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A Comparison of the Reinforcing Efficacy of Alcohol in Alcohol-Preferring (P) and Alcohol-Nonpreferring (NP) Rats

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HEYMAN, G. *A comparison of the reinforcing efficacy of alcohol in alcohol-preferring (P) and alcohol-nonpreferring (NP) rats.* PHARMACOL BIOCHEM BEHAV **66**(2) 455–463, 2000.—A key feature of the selective breeding program that produced alcohol-preferring (P) and alcohol-nonpreferring (NP) rats is that the alcohol was mixed with water. However, humans typically drink sweetened or palatably flavored alcohol. The experiments in this study tested whether the differences in P and NP rats generalize to sweetened alcohol. In Experiment 1, P rats drank more alcohol than NP rats when the vehicle was water, but NP rats drank about as much alcohol as P rats (1.1 to 1.3 g/kg/30 min) when the vehicle was a saccharin solution. Experiment 2 tested whether P rats were more susceptible to the rewarding properties of sweetened alcohol than were NP rats. The criterion for reward strength was the degree to which alcohol-reinforced lever pressing persisted, despite increases in the schedule requirements for the alcohol reward. In baseline, lever presses were reinforced with sweetened alcohol and an isocaloric Polycose solution according to two, concurrent, variable-interval 5-s schedules. In subsequent conditions, the interval schedule for alcohol was increased, and then, after a return to baseline, the interval schedule for Polycose was increased. By the criterion of resistance to change, alcohol was a stronger reinforcer than was Polycose, and alcohol was a stronger reinforcer in NP rats than in P rats. © 2000 Elsevier Science Inc.

Alcohol preference Alcohol reward P rats NP rats Reinforcement strength Resistance to change Variable-interval schedules Animal model Alcoholism

RATS, like people, differ in terms of their initial response to alcohol (16,23). Consequently, researchers have been able to selectively breed populations of rats that reliably drink different amounts of alcohol under similar circumstances. The most widely used lines are the alcohol-preferring, P, rats and the alcohol nonpreferring, NP, rats (16). As their names imply, P rats drink more alcohol than do NP rats. A widely accepted explanation for this difference is that P rats are more susceptible to the rewarding properties of alcohol, and in particular, more susceptible to the postingestive pharmacological rewards (18,27). The two experiments presented in this report evaluate 1) the generality of greater drinking by P rats, and 2) the claim that P and NP rats differ in the degree to which they are susceptible to the rewarding properties of alcohol.

The differences between P and NP rats were established in experiments in which alcohol was mixed with water. However, humans typically drink flavored and sweetened alcohol, and have continued to do so even after the development of stronger, laboratory alcohols. Experiment 1 tests whether the differences that were established with water as the vehicle would generalize to a setting in which the vehicle included a sweetener. In the first phase of the study, alcohol was mixed with water. In the second phase, alcohol was mixed with water plus saccharin. If the postingestive rewarding effects of alcohol are what matter most, then the differences between P and NP rats should generalize. On the other hand, if taste is what matters most, differences in alcohol consumption should shrink. There was also an isocaloric food control to ensure that alcohol was not the only source of calories during the experimental session. The results will provide information about the generality of P and NP differences in alcohol consumption.

Experiment 2 tested the reinforcing efficacy of the alcohol plus saccharin solution relative to an isocaloric starch solution (Polycose) in P and NP rats. This experiment differed from the procedure used to establish the P and NP lines in three ways. First, alcohol was flavored with saccharin. Second, there was a concurrently available, isocaloric solution of Polycose. Third, the measure of reinforcing efficacy was the degree to which behavior persisted under a series of constraints or challenges. The challenge was an increase in the requirements (waiting time) for obtaining a reinforcer. For example, the wait times for obtaining a serving of alcohol were in-

creased from an average value of 5 s to an average value of 30 s. The rationale for taking this approach includes the following findings and methodological issues.

There are a variety of ways of measuring reinforcing efficacy [(4) and (29) for reviews]. One of the oldest and widely used is resistance to change [e.g., Skinner, 1938, (25)]. The idea can be illustrated by the following example and findings. Two buildings may differ in height, but be of equal strength in that they are equally difficult to knock down. Similarly, in studies with rats, response rates maintained by food were higher than response rates maintained by alcohol in baseline conditions, but when the requirements for obtaining a reinforcer were increased, responding maintained by food decreased considerably more than did responding maintained by alcohol (9,11). As it was harder to weaken alcohol-reinforced behavior, alcohol can be said to be the stronger reinforcer, despite the baseline differences. (The features of alcohol that may have contributed to this advantage are reviewed in the Discussion section of this article). Recently, Nevin and Case (19) introduced a quantitative theory of reinforcement strength based on the resistance to change idea, and economists have developed a parallel theory based on the relationship between consumption and price increases, which they refer to as "inelasticity of demand." Thus, Experiment 2 uses a method for measuring the reinforcing efficacy that controls for differences in baseline consumption levels and which reflects widely shared ideas about what is meant by the term "reinforcement strength."

METHOD

Animals

The subjects were seven, inbred, generation 15, male alcohol-preferring (P) rats and eight, inbred, generation 15, male alcohol-nonpreferring (NP) rats from the laboratories of the Indiana University School of Medicine. At arrival the P rats weighed on average 202 g, and the NP rats weighed on average 172 g. The rats were individually housed in standard hanging cages. The colony room had a 12L:12D cycle, with lights on at 0700h. Throughout the study there was free access to water in the home cage, and during training and the first two parts of Experiment 1 (see below), there was also free access to chow in the home cage.

Apparatus

The experiments were conducted in eight standard operant chambers (MED Associates: 28 cm, 20.5 cm, 26 cm). Two levers, left and right, were inserted into the front wall, 7 cm above the floor, and 1 cm from each side. The levers (5 cm wide) were operated with a force of approximately 0.25 N. Just below each lever (2 cm) was an opening into which an 0.1 ml dipper could be raised. Each dipper sat in its own trough, so that it was possible to serve two different solutions. Experimental events were arranged and recorded with an IBM compatible personal computer that used MED-PC software (26).

Experiment 1

Procedure. Responses at one lever provided access to an 0.1-ml dipper of alcohol, and responses at the other lever provided access to an 0.1-ml dipper of water or Polycose. At each lever, the relationship between presses and dipper operations was determined by a variable-interval (VI) schedule. The list of intervals for each schedule was identical, with a range of 0.3 to 16 s, a mean of 5 s, and a distribution that was approximately Poisson (3). The two VI timers ran independently of one another. For example, while the subject was responding on the left lever, the right timer interval could elapse and set up a reinforcer for a right lever response, and vice versa. The reinforcer consisted of 3 s access to the dipper. Following the reinforcement period, there was a 1.5 s period during which responses had no programmed effects. In addition, responses just following a switch from one to the other lever were not eligible for reinforcement until a brief delay elapsed (1.5 s). This contingency eliminates adventitious switching. Thus, responses produced dippers of sweetened alcohol or food, and the rate of delivery depended on the schedule and the rate and pattern of responding. Sessions lasted 30 min and occurred 6 or 7 days a week.

Introducing alcohol. Initially, one dipper provided alcohol and the other dipper provided water. The concentration of the alcohol solution was increased from 2.5 to 10% in 2.5% increments over a 16-session period, with four or six sessions at each of the intermediary concentrations. The alcohol solutions were mixed daily and stored in sealed flasks. The other dipper provided water. The location of the two solutions alternated between the left and right troughs each session. In the home cage, as noted above, the rats had free access to chow and water. These conditions were in effect for 32 sessions.

Introducing Polycose. Following determination of preference for 10% alcohol relative to water, Polycose was substituted for water. The concentration was increased from 2.5 to 14.2% in 2.5% increments (except for the last step). The changes took place over a 12-session period, with two to three sessions at each of the intermediary concentrations. Polycose yields approximately 3.8 calories/g, and alcohol yields approximately 7.1 calories/g. Hence, the 10% alcohol solution provided 5.6 calories/ml [taking into consideration its density (0.79)], and the 14.2% Polycose solution provided 5.4 calories/ml. The location of the solutions alternated between sessions. And, as in Part 1, the rats had free access to chow and water in the home cage. The final condition remained in effect for five sessions.

Establishing baseline conditions for Experiment 2. The purpose of this part of the study was to establish baseline conditions for measuring resistance to change. First, body weights were fixed at 90% of their current level. The P rats had gained on average 227 g, so that their average 90% body weight was 386 g. The NP rats had gained on average 297 g, so that their average 90% body weight was 422 g. Second, 2.5 g of saccharin was added to each 1000 ml of the 10% alcohol solution. Third, the location of the solutions was fixed. The alcohol–saccharin solution was assigned to the right dipper, and the Polycose solution was assigned to the left dipper. Thus, in the final condition the left dipper provided a 14.2% Polycose solution and the right dipper provided a 10% alcohol plus 0.25% saccharin solution.

Experiment 2

Interval schedules were used to measure resistance to change. In Part I, the schedule for alcohol was increased. In the first condition the average interval value was 5 s; in subsequent conditions, the average intervals, in order, were 7.5, 10, 15, and 30 s. Each requirement was kept in the effect at least five sessions, and until there was no strictly increasing or decreasing trends in response rates over the just previous three sessions. Throughout this phase of the study, the average interval requirement for obtaining Polycose was 5 s.

Part 2. After the VI 30-s condition, the baseline conditions were reestablished, and the schedule requirements for Polycose were increased. In this phase of the study, the average in-

terval for the alcohol–saccharin solution was held at 5 s. The subjects and apparatus were the same as in Experiment 1.

Statistical Analyses

Repeated-measures analysis of variance and *t*-tests were used to evaluate the influence of experimental conditions and group differences. As was appropriate, focused contrasts tests (22) were used to evaluate more precise hypotheses regarding the nature of the relationship between the variables (e.g., whether schedule increases produced linear or higher order changes in response rate).

Alcohol Consumption

The number of alcohol reinforcers was used to index alcohol consumption. Three observations indicate that the nominal amounts approximated the obtained amounts. First, the difference between pre- and postsession trough volumes closely approximated the intake as determined from the number of reinforcers (within 10%). Second, overall alcohol consumption was approximately constant in an experiment in which the rats drank varying amounts from a dish prior to the session and from the dippers during the session (5). The constancy suggests alcohol consumption as measured by the number of dipper operations is equivalent to alcohol consumption as measured by the graduated cylinder used to fill the dish. Third, blood alcohol levels were an approximately linear function of number of alcohol reinforcers (6), and in an experiment that used the same baseline procedure as the one described in this article, the average blood alcohol levels were 139 mg/dl (10).

RESULTS

Experiment 1

The top panel of Fig. 1 shows response rates at the alcohol lever for P and NP rats in Experiment 1. When alcohol was not flavored with saccharin—the first three conditions—P rats responded at higher rates than did NP rats [omnibus, $F(1, 13) = 19.2, p < 0.001$), and in each of the three conditions, the differences were significant (see Fig. 1 for group comparisons in each condition). In contrast, when alcohol was flavored with saccharin—the fourth condition—the two groups responded at approximately the same rates, $t(13) = 0.23, p < 0.82$. For the P rats, alcohol-reinforced responding increased by about fourfold, to an average of 19.0 responses/min, and for the NP rats, alcohol-reinforced responding increased about 11-fold, to an average of 19.9 responses/min.

Alcohol-reinforced responding also changed as a function of differences in the solution provided by the concurrent, nonalcohol dipper. When 14.2% Polycose was substituted for water—the second condition—responding at the alcohol lever decreased in five of seven P rats and in seven of eight NP rats. Although, the changes were small, they were reliable, and in the NP rats the decrease was significant [relative to the first condition; $t(7) = 4.2, p < 0.004$].

In the third condition, the rats were taken off of free feed, and body weight was stabilized at 90% of the free-feeding value. In both P and NP rats, the change in feeding conditions and body weight had no systematic effect on alcohol-reinforced responding. For instance, between-condition, within-group comparisons of response rates in the second and third conditions were not significant, $t(6) = 0.24, p < 0.82$; $t(7) = 0.99, p < 0.35$, for P and NP rats, respectively.

The bottom panel shows the average number of alcohol reinforcers (0.1 ml dippers of 10% alcohol) for P and NP rats in Experiment 1. As the average interval was rather short, just 5 s, the number of reinforcers varied directly with changes in response rate. Consequently, changes in alcohol consumption approximated changes in response rate.

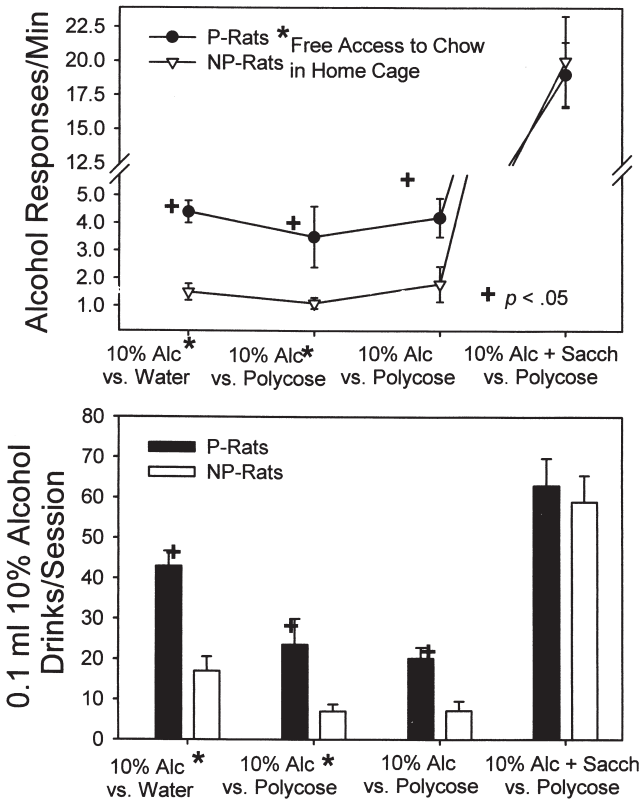

FIG. 1. The top panel shows alcohol-reinforced response rates for P and NP rats in Experiment 1. In the first two conditions, the rats had free access to chow in the home cage. In the third and fourth conditions, they were kept at a target weight of 90% of their free-feeding weight. When alcohol was unsweetened, P rats responded at higher rates (see text for *F*-value), and the difference was significant in each of the three conditions: $t(13) = 5.6, p < 0.0001$; $t(13) = 2.1, p < 0.05$; $t(13) = 2.6, p < 0.02$, respectively. In the fourth condition, alcohol was flavored with saccharin, and P and NP rats responded at about the same rate. The bottom panel shows the number of alcohol drinks for the four conditions of Experiment 1. P rats consumed more alcohol when it was unsweetened (see text for *F*-value), and as with response rate, the differences were significant in each of the three conditions as well: $t(13) = 4.9, p < 0.0003$; $t(13) = 2.7, p < 0.02$; $t(13) = 3.6, p < 0.003$. When alcohol was flavored, P and NP rats drank about the same amount.

When alcohol was not flavored with saccharin, P rats consumed two and a half to three times more alcohol than did the NP rats [omnibus ANOVA, $F(1, 13) = 31.4, p < 0.001$]. As with response rates, the group means were significantly different from one another in each condition (see Fig. 1 for *t*-test results). However, when alcohol was flavored with saccharin, NP rats drank about as much alcohol as did P rats. The mean consumption levels were 0.63 and 0.59 ml for P and NP rats, respectively (100% alcohol; for g/kg; see Table 1). Relative to the no-saccharin condition, P rats drank about 1.5 times more alcohol and NP rats drank about 3.5 times more alcohol.

When the competing dipper served Polycose rather than water (the second condition), alcohol consumption decreased

TABLE 1
GRAMS/KILOGRAMS ALCOHOL IN EXPERIMENT 1

	Alc vs. Water*	Alc vs. Polycose*	Alc vs. Polycose	Alc+Sacch vs. Polycose
P Rat	0.81 (0.07)	0.43 (0.07)	0.43 (0.06)	1.32 (0.14)
NP Rat	0.3 (0.07)	0.12 (0.04)	0.14 (0.05)	1.12 (0.14)

*Rats on free feed in the home cage.

in P and NP rats. The average changes were −42% and −55% for P and NP rats, respectively, and within-group tests (paired-*t*) were significant, $t(6) = 2.99$, $p < 0.02$; $t(7) = 4.4$, $p < 0.003$. The decreases in consumption were due to the small but reliable decreases in response rate (discussed above) and to changes in the temporal pattern of responding that accompanied the substitution of Polycose for water in the second dipper (see Discussion section for further comments).

Table 1 lists alcohol consumption in Experiment 1 as measured in g/kg. This measure is included because the rats gained weight during training and the first two conditions of the study. Upon arrival the average body weights were 202 and 179 g for the P and NP rats. During the free-feeding phase of the study (training and the first two conditions), the average gain was 220 g for the P rats and 308 g for the NP rats.

The top panel of Fig. 2 shows response rates at the lever that operated the nonalcohol dipper in Experiment 1. When this dipper served water, P and NP rats responded intermittently at a rate of only 1/min—the rats were not water deprived. However, when this dipper served Polycose, response rates increased to 10/min for P rats and 12/min for NP rats. Taking the rats off of free feed (third condition) produced further increases in Polycose-reinforced responding (paired *t*-tests on conditions 2 and 3 for between-condition, within-group differences had values of: $t(6) = 6.7$, $p < 0.0005$; $t(7) = 11.1$, $p < 0.0001$, and the increases were larger for the NP rats than for the P rats [between group comparisons of changes in response rate: $t(13) = 2.6$, $p < 0.02$].

The bottom panel of Fig. 2 shows the number of Polycose reinforcers in each condition. NP rats tended to earn more Polycose drinks, and with the introduction of the feeding constraint, the difference was significant at the 0.05 level, $t(13) = 3.1$, $p < 0.01$. However, in the other conditions, group differences were not this large, and the omnibus analysis of variance for group differences in Polycose consumption fell just short of the 0.05 level, $F(1, 13) = 4.4$, $p < 0.06$.

Summary of results from Experiment 1

When alcohol was not flavored with saccharin, P rats consumed more alcohol than did the NP rats. However, with saccharin added, NP rats consumed almost as much alcohol as did the P rats. NP rats tended to consume more Polycose than the P rats, but this difference was not consistent. Removing the free-feed conditions and stabilizing body weights, increased Polycose-reinforced responding but did not increase alcohol-reinforced responding.

Experiment 2a

Figure 3 summarizes the relationship between changes in the schedule requirement for alcohol and changes in alcohol-reinforced responding. The results from the final condition of Experiment 1 served as the first ("baseline") condition.

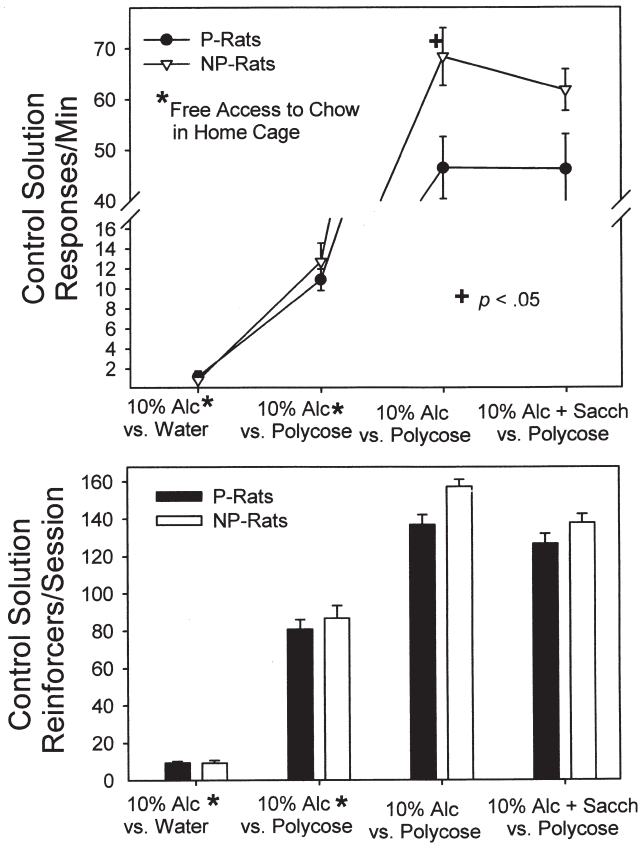

FIG. 2. The top panel shows response rates at the lever that operated the control solution dipper in Experiment 1 (water in the first condition and isocaloric Polycose in conditions 2 to 4). In conditions 3 and 4, rats were kept at 90% free-feeding body weight. According to a *t*-test, response rate differences were significant in the third condition: $t(13) = 2.6$, $p < 0.02$. The bottom panel shows the average number of control reinforcers in each condition. There were no significant differences.

Throughout Experiment 2a, the average interval requirement for Polycose was 5 s, and the average interval requirements for the alcohol-saccharin mixture were increased from 5 to 30 s (alcohol was made less accessible).

For the P rats, alcohol-reinforced responding remained at close to baseline levels for the first three schedule increases (VI 7.5 to VI 15 s), and then increased in the VI 30-s condition, $F(1, 6) = 9.8$, $p < 0.02$, for the contrast between VI 30-s and VI 5-s response rates.

For the NP rats, response rates increased with schedule requirement increases, and the relationship was approximately linear, $F(1, 7) = 10.2$, $p < 0.015$. In contrast to the P rats, the increases relative to baseline (VI 5 s) were significant at each new schedule value (the *p*-values for the focused contrast tests were < 0.053, 0.014, 0.023, and 0.004).

Between-group statistical comparisons were performed on the percentage change in response rate scores. This makes it possible to control for individual differences in baseline (VI 5-s) responding. The third panel shows the resulting comparisons. Change in response rate ranged from 5 to 49% for P rats and from 34 to 100% for NP rats. The omnibus, between-group ANOVA test was significant, $F(1, 13) = 5.8$, $p < 0.032$.

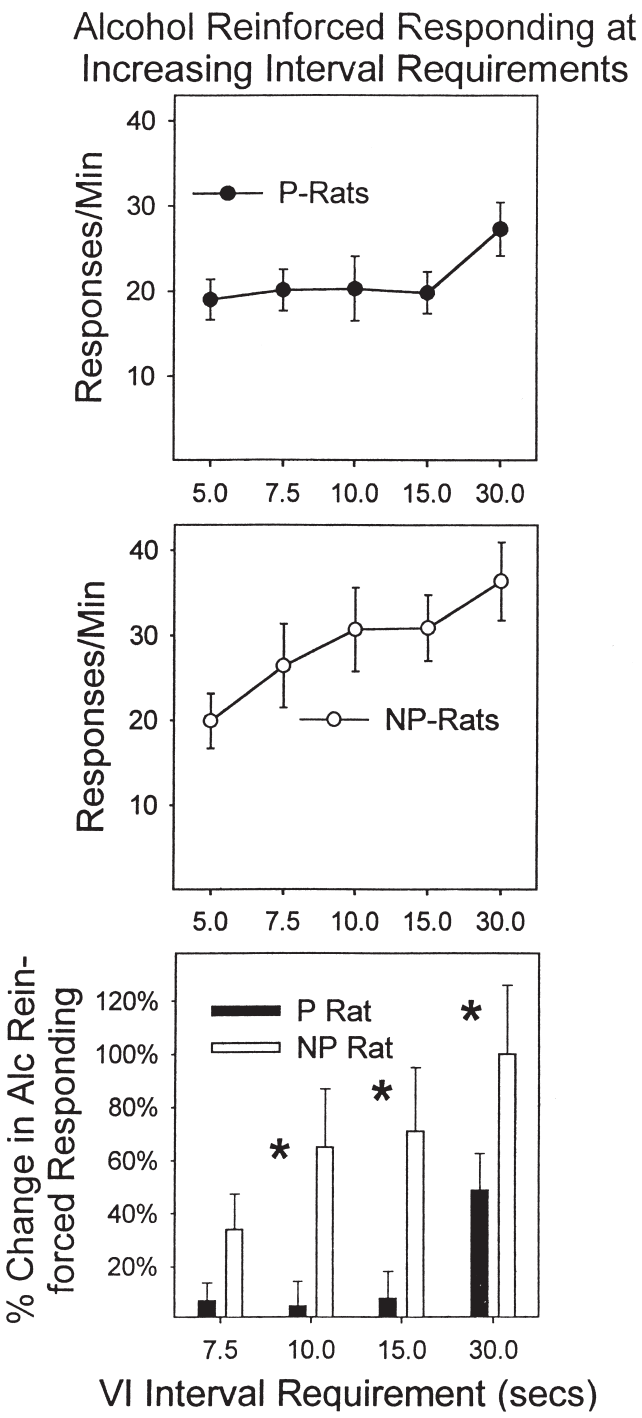

FIG. 3. The relationship between response rate and increases in the schedule requirements for alcohol in Experiment 2. The top panel shows response rates for P rats; the middle panel shows response rates for NP rats; and the bottom panel shows the change in response rates reinforced by alcohol, relative to the baseline (VI 5-s) condition. NP rats made a stronger adjustment to decreased access to alcohol as measured by response rate increases (see text for F-value). The between-group comparisons yielded t-test values of: $t(13) = 1.7$, $p < 0.11$; $t(13) = 2.4$, $p < 0.03$; $t(13) = 2.4$, $p < 0.03$).

Comparisons at the different schedule values were significant in all but the VI 7.5-s condition (see Fig. 3 for results).

The left top panel of Fig. 4 shows the obtained number of alcohol reinforcers. As the average interval values increased in duration, the rate of reinforcement depended more on the arranged schedule times rather than on variations in response rate. Nevertheless, there was a tendency for the NP rats to earn more alcohol drinks than did the P rats. The difference was not, however, significant at the 0.05 level, $F(1, 13) = 1.6$, $p < 0.24$.

Table 2 lists Polycose response rates and reinforcers for this phase of the study (recall that the average interval requirement for Polycose remained at 5 s while the schedule requirement for alcohol was increased). For both P and NP rats, changes in Polycose-reinforced responding were small and nonsystematic. However, the number of Polycose reinforcers tended to decrease. As response rates remained close to their initial levels, this decrease was primarily due to changes in the pattern of responding that accompanied the increases in alcohol interval requirements.

Experiment 2b

Following the 30-s interval requirement for alcohol, baseline conditions were restored (VI 5-s requirement for both reinforcers), and the interval requirements for Polycose were increased. The increments were the same as in the alcohol experiment. Figure 5 shows the results. On the x-axis are the average interval requirements for Polycose. On the y-axis are the average response rates, as calculated from the last three sessions of each condition.

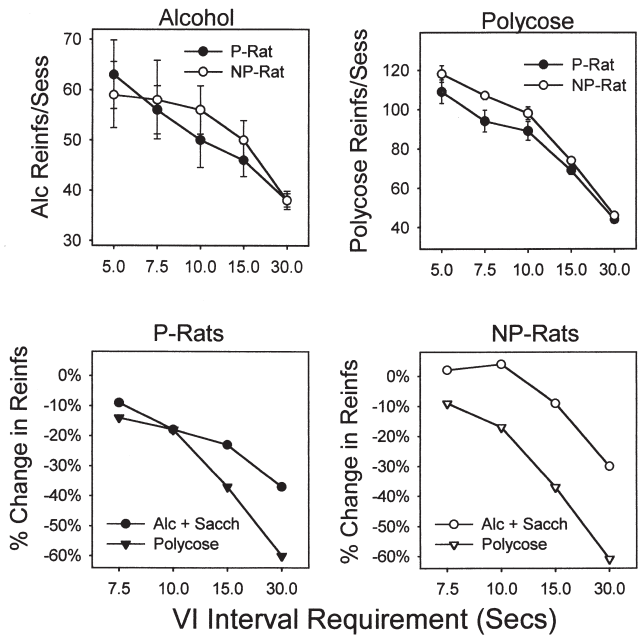

FIG. 4. The relationship between consumption and change in schedule requirements. The top panel shows changes in alcohol and Polycose consumption as a function of schedule requirement and group. The bottom panel shows changes in consumption relative to the initial VI 5-s condition for P and NP rats.

TABLE 2
POLYCOSE RESPONSE RATE AND POLYCOSE REINFORCERS UNDER A VI 5-S SCHEDULE, WHILE SCHEDULE FOR ALCOHOL SOLUTION WAS INCREASED FROM VI 5-S TO VI 30-S (EXPERIMENT 2A)

	P-Rats		NP-Rats	
Schedules (s)	Polycose Resp/Minute	Polycose Reinfs/Session	Polycose Resp/Minute	Polycose Reinfs/Session
VI 5 VI 5	46 (6.9)	127 (5.5)	62 (4.4)	138 (5.2)
VI 5 VI 7.5	51 (5.5)	133 (3.8)	62 (5.7)	134 (5.6)
VI 5 VI 10	47 (6.5)	127 (5.5)	57 (4.1)	130 (3.0)
VI 5 VI 15	46 (6.2)	125 (6.4)	62 (3.5)	132 (3.9)
VI 5 VI 30	43 (5.1)	124 (4.4)	56 (2.8)	126 (4.7)

For P rats response rates increased in the VI 7.5- and VI 10-s schedules, but not in the VI 15- and VI 30-s conditions. Polynomial contrast tests revealed a significant quadratic trend, $F(1, 6) = 9.2$, $p < 0.023$, and a significant fourth order trend, $F(1, 6) = 6.7$, $p < 0.041$, but not significant linear or third order trends. These tests had no theoretical basis, but, as shown next, turn out to be useful for purposes of comparison.

The pattern of response rate changes for the NP rats was similar. Response rates increased in the VI 7.5- and VI 10-s schedules, but not in the VI 15- and VI 30-s conditions. As with the P rats, polynomial contrast tests revealed significant quadratic and fourth order trends, $F(1, 7) = 33.7$, $p < 0.001$, and $F(1, 7) = 5.9$, $p < 0.046$, but not significant linear or third order trends.

As a way of controlling for differences in baseline response rate, the bottom panel shows the percent change in Polycose-reinforced responding. The changes in relative measures were quite similar, $F(1, 13) = 0.003$, $p < 0.95$.

The top right panel of Fig. 4 shows the number of Polycose reinforcers. Because the schedule values set a minimum interval to the next reinforcer, Polycose reinforcement rate decreased for both P and NP rats. Finally, the two bottom panels of Fig. 4 show percent change in alcohol and Polycose reinforcement rate for P and NP rats. The NP rats kept alcohol consumption at baseline levels over the first two schedule increases (7.5 and 10 s), and the third increase (VI 15 s) brought about a 10% decrease in alcohol intake. In contrast, the initial schedule increase reduced alcohol consumption in the P rats, and when the requirement was 15 s, the decrease in alcohol consumption was 20%—twice as great as it was for the NP rats. These differences follow from the differences in response rates shown in Fig. 3. NP rats adjusted to the schedule challenge by responding more at the alcohol lever. In contrast, under the same challenge, P rats responded at baseline levels in all but the last condition (VI 30 s).

Table 3 lists alcohol reinforcers and response rates during the sessions that the VI schedule for Polycose was manipulated and the VI schedule for alcohol remained at an average value of 5 s. Alcohol-reinforced responding tended to decrease. However, the changes were not significant at the 0.05 level for either the P or NP rats.

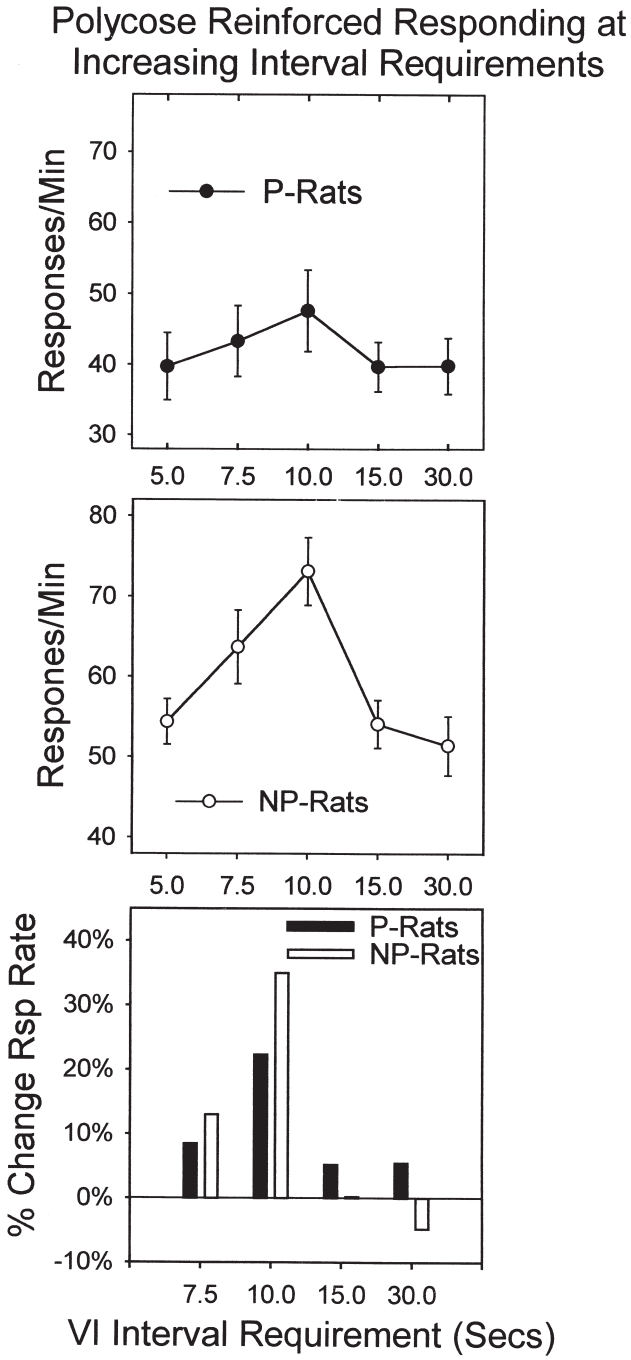

FIG. 5. The relationship between Polycose-reinforced responding and increases in the schedule requirements for Polycose. The top panel shows response rates for P rats; the middle panel shows response rates for NP rats; and the bottom panel shows change in response rate relative to the baseline (VI 5-s) condition. The two groups adjusted similarly to decreased access to Polycose, as measured by changes in Polycose-reinforced responding.

DISCUSSION

This study tested the generality of differences in P and NP rats that had been established with mixtures of alcohol plus water. The key finding was that the results did not generalize. When saccharin was added to the solution, NP rats drank about as much alcohol as did P rats, and sweetened alcohol was more reinforcing for NP rats than for P rats. The control conditions included a concurrent, isocaloric Polycose solution so that it was possible to compare the reinforcing efficacy of alcohol relative to food. According to the resistance to

TABLE 3

ALCOHOL RESPONSE RATE AND ALCOHOL REINFORCERS UNDER A VI 5-S SCHEDULE, WHILE SCHEDULE FOR POLYCOSE SOLUTION WAS INCREASED FROM VI 5- TO VI 30-S (EXPERIMENT 2B)

	P Rats		NP Rats	
Schedules (s)	Alcohol Resp/Minute	Alcohol Reinfs/Session	Alcohol Resp/Minute	Alcohol Reinfs/Session
VI 5 VI 5	28 (5.8)	84 (9.5)	31 (9.7)	78 (6.5)
VI 5 VI 7.5	25 (3.7)	81 (7.1)	30 (11.5)	76 (8.4)
VI 5 VI 10	23 (3.9)	76 (6.7)	22 (2.6)	63 (7.3)
VI 5 VI 15	25 (4.2)	87 (7.1)	29 (3.8)	86 (7.9)
VI 5 VI 30	20 (3.3)	78 (7.5)	22 (2.0)	82 (5.3)

change criterion, alcohol was more reinforcing than was Polycose for both rat strains. These results are consistent the hypotheses that preference for alcohol was based on its taste and/or its pharmacology. These are not mutually exclusive interpretations, and, as is described next, there is evidence for both views.

The finding that saccharin reduced the differences in P and NP rat alcohol consumption has a precedent. In a home-cage drinking experiment on the development of dependence in P and NP rats (28), saccharin and salt were added to 10% alcohol. As in the present study, alcohol consumption markedly increased for both groups, with the daily totals rising to approximately 14 and 12 g/day. The conditions of this study were very different from those of Experiment 1, so that the influence of saccharin on P and NP rats is likely quite robust.

The simplest interpretation of these results is that saccharin made the alcohol solution more palatable, suggesting that when alcohol is mixed with water it is more aversive for NP than P rats. However, there are two potential problems with this interpretation. First, it could be argued that the NP rats were not more sensitive to alcohol's aversive effects but, instead, were more responsive to saccharin's palatable taste. This idea fits the data, but saccharin also increased alcohol consumption in the P rats, and in a series of experiments on taste, P rats typically showed greater preference for saccharin than did NP rats (14).

Second, there are findings that suggest that P and NP rats respond similarly to the taste of alcohol (2). Building on the observation that sucrose and quinine produce different orofacial responses in rats, Kiefer and his colleagues compared the mouth and facial reactions of P and NP rats to a variety of tastants, including alcohol. P and NP rats responded similarly to alcohol. This was interpreted as evidence that the two strains did not differ in regards to their hedonic reaction to the taste of alcohol [e.g., Kampov-Polevoy et al., (14)]. However, this conclusion may be premature. There may not be a perfect correlation between facial gustatory reactions and palatability, and/or the researchers may have missed subtle differences. Also, there may be other limitations with the method. One of the figures in the article on taste reactivity in P and NP rats [(2); Fig. 4] shows that exposure to water was followed by the same number of "aversive" responses as was exposure to alcohol. This suggests that orofacial reactions are not a sufficiently discriminating index of hedonic states. Also facial reactions changed as a function of experience (2), suggesting that they reflect postingestive as well as preingestive effects.

Thus, the simplest account of Experiment 1 is that when alcohol was mixed with water, NP rats were more sensitive to the preingestive aversive properties of alcohol than were the P rats, but that when alcohol was mixed with saccharin, it was more palatable, and thus the NP rats drank as much as did the P rats.

In Experiment 2, alcohol-reinforced behavior was more resistant to change in the NP rats. According to economic and reinforcement theory, resistance to change is determined by the importance of the reinforcer and the availability of competing reinforcers. In support of these points, resistance to change has been greatest in studies in which the two reinforcers were quite different, such as food and water, and at a minimum when the two reinforcers were identical (7,12). Thus, according to theory and previous findings, sweetened alcohol was a more unique reinforcer for the NP rats. Possibly this was due to the saccharin, rather than the alcohol. However, as noted above, P rats showed stronger preferences for saccharin than did NP rats (14). Thus, differences in the response to alcohol remain the most likely hypothesis.

For both P and NP rats, responding reinforced by alcohol was more resistant to change than was responding reinforced by an isocaloric food. This replicates the results from a series of earlier studies in which Wistar rats served as subjects (7,9,11). These experiments included controls for assessing whether differences in taste influenced the findings. For instance, one experiment used the same procedure as did Experiment 2 of this report, except that the reinforcers were 10% sucrose and 10% sucrose plus quinine (8). In baseline, the rats favored the sucrose solution that did not contain quinine by about a four-to-one margin. However, when the schedule requirement for sucrose was increased, the rats readily shifted to sucrose plus quinine, and vice versa when the schedule requirements for sucrose plus quinine were increased. Thus, taste influenced consumption but not resistance to change. Similar results were obtained in an experiment in which the reinforcers were isocaloric concentrations of sucrose and Polycose plus saccharin (9). Thus, it is unlikely that taste explains the greater reinforcing properties of alcohol in Experiment 2.

In contrast, earlier results support the idea that differences in resistance to change in Experiment 2 were related to alcohol's pharmacological effects. For instance, in experiments that varied feeding conditions, rats drank an approximately constant amount of alcohol, independent of large changes in body weight and presession meals of sucrose and chow (5). Second, the rate of alcohol consumption varied as a function of how much alcohol had been consumed, but not as a function of how much food had been consumed (5,11). Third, pharmacological agents selectively influenced alcohol consumption. R0 15-4513, a benzodiazepine inverse agonist, had a significantly larger impact on responding reinforced by an alcohol–sucrose mixture than on responding reinforced by sucrose (20). Daidzin, an isoflavone, decreased consumption of saccharin-flavored alcohol at doses that did not decrease consumption of an isocaloric Polycose solution (10). The simplest account of these results is that alcohol's reinforcing efficacy was a function, at least in part, of its pharmacology. As the design of the current experiment is similar to those just reviewed, it is plausible that in Experiment 2, alcohol's pharmacological effects made it more reinforcing than food.

The results from this study raise questions about the advantages and disadvantages of adding sweeteners and flavorings in animal models of human alcohol consumption. This topic deserves an extended review. However, several key points can be outlined briefly.

Solutions of alcohol mixed with water stimulate both "sweet" and "bitter" reactions (15), and as the concentrations

of alcohol increases, the aversive consequences dominate (21). For example, rats trained on alcohol solutions of 3 to 9%, generalized to a solution of quinine plus sucrose, and the generalization was greater for the two higher concentrations (15). This means that the standard 10% alcohol solution contains an aversive, quinine-like component. In support of this point, rats invariably consumed considerably more alcohol when its gustatory effects were bypassed or countered with palatable tastants (1,13,28). Thus, a selective breeding program for alcohol consumption that is based exclusively on alcohol and water mixtures may end up with subjects that differ more in terms of alcohol's preingestive, aversive properties than its postingestive, positive rewarding properties.

The same arguments, of course, apply to the use of sweetened alcohol, but with a bias toward subjects who respond more positively to sweet tastes. That is, as taste is inherent to orally consumed alcohol, there is no simple way to remove it as a possible determinant of consumption. [There is at least one study with anosmic rats (13).] Thus, we should ask, whether research goals are best realized by sweetened or unsweetened alcohol solutions, recognizing that with each approach it is necessary to take some steps to control for gustatory influences. The advantages of using sweetened solutions for studies of preference for alcohol include the following points. For studies with different aims, the list would, of course, be different.

First, under comparable conditions, saccharin increases alcohol intake by more than a factor of 2. For example, blood alcohol levels in nonselected, commercial rats were two to four times higher than reported for P rats (10,24). As pharmacological control is a function of blood alcohol levels, this means that the sweetened alcohol approach greatly increases the role of pharmacology in preference. A host of studies that used concurrent food controls support this point (5,8,9,11). Second, the introduction of a concurrent palatable food reduces alcohol consumption to negligible levels when the alcohol vehicle does not include a palatable tastant. Importantly, this is true for P rats as well as for NP rats (24). The methodological implication is that you cannot use isocaloric, palatable control solutions. Consequently, with the water vehicle approach, there will always remain the possibility that alcohol consumption was based on its calories or other food-like properties. In contrast, as demonstrated in this and other studies, when alcohol is flavored, it is possible to maintain high consumption levels even when there is access to rich and palatable foods, such as starch and sucrose solutions. This makes it possible to conduct experiments with controls for calories, and to some degree, controls for taste. Third, as pointed out in the introduction to this article, humans typically drink flavored and sweetened alcohol. Thus, experiments conducted with alcohol plus saccharin are more likely to be relevant to human drinking than are experiments in which alcohol is simply mixed with water.

These comparisons suggest three, nonmutually exclusive, strategies for animal models of alcohol consumption. 1) Use a variety of vehicle solutions, including just water. 2) Use measures of reward efficacy that are independent of the initial consumption level, such as resistance to change. For example, recall that when foods differed only in regard to the presence of quinine, there were large differences in baseline consumption levels but not in reinforcing efficacy, as measured by resistance to change. [This dissociation has not been investigated, but it has been replicated numerous times (19).] 3) Use procedures that allow for concurrently available, palatable caloric sources so that the specificity of experimental manipulations (such as drug treatments) can be pursued.

One additional empirical finding deserve some comment. Reducing food availability in Experiment 1 produced pronounced changes in Polycose-reinforced responding but no change in alcohol-reinforced responding. This replicates earlier findings (5), and it implies that the determinants of alcohol and of food consumption differed (although there may well have been common factors as well). However, the dissociation between food and alcohol may be context specific.

In experiments in which alcohol was mixed with water, and there was no concurrently available food source, changes in feeding conditions systematically altered alcohol consumption (17). In contrast, when alcohol was mixed with a sweetener, and there was a concurrent food source available, changes in feeding conditions had little influence on alcohol consumption (5). This difference suggests that the nature of alcohol's reinforcing effects depend on the context. For instance, if alcohol is the only source of calories and pharmacological effects, its consumption should vary as a function of both factors. However, if a palatable food is concurrently available, the rats can fill up first on alcohol and then switch to food (11). Thus, that calories did not predict alcohol consumption in the concurrent food procedure does not mean that caloric effects are absent in the alcohol vs. water procedure.

SUMMARY AND CONCLUSION

For casual and problem drinkers, alcohol provides a unique array of sensory and central effects. For example, caloric foods and drinks are not good substitutes for either the social drinker or the alcohol addict. Soda is not the equivalent to wine at the dinner table, or a passable replacement for wine in the service of withdrawal symptoms. In the procedures used in this report, food consistently failed to substitute for alcohol. Thus, there is a parallel between the relationships of food and alcohol in the two settings. This suggests that an analysis of the mechanisms that mediate preference for alcohol in the experimental setting will shed light on the mechanisms that make alcohol such a powerful reinforcer for both social and problem drinkers in nonexperimental settings.

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