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Glucose- and Fructose-Conditioned Flavor Preferences in Rats: Taste Versus Postingestive Conditioning

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SCLAFANI, A. AND K. ACKROFF. *Glucose- and fructose-conditioned flavor preferences in rats: Taste versus postingestive conditioning.* PHYSIOL BEHAV **56**(2) 399–405, 1994.—Flavor preferences conditioned by glucose and fructose were compared using two training methods. With the simultaneous method preferences can be reinforced by the flavor and/or the postingestive consequences of nutrients, whereas with the delayed method preferences are reinforced only by postingestive nutritive effects. In Experiment 1, food-deprived rats displayed similar preferences for flavors (CS+) added to an 8% glucose or 8% fructose solution over flavors (CS−) added to a noncaloric saccharin solution (simultaneous conditioning). Other rats learned to prefer a CS+ flavor paired with the delayed (10 min) presentation of 8% glucose over a CS− flavor paired with delayed saccharin. Fructose failed to condition a flavor preference with the delayed paradigm. Taken together, these data suggest that the preference for a flavor mixed in a fructose solution is reinforced by the sweet taste, not the postingestive effects of the sugar. Experiment 2 tested this idea by devaluing the taste of the sugar solutions by quinine adulteration. Rats initially avoided both glucose–quinine and fructose–quinine solutions in favor of a saccharin solution. Following one-bottle training, they came to prefer the glucose–quinine but not the fructose–quinine solution over the saccharin solution. The glucose-trained rats also showed stronger preferences for sucrose–quinine solutions than did the fructose-trained rats. These findings, along with other recent data, indicate that fructose-conditioned preferences are based primarily on the sugar's palatable taste. Glucose, in contrast, can condition strong preferences based on its taste as well as its postingestive actions.

Flavor–flavor conditioning Flavor–nutrient conditioning Simultaneous training Delayed training Sucrose Quinine

IN recent studies Ackroff and Sclafani (1,2) reported that rats develop preferences for solutions containing glucose-based carbohydrates (glucose, maltose, Polycose) over carbohydrates that include fructose (fructose, sucrose). These preferences were not apparent in initial test sessions, but developed after experience with the saccharide solutions, and thus appeared to be dependent upon postingestive actions of the carbohydrates. Consistent with this interpretation, rats also developed strong preferences for a cue flavor mixed with glucose over a different flavor mixed with fructose (1). Other animals were trained to associate one flavor with a sugar solution (glucose or fructose) and another flavor with a noncaloric saccharin solution (1). In subsequent choice tests, the sugar-paired flavor was preferred to the saccharin-paired flavor. The glucose-reinforced flavor preference tended to be stronger than the fructose-reinforced preference but the difference was not significant. Based on these findings, Ackroff and Sclafani (1) concluded that glucose has a more potent postingestive reinforcing effect than does fructose [but see (20)].

In a more direct comparison of the postingestive reinforcing actions of the two sugars, Sclafani et al. (16) trained separate groups of rats to associate a cue flavor with intragastric (IG) infusions of glucose or fructose and another flavor with IG water infusions. In two different experiments, nondeprived and food-deprived groups rapidly acquired strong preferences (89% and 95%, respectively) for the flavor paired with glucose, but acquired only weak and slowly developed preferences (62% and 67%) for the flavor paired with fructose. In a third experiment, rats trained with one flavor paired with IG glucose and another flavor paired with IG fructose displayed a significant preference (82%) for the glucose-paired flavor. These findings are consistent with the results cited above and demonstrate that it is the postingestive rather than taste properties of glucose and fructose that are responsible for the differential reinforcing effects of the two monosaccharides.

The present study further compared glucose- and fructose-conditioned flavor preferences. As noted above, rats learn to prefer a flavor mixed with fructose over a flavor mixed with saccharin. The unconditioned stimulus (US) reinforcing this preference was assumed to be related to the postingestive nutritive actions of fructose. The subsequent observation that IG fruc-

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tose infusions are relatively ineffective in conditioning flavor preferences questions this interpretation (16). It may be that the conditioned preference obtained with flavored fructose solutions results primarily from the sugar's sweet taste (flavor–flavor conditioning) rather than from its postingestive nutritive effects (flavor–nutrient conditioning). One interesting way to separate flavor–nutrient and flavor–flavor conditioning is to separate the conditioned stimulus (CS; i.e., cue flavor) and the unconditioned stimulus (US; i.e., the flavor or nutrient). Prior work shows that rats learn to prefer a CS flavor mixed with a palatable, nonnutritive US (e.g., saccharin, mineral oil), but do not come to prefer that CS flavor when it is presented several minutes before the nonnutritive US (6,8). On the other hand, with nutritive USs (e.g., glucose, corn oil), flavor preferences are established when the CS precedes the US (delay conditioning) as well as when the CS is mixed into the US (simultaneous conditioning) (6,8). Fructose, being a nutrient, should condition flavor preferences using the delayed conditioning procedure. However if, as our recent IG study (16) suggests, fructose has only a weak postingestive reinforcing effect, then fructose, unlike glucose, may be ineffective in conditioning a flavor preference using a CS–US delay procedure. Also, if the fructose-conditioned flavor preference obtained with the CS–US simultaneous procedure is reinforced primarily by the sugars' palatable taste, then devaluing this taste should attenuate preference conditioning. These predictions were tested in the present study.

EXPERIMENT 1

Separate groups of rats were trained to associate one CS flavor (the CS+) with glucose or fructose, and another flavor (the CS−) with a noncaloric saccharin solution. Some animals were trained with the flavors mixed into the sugar and saccharin solutions (simultaneous conditioning procedure) and others were trained with the CS flavors followed by the delayed presentation of unflavored sugar and saccharin solutions (delayed conditioning procedure). All rats were then tested for their flavor preferences using an identical procedure so that the two conditioning methods could be compared. The preference test was extended to eight sessions to determine the persistence of the sugar-conditioned flavor preferences in the absence of reinforcement. As in previous experiments (6,8), the rats were trained and tested while food deprived; prior work indicates that food deprivation enhances the expression of conditioned flavor preferences (7).

METHOD

Subjects

Thirty-four female CD rats were obtained from Charles River Laboratories (Wilmington, MA). They were 80 days old at the start of testing and were individually housed in standard wire-mesh cages in a vivarium maintained at 21°C under a 12:12 h light:dark cycle.

Test Solutions

The training solutions used in the simultaneous conditioning procedure consisted of 8% glucose, 8% fructose, and 0.2% sodium saccharin (Sigma Chemical) solutions flavored with 0.05% grape or cherry Kool-Aid (General Foods, White Plains, NY). For half the rats grape was the CS+ flavor paired with glucose (CS+G) or fructose (CS+F), and cherry was the CS− flavor paired with saccharin (CS−s); the flavors were reversed for the remaining rats. In the preference tests, only flavored saccharin solutions were used; the CS−s was the same solution used during training and the CS+s was a saccharin solution with the flavor previously paired with glucose or fructose.

In the delay conditioning procedure, the CS solutions consisted of 0.2% saccharin solutions flavored with 0.05% grape or cherry Kool-Aid. One flavored saccharin solution (CS+s) was paired with the delayed presentation of unflavored sugar solution (8% glucose or fructose), and the other flavored saccharin solution (CS−s) was paired with the delayed presentation of unflavored saccharin solution. The same CS+s and CS−s solutions were used in the preference tests.

All solutions were prepared on a weight/volume basis and were presented in 50-ml graduated tubes. Intakes were recorded to the nearest 0.5 ml.

Procedure

The rats were familiarized with unflavored 0.2% saccharin solution by giving them ad lib access to saccharin and plain water for 2 days. They were then food restricted and maintained at 85% of ad lib body weight for the remainder of the experiment. The rats were trained to drink the saccharin solution during brief daily tests by offering them the solution for 30 min (2 days), 20 min (3 days), and 10 min (2 days). Following this preliminary training, the animals were divided into four groups equated for their 10-min saccharin intake and body weight (235–238 g).

Two groups (n = 8 each) were trained using the simultaneous procedure for 10 days. On odd-numbered days they were given 24 ml of the CS+G (glucose-simultaneous or G-S group) or the CS+F (F-S group) solution. On even-numbered days, both groups were given 24 ml of the CS−s solution. The solutions were presented at midday, and 2 h later the rats were given their chow ration and tap water; any unfinished solution remained available until the next day.

The two other groups (n = 9 each) were trained using the delay procedure for 10 days. On odd-numbered days they were given 10-min access to the CS+s solution, and then after a 10-min delay, 24 ml of the unflavored glucose (glucose-delay or G-D group) or fructose (F-D group) solution. On even-numbered days, the rats were given 10-min access to the CS−s solution, and then after a 10-min delay, 24 ml of the unflavored saccharin solution. Two hours after the unflavored sugar and saccharin solutions were presented, the rats were given their chow ration and tap water; any unfinished solution remained available until the next day.

Following training, a two-bottle test was conducted during which all rats were given 2 h/day access to the CS+s and CS−s for 8 days. The left–right position of the solutions alternated daily and intakes were recorded to the nearest 0.5 ml. Intakes were averaged over 2-day blocks and evaluated with repeated measures analyses of variance (ANOVAs); individual comparisons were evaluated with simple main effects and Newman–Keuls tests where appropriate. Reported differences were significant at the 0.05 level or less.

RESULTS

Figure 1 summarizes the results of the two-bottle CS+s vs. CS−s preference test. Within-group analyses revealed that the rats in the G-S, F-S, and G-D groups consumed more CS+s than CS−s [$F(1, 7) = 13.6, p < 0.01$; $F(1, 7) = 45.9, p < 0.001$; $F(1, 8) = 19.8, p < 0.01$]. In contrast, the rats in the F-D group did not reliably differ in their CS+s and CS−s intakes. The CS+s preferences of the F-S and G-D groups as well as the lack of preference in the F-D group remained relatively stable over the course of testing. On the other hand, the CS+ preference of the G-S group declined with repeated testing [CS × block interac-

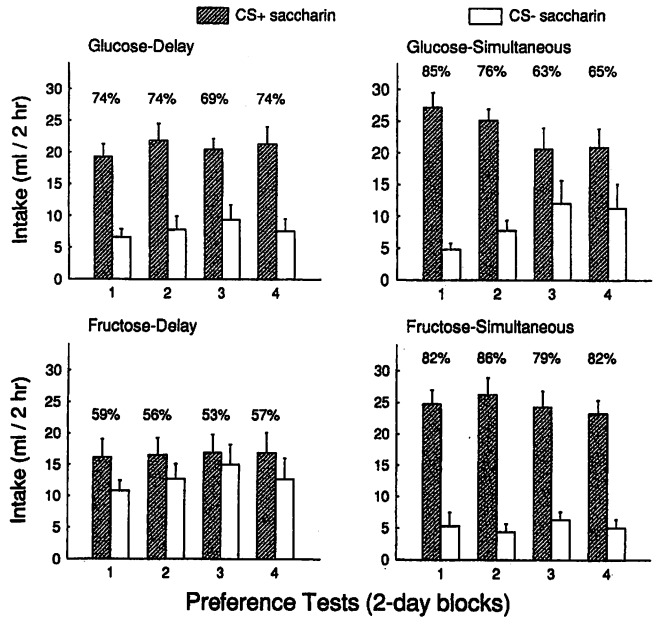

FIG. 1. Experiment 1. Mean + SEM intakes of CS+ and CS− flavored saccharin solutions of the glucose-simultaneous (G-S), glucose-delay (G-D), fructose-simultaneous (F-S), and fructose-delay (F-D) groups. The CS flavors were grape and cherry. Each bar represents the mean of two 2 h/day test sessions. Percentages atop bars indicate the percent intake of the CS+ flavored solution.

tion, $F(3, 21) = 3.5, p < 0.05$] and by test blocks three and four CS+s intake did not reliably exceed CS−s intake (Newman–Keuls tests, NS).

A between-group analysis based on all four test blocks indicated that, overall, CS+s intake was greater than CS−s intake, $F(1, 30) = 51.1, p < 0.001$, and this difference was greater for the simultaneous conditioning groups (24.0 vs. 7.1 ml) than for the delay conditioning groups (18.6 vs. 10.3 ml) [CS × training method interaction, $F(1, 30) = 5.9, p < 0.05$]. The differential effect of training method on CS preference tended to be more pronounced with fructose than with glucose; the three-way interaction CS × sugar × training method just failed to reach significance, $F(1, 30) = 3.9, p = 0.056$. Separate analyses were performed using the data from the first preference test block when extinction effects were minimal. Both glucose groups consumed significantly more CS+s than CS−s during test block 1, but the CS+s preference was stronger in the G-S than in the G-D group [CS × group interaction, $F(1, 15) = 6.8, p < 0.05$, and simple main effects tests]. The CS intakes of the two fructose groups also differed, but in this case only the F-S group consumed reliably more CS+s than CS−s [CS × group interaction, $F(1, 15) = 10.1, p < 0.01$, and simple main effects tests].

The CS+s and CS−s intakes of the G-D and F-D groups during the 10 one-bottle training sessions were also analyzed. The two groups did not differ in their CS intakes during the first four training sessions. However, during the last six sessions the G-D rats consumed more CS+s than CS−s [6.1 vs. 4.2 ml/10 min, $F(1, 16) = 13.8, p < 0.01$], whereas the F-D rats consumed similar amounts of the CS+s and CS−s (4.9 vs. 5.2 ml/10 min, NS) [group × CS interaction, $F(1, 16) = 9.5, p < 0.01$].

DISCUSSION

In confirmation of previous results (1), both glucose and fructose conditioned a preference for a CS+ flavor mixed into the sugar solutions over a CS− flavor mixed into a saccharin solution. The new finding here is that only glucose conditioned a preference when the CS+ flavor was presented 10 min before the sugar solution.

In the first choice test following training, the F-S and G-S groups displayed comparable preferences for the CS+ flavor (82%). This contrasts with our previous finding (1) of a weaker preference in F-S rats than in G-S rats (66% vs. 82%). Similar procedures were used in the two studies and the reason for the discrepant results is not clear. The fructose-conditioned preference of the F-S group remained stable with repeated testing even though the animals were no longer reinforced. Unexpectedly, the glucose-conditioned preference in the G-S group declined with repeated testing. One possible explanation why the CS+ preference extinguished in the G-S group but not the F-S group is offered below.

In marked contrast with the results obtained in the F-S group, the F-D group did not acquire a preference for the flavor paired with the delayed presentation of fructose. On the other hand, the G-D group displayed a significant and stable preference for the flavor that preceded the delayed presentation of glucose. The two delay groups also differed in that the G-D rats, but not the F-D rats, consumed more CS+s than CS−s during training. Prior studies indicate that flavor–flavor associations are blocked with the CS–US delay paradigm [(6,8), see also (9)]; thus any preferences obtained are thought to be mediated by the postingestive consequences of the nutrient. The failure of the F-D group to develop a CS+ preference, therefore, indicates that the postingestive actions of fructose are not reinforcing. This is consistent with the observation that IG fructose infusions condition only weak flavor preferences (16). Taken together, these results suggest that the flavor preference observed in the F-S group was due primarily to the taste rather than the postingestive effects of fructose. In support of this interpretation, short-term taste tests demonstrate that 8% fructose is strongly preferred to 0.2% saccharin (unpublished observations).

The initial CS+ preference displayed by the G-D rats was less than that shown by the G-S rats. This may be because with the simultaneous conditioning procedure, both the sweet taste and postingestive effects of glucose are available to reinforce the flavor preference, whereas with the delay procedure only postingestive reinforcement is effective. The double reinforcing effect obtained with the simultaneous procedure may also explain why the CS+ preference extinguished in the G-S group but not in the G-D group. During preference testing the CS+ and CS− flavors were both presented in saccharin solutions. Thus, the G-S group was missing both the taste and postingestive reinforcing actions of glucose during testing, whereas the G-D group was missing only the postingestive reinforcement. The greater contrast between training and test conditions for the G-S group may account for their weakening CS+ preference over test sessions. This analysis suggests that the F-S group did not extinguish their CS+ preference because they too were missing only one reinforcer, in this case the taste of fructose, during the test sessions with the CS+s and CS−s solutions.

EXPERIMENT 2

The results of the first experiment suggest that conditioned preferences for CS+ flavors mixed into a fructose solution are reinforced primarily by the sugar's palatable taste rather than its postingestive actions. According to this interpretation, if the taste of the fructose solution were made less palatable then preference conditioning would be attenuated. Reducing the palatability of a glucose solution would be less effective in blocking conditioning because of this sugar's postingestive reinforcing effect. Boakes et al. (4), in fact, reported that rats learned to prefer a flavor mixed in a glucose–quinine solution over a flavor mixed in a saccharin solution even though the glucose–quinine solution was initially less preferred than the saccharin solution. The present experiment compared the effects of quinine adulteration on preference conditioning produced by fructose and glucose solutions.

METHOD

Subjects

Twenty female CD rats born in our laboratory from Charles River stock were used. The animals were 90 days old at the start of the study and were housed as in Experiment 1.

Test Solutions

The training sugar solutions consisted of 8% glucose or 8% fructose flavored with 0.05% grape or cherry Kool-Aid and 0.01% quinine hydrochloride (Sigma Chemical); the training saccharin solution contained 0.2% saccharin and 0.05% grape or cherry Kool-Aid. For half the rats grape was the CS+ flavor paired with glucose–quinine (CS+Gq) or fructose–quinine (CS+Fq), and cherry was the CS− flavor paired with saccharin (CS−s); the flavors were reversed for the remaining rats. Preference tests were conducted with these training solutions as well as with a saccharin solution containing the CS+ flavor (CS+s solution).

Procedure

The rats were familiarized with unflavored 0.2% saccharin solution by giving them ad lib access to saccharin and plain water for 2 days. They were then food restricted and maintained at 85% of ad lib body weight for the remainder of the experiment. The rats were adapted to drink unflavored saccharin during daily 2-h sessions for 9 days. They were then divided into two groups (n = 10 each) equated for their saccharin intake. The glucose group was given a two-bottle preference test (test 1) with the CS+Gq solution vs. the CS−s solution. This pretest assessed the rats' initial preference for the training solutions. The rats were next given one-bottle training with the sugar and saccharin solutions for a total of 10 sessions. Each day the animals were given their food ration and water for 2 h in the morning, followed by water only for 2 h. They were then given overnight access to 24 ml of the CS+Gq or CS−s solution on alternate days. To ensure that the rats consumed the CS+Gq solution, water was not available overnight during the first 9 training days. On the last training day (with CS−s) the rats had water ad lib so that they would not be thirsty prior to the preference test conducted the next day. In this preference test (test 2) the animals were given the choice between the CS+Gq and CS−s solutions. They were next given a preference test with the CS+s vs. CS−s solutions (test 3) followed by another test with their training solutions (test 4; CS+Gq vs. CS−s). All preference tests consisted of two 2-h/day sessions with the left–right position of the flavors alternating over days. The tests were conducted in the morning and the rats' daily food ration and ad lib water were presented 1 h after the end of the test session.

The fructose group was treated identically to the glucose group except, of course, it was trained and tested with fructose instead of glucose.

RESULTS

Figure 2 summarizes the results of the two-bottle preference tests. In the initial preference test both the glucose and fructose groups rejected the CS+ flavored sugar–quinine solutions in favor of the CS− saccharin solution, $F(1, 18) = 106.2, p < 0.0001$; the percent of total solution consumed as CS+Gq and CS+Fq was only 1.0% and 1.4%, respectively. During the subsequent one-bottle training days the animals consumed the CS+ quinine–sugar solutions when they were the only fluids available overnight on alternate days. (On the first training day, three of the glucose rats and four of the fructose rats did not consume all of the CS+ sugar–quinine solution but thereafter all rats consumed the entire 24 ml/day allotment.)

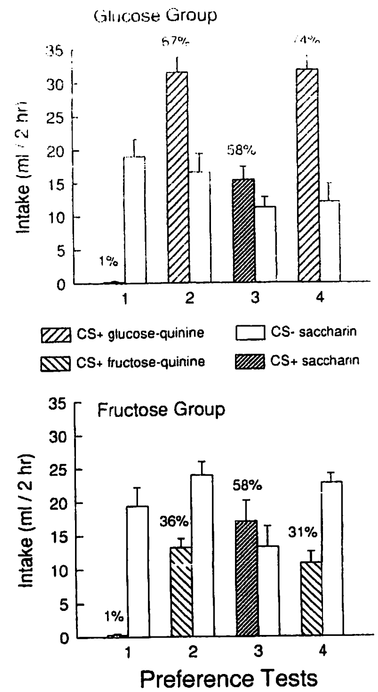

FIG. 2. Experiment 2. Mean + SEM intakes of CS+ and CS− flavored solutions of the glucose and fructose groups during 2 h/day preference tests. The CS flavors were grape and cherry. In tests 1, 2, and 4 the rats were offered the choice between CS+ glucose–quinine (glucose group) or CS+ fructose–quinine (fructose group) vs. CS− saccharin. In test 3 CS+ saccharin vs. CS− saccharin solutions were used. Percentages atop bars indicate the percent intake of the CS+ flavored solution.

In the posttraining preference test (test 2), both groups substantially increased their CS+ sugar–quinine solution intake compared to the pretraining test (test 1) [test × solution interaction, $F(1, 18) = 128.9, p < 0.001$], but this increase was much greater for the glucose group than the fructose group [group × test × solution interaction, $F(1, 18) = 48.3, p < 0.001$]. In test 2 the glucose group consumed more CS+Gq than CS−s whereas the fructose group drank less CS+Fq than CS−s [group × solution interaction, $F(1, 18) = 29.1, p < 0.001$]; percent CS+Gq and CS+Fq intakes were 67% and 36%, respectively. In addition, the glucose group consumed more ($p < 0.01$) CS+ sugar–quinine and less ($p < 0.05$) CS− saccharin than did the fructose group. When offered the CS+ and CS− flavored saccharin solutions in test 3, both groups showed small and unreliable preferences for the CS+s solution; the solution intakes of the two groups did not differ. In test 4 the rats were again offered their original training solutions and the results were similar to test 2: the glucose group significantly preferred the CS+Gq solution whereas the fructose group preferred the CS−s solution [group × solution interaction, $F(1, 18) = 59.8, p < 0.001$]; the percent

CS+Gq and CS+Fq intakes were now 74% and 31%, respectively.

DISCUSSION

Both groups increased their intake of the CS+ flavored sugar–quinine solutions following one-bottle training, but this increase was much greater in the glucose group, which, unlike the fructose group, came to prefer the CS+ sugar–quinine solution to the CS− saccharin solution. However, the groups did not differ in their responses to the CS+ flavor when it was presented in a saccharin solution; neither group reliably preferred the CS+s to the CS−s. It may be that the cherry and grape flavors were not effective as CS+ cues, as they were in Experiment 1, because they were overshadowed by the bitter taste of the glucose–quinine solution (10).

The failure to obtain a significant CS+s preference in the glucose group contrasts with the findings reported by Boakes et al. (4). Differences in the training stimuli may account for the discrepant findings. In addition to using different, and perhaps stronger, cue flavors (coffee and vinegar), the earlier experiment used more concentrated glucose (15%) and less concentrated saccharin (0.1%) solutions than used here; the quinine concentration was the same in both experiments. Given these differences, it is not surprising that the rats in the present experiment more strongly avoided the glucose–quinine solution in the pretraining preference test than did the rats in the Boakes et al. study (1% vs. 21% CS+Gq intakes). Nevertheless, the posttraining preference for the glucose–quinine solution in the present and previous experiments were similar (67% and 64%).

The rats' strong avoidance of the CS+ sugar–quinine solutions in the pretraining test (test 1) may represent a combination of an aversion to bitter taste, in particular, and a neophobic response to novel flavor. Thus, the increased intakes of CS+ sugar–quinine solutions following one-bottle training can be attributed in part to a familiarization effect, i.e., loss of their neophobic reaction to the solutions [see (4)]. In addition, the rats may have acquired an increased preference for the CS+ sugar–quinine solutions during training as they associated its bittersweet taste with the postingestive reinforcing action of the sugar. The much stronger posttraining CS+ sugar–quinine preference displayed by the glucose group compared to the fructose group is consistent with the results of Experiment 1 and prior studies (1,16) that glucose has a more potent postingestive reinforcing effect than does fructose.

Because the glucose and fructose groups did not differ when tested with the CS+ saccharin solution but differed only when tested with the CS+ sugar–quinine solutions, the present data, by themselves, do not provide conclusive evidence that glucose conditions stronger flavor preferences than does fructose. It could be argued that unconditioned responses to the different taste or postingestive properties of glucose and fructose were responsible for the greater CS+ sugar–quinine intake of the glucose group compared to the fructose group. For example, the present data could be accounted for if rats are inherently more attracted to the taste of glucose than fructose. Food-deprived rats in a prior experiment did, in fact, prefer 8% glucose to 8% fructose in a pretraining choice test, but whether this was due to unlearned taste preference or a rapid learning effect is uncertain. Other data indicate that when postingestive factors are minimized, rats tend to prefer fructose to glucose at midrange concentrations (17). Nevertheless, given the ambiguous nature of the present findings, Experiment 3 further evaluated the response of the glucose and fructose groups to sugar–quinine solutions.

EXPERIMENT 3

The rats in Experiment 2 may have consumed more of the CS+ glucose–quinine solution than of the CS+ fructose–quinine solution after training based on 1) conditioned responses to the different postingestive reinforcing effects of the two sugars or 2) unconditioned responses to the taste or postingestive properties of the two sugars. To distinguish between these two possibilities, the present experiment gave the glucose and fructose rats preference tests with CS+ sucrose–quinine solutions. If the glucose rats consume more sucrose–quinine solution than the fructose rats, this would support the idea that they acquired a learned preference for bittersweet solutions based on the postingestive reinforcing actions of glucose. On the other hand, if the two groups consumed comparable amounts when tested with the same sucrose–quinine solutions, this would indicate that their differential intakes of glucose–quinine and fructose–quinine solutions were due to unconditioned responses to the two sugars.

METHOD

Test Solutions

The flavored glucose (CS+Gq), fructose (CS+Fq), and saccharin (CS−s) solutions described in Experiment 2 were used. In addition, flavored sucrose solutions were prepared containing 4%, 6%, or 8% sucrose, 0.05% grape or cherry Kool Aid, and 0.01% quinine hydrochloride. (Three concentrations were tested because it was not known what sucrose concentration would most closely match the sweet taste of the glucose and fructose solutions.) Each rat was tested with sucrose solutions containing the flavor (grape or cherry) used in their original training sugar solution (CS+Gq or CS+Fq).

Procedure

Following the last preference test of Experiment 2, the glucose and fructose groups were given a series of two-bottle tests with CS+ sucrose–quinine vs. CS− saccharin at sucrose concentrations of 8%, 4%, and 6%, in that order. After each sucrose test the animals were given a two-bottle test with their original training solutions (CS+Gq or CS+Fq vs. CS−s). The preference tests were conducted as in Experiment 2.

RESULTS

As illustrated in Fig. 3, when retested for their preference for their original training solutions, the glucose group preferred the CS+Gq to the CS−s, whereas the fructose group consumed more CS−s than CS+Fq [group × solution interaction; $F(1, 18) = 28.6$, $p < 0.001$]. In addition, the glucose group consumed more ($p < 0.001$) sugar–quinine and less ($p < 0.05$) saccharin than did the fructose group. The groups also differed in their response to the CS+ sucrose–quinine solutions [group × solution interaction, $F(1, 18) = 5.0$, $p < 0.05$]. Over all concentrations, the glucose group consumed more CS+ sucrose–quinine and less CS− saccharin than did the fructose group. Both groups increased their CS+ sucrose–quinine intake, and decreased their CS−s intake as sucrose concentration increased [concentration × solution interaction, $F(2, 36) = 52.3$, $p < 0.001$]. Note that the preferences displayed by the fructose group for the 6% and 8% sucrose–quinine solutions were comparable to those displayed by the glucose group for the 4% and 6% sucrose–quinine solution, respectively. Also, the fructose rats avoided the 4% sucrose–quinine solution in favor of the CS− saccharin solution

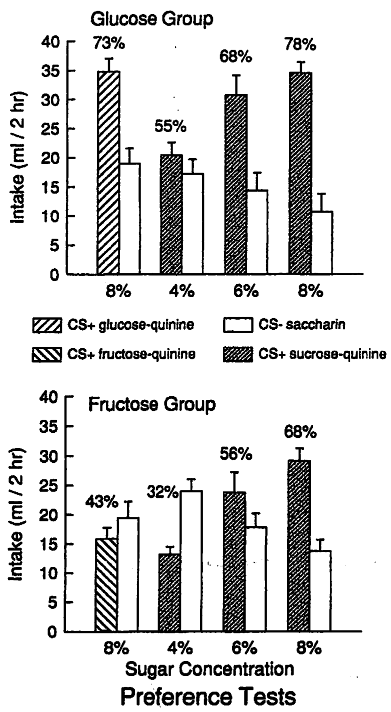

FIG. 3. Experiment 3. Mean + SEM intakes of CS+ and CS− flavored solutions of the glucose and fructose groups during 2 h/day preference tests. The CS flavors were grape and cherry. The glucose and fructose groups were both tested with CS+ sucrose–quinine vs. CS− saccharin solutions at concentrations of 4%, 6%, and 8%; the data presented are the mean of two sessions at each concentration. After each sucrose test, the rats were offered CS+ glucose–quinine (glucose group) or CS− fructose–quinine (fructose group) vs. CS− saccharin; the data presented are the mean of six sessions. Percentages atop bars indicate the percent intake of the CS+ flavored solution.

whereas the glucose group showed a slight preference for the 4% sucrose–quinine solution.

DISCUSSION

The groups differed not only in their intakes of their respective sugar–quinine solutions, but also in their intakes of the CS+ sucrose–quinine solutions. This latter finding supports the hypothesis that the rats' differential intakes of the glucose–quinine and fructose–quinine solutions were due to the more potent postingestive reinforcing effect of glucose. The CS+ sucrose–quinine results, along with the CS+ saccharin findings of the previous experiment, indicate that the effective CS+ was not the grape or cherry flavor alone, but the flavor combined with the bittersweet taste of the sugar–quinine solution.

At all concentrations tested, the glucose rats displayed stronger preferences for the CS+ sucrose–quinine solutions than did the fructose rats. Both groups were responsive to increasing sucrose concentration; the fructose rats simply required a higher sucrose concentration than did the glucose rats to overcome their avoidance of the bittersweet sucrose–quinine solution. The isohedonic sucrose concentration needed to match the rats' attraction to the saccharin solution was estimated to be 3.2% for the glucose group and 5.7% for the fructose group (this estimate was based on a regression analysis using the data from the three sucrose concentrations tested). Thus, prior experience with the postingestive reinforcing effect of glucose appears to improve the palatability of the CS+ sugar–quinine solution in a manner comparable to increasing its sweet taste.

GENERAL DISCUSSION

The present findings further specify the flavor preference conditioning effects of glucose and fructose. The two sugars were equally effective in conditioning a flavor preference when the CS+ flavor was mixed into the sugar solutions, but only glucose supported preference conditioning when the CS+ flavor preceded the sugar by a short delay. In addition, degrading the taste of the sugar by quinine adulteration blocked the development of a preference for a flavored fructose solution but not for a flavored glucose solution. Prior work also shows that IG glucose infusions are much more effective than IG fructose infusions in conditioning flavor preferences, and rats readily learn to prefer flavors paired with glucose over flavors paired with fructose (1,3,16). We have also reported preferences for flavored chow paired with a glucose solution over flavored chow paired with a fructose solution (1), although Tordoff et al. (20) obtained conflicting results.

Taken together, these results indicate that fructose can condition a flavor preference based on its palatable taste, but its postingestive actions are minimally effective in supporting preference conditioning. Glucose, on the other hand, can condition flavor preferences both by its sweet taste and postingestive actions. Because of its dual reinforcing effect, glucose should produce stronger flavor preferences than fructose using the simultaneous conditioning procedure. For some reason this outcome was observed in a prior study but not in Experiment 1 of the present study. Conceivably, the taste of fructose may be more reinforcing than the taste of glucose, which would partially counteract glucose's postingestive reinforcing action. Further work is needed to compare the conditioning effects of the glucose and fructose tastes when postingestive factors are eliminated. This could be accomplished by testing rats with flavored sugar and saccharin solutions as in Experiment 1 but under sham-feeding test conditions.

Why glucose has a more potent postingestive reinforcing effect than fructose remains to be determined. It cannot be attributed to differences in energy value or satiating effects because the two sugars are isocaloric and appear to be equally satiating to rats (5,11,19). Rather, more specific differences in the pre- and/or postabsorptive actions of the two sugars must account for their differential reinforcing effects. One possibility is that sugar-stimulated vagal afferent activity reinforces flavor preferences. Prior work indicates that intestinal and hepatic vagal afferents are more responsive to glucose infusions than to fructose infusions (12,15). Neuroendocrine responses may also be involved in the differential reinforcing effects of the two sugars (13,14). However, insulin does not appear to be a critical hormone because streptozotocin-diabetic rats, like normal animals, learn to prefer glucose-paired flavors to fructose-paired flavors (3). We have previously speculated that fructose might have negative postingestive consequences related to its slow absorption that might limit its positive postingestive reinforcing effects (16). Arguing against this idea is the strong flavor preference conditioned by fructose in the F-S group of the present study. Nevertheless, it may be adaptive for fructose to have only weak postingestive reinforcing action in view of its slow absorption. Another adaptive explanation is that the postingestive reinforcing effect of glucose functions primarily to increase the animal's preference for complex carbohydrates (starch), not for sugars. The sweet taste of sugars, including fructose, may be sufficiently rewarding to maintain the animal's attraction to sugar-rich foods.

Because of their different physiological sites of action, glucose and fructose have proven useful in the study of energy intake regulation (18). The present results, along with other recent findings (1,16), indicate that these two sugars also have different reinforcing effects and are thus useful tools to investigate the physiological and behavioral mechanisms mediating food preference learning.

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