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The Relationships Among Saccharin Consumption, Oral Ethanol, and IV Cocaine Self-Administration

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GAHTAN, E., L. P. LABOUNTY, C. WYVELL AND M. E. CARROLL. *The relationships among saccharin consumption, oral ethanol, and IV cocaine self-administration.* PHARMACOL BIOCHEM BEHAV **53**(4) 919–925, 1996.– The purpose of the present experiment was to replicate previously reported observations of a relationship between saccharin consumption and oral ethanol self-administration in rats using operant measures (2,8) and to determine whether saccharin intake was related to the rate of acquisition of IV cocaine self-administration. Groups of Wistar rats selected for high and low saccharin (0.1% wt/vol) intake were tested for rate of acquisition of IV cocaine (0.2 mg/kg/infusion) self-administration using an autoshaping procedure. They were subsequently tested for self-administration of oral ethanol (8% wt/vol) under ascending fixed-ratio (FR) schedules (FR 1, 2, 4, and 8). Finally, ethanol deliveries were compared under food-deprivation and food-satiation conditions under an FR 8 schedule. Saccharin intake was redetermined after each phase of the experiment. No significant differences between high and low saccharin groups were found in rate of acquisition of IV cocaine self-administration, and there was not a significant correlation between saccharin and cocaine consumption. However, the high saccharin group drank significantly more ethanol than the low saccharin group during the FR 8 food satiation component. A significant correlation between saccharin and ethanol consumption was also found. For high and low saccharin groups, responding for ethanol increased proportionally with increases in FR such that consumption of ethanol remained relatively constant as FR increased. Ethanol consumption was significantly increased under food deprivation relative to food satiation conditions for both saccharin groups. A significant correlation between ethanol consumption and cocaine consumption was also found. Significant increases in saccharin consumption across successive saccharin consumption tests were found for both groups, although relative intake for the high and low saccharin groups remained stable throughout the experiment. These results indicate that higher ethanol intake is predicted by higher saccharin intake, but saccharin intake did not predict the rate of acquisition of IV cocaine self-administration.

Cocaine Ethanol Saccharin Self-administration IV Oral Rats

RECENTLY, a number of studies have shown a relationship between consumption of saccharin and ethanol self-administration in rats using home-cage drinking techniques. Except for recent studies with outbred rat strains [e.g., (8)], most of these studies have investigated the relationship between ethanol and saccharin intake in rat strains bred specifically for high or low ethanol preference. In these inbred strains, strong relationships between saccharin consumption and ethanol consumption were found (10,16,18). There is evidence to suggest that the relationship between the consumption of saccharin and ethanol self-administration exists because of the postingestional effects of these substances (vs. the taste sensitivity of the rats). For example, rat strains selected for high and low oral ethanol consumption have corresponding rates of intracranial (14) and intragastric (20) ethanol self-administration, indicating that differences in the postingestional effects of ethanol play a large role in the differences in oral ethanol consumption. Gosnell et al. (9) showed that outbred

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Sprague–Dawley rats selected for high and low saccharin consumption had corresponding rates of IV morphine self-administration. Finally, Ganchrow et al. (7) showed that rats bred for high or low rates of intracranial self-stimulation (ICSS) have corresponding high and low saccharin intakes. The positive relationships between oral, intragastric, and intracranial ethanol self-administration, IV morphine self-administration, rate of ICSS, and saccharin sumption suggest that the taste of ethanol is not a crucial determinant of the predictive effect of saccharin and ethanol intake.

The proposed neurological mechanisms involved in the reinforcing effects of ethanol include the mesocorticolimbic dopamine system, GABA, glutamate, serotonin, and opioidergic systems (12). Beczkowska et al. (1) and Touzani et al. (19) have provided evidence that saccharin activates the opioidergic system. Thus, the relationship between saccharin and ethanol consumption may coincide with their overlapping pharmacological actions. However, the research cited above is limited in its generality because inbred strains of rats, selected for particular substance or ICSS preferences, were used.

Two recent studies examined the relationship between saccharin and ethanol consumption in outbred Wistar rats. Here, a much weaker but positive relationship between preferences for saccharin and ethanol self-administration was found (2,8). Gosnell and Krahn (8) found a statistically significant relationship between ethanol and saccharin consumption when rats were fed ad lib, but differences did not reach statistical significance when the animals were food deprived. Bell et al. (2) extended this work to an operant paradigm, and they found a consistent relationship between saccharin and ethanol consumption across 23 of 24 measures, but only one derived measure reached statistical significance. One purpose of the present research was to further investigate the relationship of saccharin and ethanol preference in Wistar rats to bring more evidence to bear on the reliability and generality of previous findings.

As might be expected if the opioidergic system is involved in the reinforcing effects of saccharin, there would also be a relationship between saccharin consumption and opioid consumption. Nichols and Hsiao (15) found that rats selected for high and low receptivity to oral opiate self-administration had corresponding high and low receptivity to ethanol self-administration. More recently, Gosnell et al. (9) showed that rats selected for high and low saccharin preferences had corresponding high and low rates of IV morphine self-administration. In their study high and low saccharin groups were also tested for differences in oral morphine self-administration, but they were not found to differ.

Because animal research in this area has been limited to two pharmacological classes of drugs, ethanol, and opioids, another purpose of the present research was to examine the relation of saccharin intake to cocaine self-administration. In the present experiment a drug acquisition procedure was used that was previously found to be sensitive to individual differences in the reinforcing effects of drugs (4,5). Rats ranked high or low on saccharin intake were tested for rate of acquisition of IV cocaine self-administration. It was hypothesized that the high saccharin group would acquire cocaine-reinforced behavior more quickly than the low saccharin group. Following the cocaine acquisition phase, rats were allowed to acquire oral ethanol self-administration, and they were then were tested for steady-state oral ethanol self-administration under food deprivation and food satiation conditions. The ethanol phase of this experiment was a systematic replication of the earlier study by Bell and co-workers (2) reporting a correlation between saccharin intake and oral ethanol self-administration using an operant paradigm.

METHODS

Animals

Subjects were 60 naive male Wistar rats, approximately 6 months old at the beginning of the experiment. Their mean (±SE) body weight was 239.3 (±1.56). All subjects were housed individually in a single room with 12 L : 12 D cycles (lights on at 0600 h). Prior to the cocaine acquisition test, the rats received free access to food (Ground Purina Laboratory Chow). During cocaine acquisition, food was restricted to 20 g each day. Free-feeding weights were determined prior to the cocaine acquisition phase, and weights were reduced to 85% of free feeding weight prior to the beginning of the ethanol FR series. Free access to food was restored for the final phase of ethanol self-administration. Water was freely available in the home cages and for initial exposure to saccharin, with the exception of 24-h water deprivation before spout training in the experimental chamber. One subject from the high saccharin intake group died during the ethanol phase of the experiment, and four additional subjects, two from each saccharin group, died prior to the final saccharin preference test. All available data from these subjects were included in the statistical analysis.

Apparatus

Home cages constructed of wire mesh were 30.5 cm long, 30.5 cm wide, and 61 cm high. During the ethanol phase of the experiment 15 randomly selected rats were housed and run at Macalester College (St. Paul, MN). The dimensions of the home cages at that site were 24 cm long, 18 cm wide, and 17.5 cm deep. Saccharin consumption sessions were run at 0900 h each day.

Experimental chambers used for cocaine self-administration tests were octagonally shaped with alternating stainless steel and Plexiglas walls that were placed in sound attenuating wooden enclosures. A retractable lever and a standard programmed inactive lever were mounted on the back left and right metal panels. A house light directed upwards at the top rear of the cage, relative to the levers, provided constant illumination.

For the saccharin consumption assessment, 50 ml plastic graduated burettes with attached drinking spouts were affixed to the home cages, allowing direct measurement of volume of water or saccharin consumed. For the intravenous cocaine self-administration phase, experimental chambers were fitted with a standard water bottle and a recessed food jar containing ground food.

During the oral ethanol self-administration phase, experimentation took place at two sites. Experimental conditions and equipment were identical at both sites with the exception of the experimental chambers, and no differences in results were noted between sites. At Macalester College, rather than the octaganol chambers, standard Coulbourn Instruments Large Animal Test Environments were used. At the University of Minnesota, the same octagonal chambers were used as in the IV cocaine self-administration phase. Experimental chambers at both locations were each identically equipped with a solenoid-driven lick-operated drinking spout, a house light located above the drinking spout, and a pellet feeder delivering 45 mg food pellets. Levers were removed from the experimental chambers for the ethanol self-administration phase of

the experiment, and the IV catheters (Plastics One, Inc., Roanoke, VA) and related apparatus were removed. Tongue contacts on the drinking spout closed a low voltage electrical circuit running through the wire mesh floor of the cage, allowing lick responses to be counted and recorded. The volume of liquid deliveries was calibrated to approximately 0.025 ml per delivery. Experimental chambers were controlled and experimental events were recorded by Med Associates Inc. (St. Albans, VT) interfacing and software, which was run on IBM-compatible computers.

The IV cannula for cocaine infusions extended from the jugular vein under the skin to a back harness affixed to the skin of the rat near the scapulae. From the back harness the cannula attached to a swivel (Alice King Chatham, Inc., Hawthorne, CA) on the ceiling of the chamber that allowed the rat free movement around the chamber. An infusion pump and aspirator bottle containing the cocaine solution were housed directly outside each wooden chamber enclosure and attached to the cannula at the swivel on the chamber ceiling. Infusion pumps (Fluid Metering, Inc., Oyster Bay, NY; Model RHSYOCKC) delivered 0.2 ml/kg/infusion of cocaine HCl at a rate of 0.03 ml/s. Microcomputer Control Systems (Micro Interfaces, Inc., Minneapolis, MN) computers, located in an adjacent room, controlled and recorded experimental events.

Drugs

Cocaine HCl was obtained from the National Institute of Drug Abuse (Research Triangle Institute, Research Triangle Park, NC) and saccharin was purchased from the Sigma Chemical Company (St. Louis, MO). Ethanol (95%) was purchased from the University of Minnesota Storehouse or the Macalester College Chemistry Department. Cocaine HCl was dissolved in saline to produce a 1.6 mg/ml cocaine concentration. Dose was determined by the duration of the infusion and programmed according to the subject's body weight (1 s/100 g weight). Cocaine unit dose was 0.2 mg/kg for each infusion. Saccharin was dissolved in water to produce a 0.1% (wt/vol) solution. Ethanol (95%) was mixed in water to produce an 8% (wt/vol) solution.

Procedure

Saccharin consumption assessment. Rats were water deprived during the first 2 days of exposure to the saccharin solution to ensure sampling of the solutions. On the third day water was restored in the home cage and experimental sessions began 2 h into the light cycle (0800 h). Sixty rats were given concurrent access to water and the 0.1% saccharin solution for 1 h. Twelve sessions of concurrent water and saccharin availability were conducted, reversing the positions of the liquids each day. Volumes consumed on the last 5 of the 12 sessions were used as an index of saccharin consumption.

All rats were then tested for saccharin and water intake over 12 consecutive days during which only saccharin or water was available. Saccharin and water availability were alternated each session. The 30 rats with intermediate saccharin intakes were not used in the remainder of this study. Two to 3 weeks following the last exposure to cocaine, the single-bottle procedure for saccharin preference was repeated. A final concurrent-access saccharin–water two-bottle test occurred no less than 2 weeks following the last exposure to ethanol, and this was the final component of the experiment.

Acquisition of cocaine self-administration. Rats were implanted with chronic indwelling catheters into the left external jugular vein according to a surgical procedure described in detail previously [see (3)]. Following surgery, rats were placed in the operant chambers where they remained for the duration of the cocaine self-administration phase. They were allowed at least 5 days of recovery from surgery before cocaine infusions began. Daily sessions consisted of a 6-h autoshaping procedure (beginning at 0900 h) immediately followed by a 6-h cocaine self-administration period (beginning at 1500 h). During the 6-h autoshaping session, the active automated lever extended into the chamber 10 times per hour according to a random time 90-s schedule. The lever retracted if a response was made or when 15 s elapsed, whichever occurred sooner. One second after the lever retracted, an infusion of cocaine (0.2 mg/kg) was delivered. The inactive (unprogrammed) lever remained extended into the chamber throughout the session, and the stimulus lights above both the active and inactive levers remained on. This autoshaping procedure has been shown to result in rapid acquisition of cocaine self-administration, and it is sensitive to differences in feeding conditions and availability of alternative nondrug reinforcers (4).

The 6-h self-administration component of the daily session was used to assess acquisition of cocaine self-administration. Active and inactive levers remained extended during the self-administration session, and each response on the active lever resulted in a cocaine infusion (FR 1). No limit was placed on the number of self-administered infusions, except responding during an infusion had no programmed consequences. Criteria for acquisition of cocaine-maintained lever pressing was a mean of 100 infusions during the 6 h self-administration session, over 5 consecutive days. Infusions during the last 2 days of that 5-day period were evaluated as an indicator of steady-state cocaine-maintained responding following acquisition.

Ethanol Self-Administration

Rats were reduced to 85% of their free-feeding weights over a period of approximately 10 days. Low and high saccharin groups did not differ significantly on mean (±SE) 85% body weights, which were 533.54 ± 16.17 g and 506.73 ± 16.07 g, respectively. Before ethanol sessions began, rats were 24-h water deprived and trained to drink water from the drinking device. A schedule-induced drinking procedure was used to establish ethanol drinking. For the duration of each 3-h session, ethanol deliveries were contingent upon one response (FR 1) on a lick-operated drinking spout. During the second and third hours of the session, 45 mg food pellets were delivered noncontingently according to a fixed-time 60-s schedule. This schedule of food delivery generates schedule-induced polydipsia, or copious drinking of a variety of liquids [see (6)]. A minimum of 20 sessions of schedule-induced ethanol drinking were conducted, and food was removed from the session when rats reached the criteria of 3 days of stable responding, defined as no steady increase or decrease in total daily responses. Four rats, three from the high saccharin intake group and one from the low group did not acquire ethanol drinking during the food-induced drinking phase, and extra training sessions were conducted with water under water-deprivation conditions. Once food deliveries were terminated, the FR lick requirement for ethanol deliveries was increased according to the following series; 1, 2, 4, 8. Subjects were exposed to each FR value for a minimum of 5 days and the FR was advanced only after 3 consecutive days of stable responding (no increasing or decreasing trend). When responding had stabilized at FR 8, rats were tested sequentially with ethanol, water, and then ethanol again, each available at FR 8. Responding for each liquid was allowed to stabilize accord-

ing to the above criteria for ethanol FR performance before changing liquids.

When this first ethanol-water-ethanol sequence was completed, subjects were given free access to food in the home cages while still being tested each day under an FR 8 schedule of ethanol deliveries. When subjects reached at least 90% of their free-feeding weights as established at the beginning of the ethanol experiment, a second ethanol-water-ethanol sequence was conducted. Table 1 summarizes the various phases of the experiment in the order that they occurred.

Data Analysis

Data were analyzed by analysis of variance procedures using Super ANOVA (Abacus Software, Inc., Berkeley, CA) and by correlation analysis using Statview (Abacus Software, Inc.). Separate *t*-tests were conducted comparing the high and low saccharin group means on the water component and two ethanol components during the food deprivation and satiation ethanol-water-ethanol series. The Bonferroni/Dunn correction procedure was employed for all posthoc comparisons, and the experiment-wise error rate was set a priori at $p = 0.05$. Overall *F*-values were calculated for multivariate ANOVAs.

RESULTS

Saccharin Consumption Tests

Figure 1 depicts liquid intakes for the high and low saccharin consumption groups across the four saccharin tests. Means were compared using paired, one-tailed *t*-tests, and $p \leq 0.05$ was considered statistically significant. In all but the final saccharin preference test, the high saccharin group, as determined by the initial group selection test, had a significantly higher mean saccharin intake than the low group. On the final saccharin test, the high group had a higher mean consumption than the low saccharin group [17.71 (±2.66) and 10.46 (±2.71), respectively], but this difference failed to reach significance. In all tests water consumption was low for both groups and not significantly different between groups.

In addition to between-group differences in saccharin consumption, significant increases in saccharin consumption occurred within groups across successive testing phases. The low saccharin group increased its saccharin consumption after exposure to cocaine ($t = -2.44$, $p < 0.05$) and again after ethanol ($t = -5.67$, $p < 0.01$), and the high group increased its saccharin consumption after ethanol exposure ($t = -2.73$, $p < 0.05$). Because water consumption was not affected by exposure to cocaine or ethanol, increases in saccharin consumption were not interpreted as part of a general increase in liquid consumption.

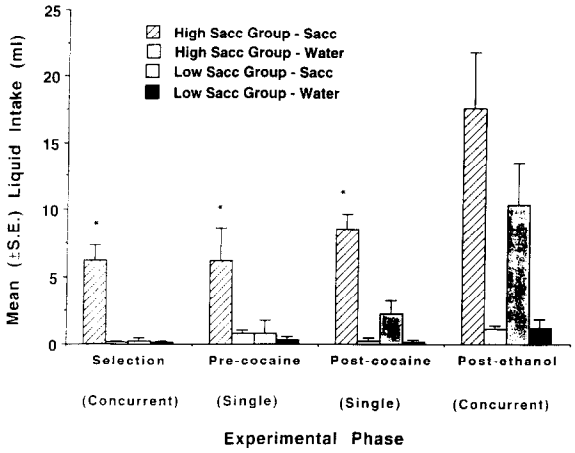

FIG. 1. Mean (±SE) of 0.1% (w/v) saccharin and water intake (ml) for the high and low saccharin groups on four sequential tests: 1) the initial selection test, 2) the precocaine self-administration test, 3) the postcocaine self-administration test, and 4) the postethanol self-administration test. During tests 1 and 4 water and saccharin were concurrently available. During tests 2 and 3 saccharin and water were available on alternate days. Each bar represents the group mean ($n = 15$) over the last 5 sessions of a 12-session series. Asterisks indicate that saccharin consumption was significantly greater in the high and low saccharin groups ($p < 0.05$).

Cocaine Self-Administration

Figure 2 depicts the rate of acquisition of IV cocaine self-administration for the high and low saccharin groups, expressed in terms of the percent of each group having reached the acquisition criteria at each successive day of training. Acquisition was defined as an average of 100 infusions per day for 5 consecutive days; thus, criteria for acquisition could not

TABLE 1

ORDER OF EXPERIMENTAL EVENTS

1. Saccharin consumption group selection
   Concurrent saccharin/water access
2. Saccharin consumption retest
   Single liquid access
3. Cocaine self-administration acquisition
4. Saccharin consumption retest
   Single liquid access
5. Ethanol self-administration
   Ascending fixed-ratio (FR) series
   Food deprivation ethanol-water-ethanol series
   Food satiation ethanol-water-ethanol series
6. Saccharin consumption retest
   Concurrent saccharin/water access

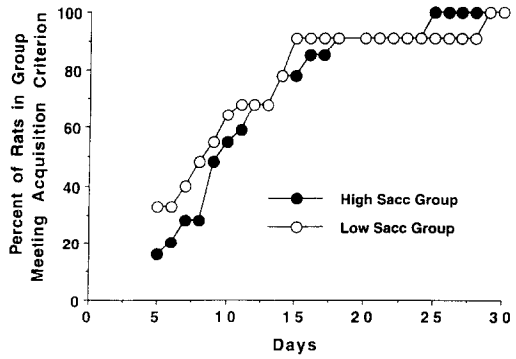

FIG. 2. The percent of rats reaching the criterion of 100 IV infusions of 0.2 mg/kg cocaine in a 6-h period is presented as a function of number of days of autoshaping. Filled circles represent the high saccharin group ($n = 15$) and open circles refer to the low saccharin group ($n = 15$).

be reached in fewer than 5 days. There was no significant difference between the high and low saccharin groups in the mean days to reach cocaine acquisition criterion: 11.20 ± 1.31 and 10.27 (± 1.56), respectively ($t = -0.458, p > 0.05$).

High and low saccharin groups were also compared on amount of cocaine consumption, defined as the mean number of cocaine infusions taken during the final 2 days of cocaine acquisition. No difference in mean (± SE) cocaine consumption was found between high and low saccharin groups [159.93 (± 9.19) and 172.93 (± 13.02)], respectively ($t = 0.815$; $p > 0.05$). Correlation analyses were also conducted between saccharin consumption and rate of cocaine acquisition and between saccharin and cocaine consumption. Saccharin group assignment was ignored for these correlation analyses. There were no significant correlations between saccharin consumption and rate of cocaine self-administration acquisition ($r = 0.058, p > 0.05$) or amount of cocaine consumed ($r = 0.036$, $p > 0.05$).

Ethanol Self-Administration

Figure 3 shows differences in mean ethanol consumption for the high and low saccharin groups at each FR in the ascending series. High and low saccharin groups did not differ in ethanol consumption across the FRs of the ascending series, $F(1, 28) = 0.121, p > 0.05$]. In both groups, responding increased with increases in FR such that there were no significant within or between group differences in mean number of deliveries across the 4 FR conditions.

Figure 4 shows mean liquid deliveries at FR 8 under both food deprivation and satiation conditions for the ethanol-water-ethanol sequence. *t*-Tests comparing saccharin group means at each of the three components of the deprivation and satiation ethanol-water-ethanol series revealed no significant differences in ethanol or water consumption during the food deprivation series or on the first ethanol and the water component of the food satiation series. However, the high saccharin group did consume significantly more ethanol than the low saccharin group during the second ethanol component of the food satiation series, $t(14) = 2.67, p < 0.05$.

Both saccharin groups consumed significantly more ethanol than vehicle (water) during both feeding conditions, $F(2, 54) = 88.18, p < 0.01$, suggesting that ethanol functioned as a reinforcer for both saccharin groups. A significant effect of feeding condition, with both groups consuming less ethanol during the food satiation vs. food deprivation condition, was also found, $F(1, 27) = 38.60, p < 0.01$. Water consumption, a measure of extinction, remained relatively low and was not significantly affected by feeding condition.

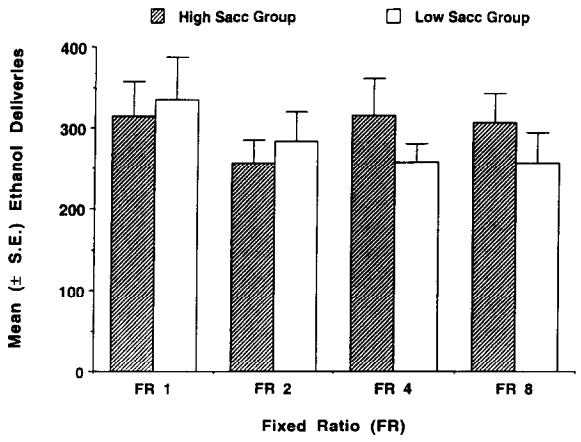

FIG. 3. Mean and SEM of ethanol consumption for the high and low saccharin groups from the last 3 days of each FR of the ascending FR series. No significant differences in means between the high and low saccharin groups were found.

Correlation analysis was also used to examine the relationship between saccharin and ethanol consumption. The mean saccharin consumption across the four saccharin consumption tests was calculated for each rat, and mean saccharin and mean ethanol consumption were compared during the two ethanol components of the food satiation ethanol-water-ethanol series. Saccharin group assignment was ignored for the correlation analysis. A significant correlation was found between these indices of saccharin and ethanol consumption ($r = 0.405, p < 0.05$).

The relationship between ethanol and cocaine self-administration was assessed by correlation analysis. Mean ethanol intake during the food satiation phase of ethanol self-administration was correlated separately with rate of acquisition of cocaine self-administration (days to criteria) and the mean number of cocaine infusions across the last 2 days of the acquisition criteria period. Rate of acquisition of cocaine self-administration was not significantly correlated with ethanol consumption ($r = -0.126, p > 0.05$); however, a significant positive correlation between cocaine and ethanol consumption was found ($r = 0.312, p < 0.05$).

DISCUSSION

The primary purposes of this experiment were to replicate the previously demonstrated positive relationship between preference for saccharin and oral ethanol self-administration in outbred rats (2,8) and to extend this line of research to a different class of drugs (e.g., cocaine) and route of administration (e.g., IV). Although the high and low saccharin groups differed significantly in ethanol consumption at only one condition of the ethanol self-administration component (second ethanol component of the food satiation series), the high saccharin group had a higher mean ethanol consumption on three of the four ethanol components at FR 8 (see Fig. 4). These results are consistent with those reported by Bell et al. (2), where the high saccharin consumption group had a higher mean ethanol intake than did the low saccharin group on 23 of 24 ethanol self-administration conditions. However, ethanol consumption differed significantly between saccharin groups on only one component of ethanol self-administration in their study. The significant correlation between saccharin and ethanol consumption found in the present study further supports the reliability of this effect.

As indicated in Fig. 4, the greatest difference in mean ethanol consumption between saccharin groups was in the second ethanol component of the food satiation ethanol-water-ethanol sequence. The larger group difference in ethanol consumption found during the later stages of the food satiation condition is consistent with the results of a previous investigation of the relationship between saccharin and ethanol consumption in rats (8). That differences in ethanol intake due to saccharin group are more readily apparent during food satiation suggests that a ceiling effect on drug intake during food deprivation may occlude group differences in consumption. However, the rats never appeared to be ataxic. Overall, when considering the present and the previous studies (2,8), there is an orderly relationship between saccharin and ethanol consumption.

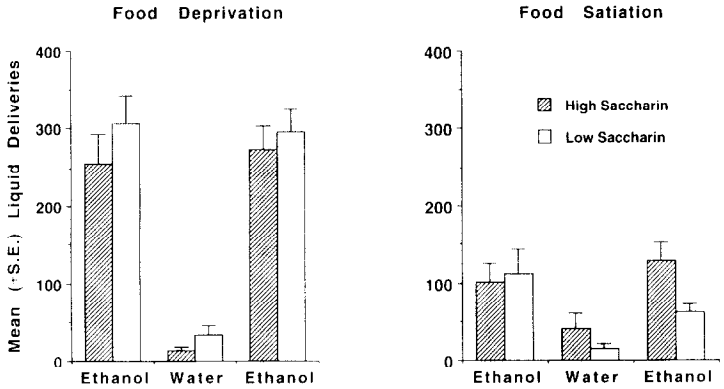

FIG. 4. Mean ethanol consumption for the high and low saccharin groups during the food deprivation (left frame) and the food satiation (right frame) ethanol-water series are shown.

The second goal of the present study was addressed by examining the relationship between saccharin intake and rate of acquisition of IV cocaine self-administration. Because the IV route diminishes orosensory factors, a relationship between IV cocaine self-administration and saccharin consumption would suggest correspondence in the sensitivity of reinforcement mechanisms for both substances. However, no differences were found between saccharin groups in either the rate of acquisition of cocaine self-administration (days to acquisition criteria) or in the amount of cocaine self-administered (based upon the final 2 days of acquisition). The absence of a relationship between saccharin consumption and cocaine self-administration was further supported by the correlation analyses between saccharin consumption and rate of cocaine acquisition and saccharin consumption and cocaine consumption. These correlations, calculated across saccharin consumption groups, were not significant. Failure to demonstrate a relationship between saccharin consumption and IV cocaine consumption could be interpreted as evidence that the replicated relationship between saccharin and ethanol consumption is mediated by taste factors. This interpretation, however, is not supported by the results of Bell et al. (2), who reported a positive relationship between saccharin consumption and IV morphine self-administration. Taste factors cannot account for this relationship since morphine, delivered intravenously, is presumably not a salient taste stimulus. Thus, the relationship between saccharin consumption and IV morphine self-administration suggests that the postingestive effects of drugs may be the critical component mediating the relationship between consumption of drug and nondrug reinforcers.

These results are consistent with pharmacological evidence that ethanol has broad and complex neurochemical effects, separate aspects of which overlap with the effects of saccharin and cocaine. For example, it is known that there is opioid receptor mediation of the self-administration of ethanol (12) and saccharin [e.g., (1,13)]. Overlapping effects in the opioidergic system may account for the relationship between saccharin and ethanol consumption. On the other hand, ethanol, but not saccharin, has consistently been shown to directly and significantly increase dopamine in the nucleus accumbens, the terminal component of the dopaminergic reinforcement pathway (11,22). Cocaine has been found to have similar effects on dopamine levels there (17,21,22). Thus, overlapping dopamine-dependent effects may account for the observed correlation between ethanol and cocaine consumption in the present experiment.

Another result worth noting in the present study was the highly stable group differences in saccharin consumption. These data support the notion that individual differences in preferences for sweet tastes are a robust phenomenon. However, it should be noted that during the first two saccharin tests the rats from both groups in the present experiment consumed less saccharin than reported in earlier studies (2,8,9). This difference may have been attributed to age, strain, and/or minor procedural variations. It is interesting to note that both the high and low saccharin groups exhibited very similar patterns of increases in saccharin consumption across the four saccharin tests (see Fig. 1). In the final two saccharin consumption tests, after exposure to cocaine and again after exposure to ethanol, the low saccharin group showed significantly greater preference for saccharin than for water. Thus, at the beginning of the experiment, the high saccharin group preferred saccharin to water, whereas, the low saccharin group did not. This distinction between groups disappeared by the postcocaine phase of the experiment. Water consumption did not change across saccharin tests, suggesting that the increase in saccharin consumption was not a result of changes in body weight or increased familiarity with the testing environment. These parallel increases in saccharin consumption in the high and low saccharin groups across testing phases may be explained by an effect of cocaine and ethanol exposure on preference for saccharin. Alternatively, the increases in saccharin intake may be due to diminished neophobia over time or a combination of factors. Gosnell and Krahn (8) also report similar increases in saccharin consumption after exposure to ethanol in high, intermediate, and low saccharin preferring groups of rats.

In summary, corresponding with previous findings (2,8) the present results provide additional evidence indicating that there is a relationship between saccharin consumption and ethanol consumption in Wistar rats. This relationship was revealed under food satiation conditions when ethanol intake is lower in contrast to food deprivation conditions when ethanol intake is maximized. There was no relationship between saccharin consumption and IV cocaine self-administration. It may be that rats show similar preferences for ethanol, saccha-

rin, and opiates because these substances have overlapping effects on a common (e.g., opioid) neurochemical system, although further research examining the mechanism of these findings is needed.

ACKNOWLEDGEMENTS

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