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# The Potency of D-1 and D-2 Receptor Antagonists Is Inversely Related to the Reward Value of Sham-Fed Corn Oil and Sucrose in Rats

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WEATHERFORD, S. C., D. GREENBERG, J. GIBBS AND G. P. SMITH. *The potency of D-1 and D-2 receptor antagonists is inversely related to the reward value of sham-fed corn oil and sucrose in rats.* PHARMACOL BIOCHEM BEHAV **37**(2) 317–323, 1990.—Intraperitoneal injection of 50 $\mu g \cdot kg^{-1}$ of the selective dopamine D-1 receptor antagonist, SCH 23390, significantly decreased sham feeding of 6% and 10% sucrose solutions, but not sham feeding of 100% corn oil. Intraperitoneal injection of raclopride, a D-2 antagonist, elicited a significant dose-dependent (200–400 $\mu g \cdot kg^{-1}$) decrease in sham intake of both sucrose concentrations and corn oil at doses that did not increase the latency to sham feed or produce overt motor impairment. The rank order of inhibitory potency for both SCH 23390 and raclopride was 6% sucrose > 10% sucrose > 100% corn oil. In a second experiment, we found that in 2-bottle preference tests, the rank order of preference for these three liquids was 100% corn oil > 10% sucrose > 6% sucrose. Assuming that preference measured the relative reward value of the liquids, the potencies of the two antagonists were inversely related to the reward value of the liquid that was sham fed. This result supports but does not prove the dopamine hypothesis of the positive reinforcing effect of orosensory stimulation by nutrients. In addition, the differential selectivity of the two antagonists for different classes of nutrients suggests that normal sensory and/or hedonic processing of sham-fed sucrose depends on stimulation of both D-1 and D-2 receptors, but the normal sensory and/or hedonic processing of sham-fed corn oil depends primarily, perhaps exclusively, on stimulation of D-2 receptors.

Dopamine D-1 receptors D-2 receptors Sham feeding Reward Feeding Fats Positive reinforcement Taste Hedonics

LIKE sucrose, fatty foods are highly preferred by rats (2,5). This preference appears to be due to the orosensory properties of fats and to their postingestive effects (5, 9, 10). The notion that the orosensory properties of fats are positively reinforcing is supported by the finding that rats sham feed corn oil even though they have never had prior experience with its postingestive metabolic effects and they sham feed mineral oil (9) which does not have metabolic effects. Since sham feeding permits the orosensory effects of nutrients to act on eating, but minimizes (14) or excludes (8) the postingestive effects, the sham feeding of corn oil and mineral oil is strong evidence that the orosensory effects of corn oil and mineral oil are positively reinforcing for the oromotor acts of licking and ingestion.

Previous work from this and other laboratories demonstrated that the ingestion of sucrose (16) but not saccharin (1), increases the metabolism and, presumably, the release of dopamine (DA) in the forebrain and that central dopaminergic synaptic activity at D-1 and D-2 receptors is necessary for the normal positive reinforcing effect of sucrose and other sweet solutions (11–13).

We have recently implicated dopamine mechanisms in the positive-reinforcing effect of sham-fed corn oil (19) by showing that the selective D-1 antagonist, SCH 23390 (6), and the selective D-2 antagonist, (−)-raclopride (7), significantly decreased 30-min sham intake of 100% corn oil in a dose-related manner. When the potency of the antagonists for decreasing corn oil intake was compared to the potencies of the same antagonists for decreasing sucrose in other experiments (13), we noted that SCH 23390 decreased corn oil less than 10% sucrose, but that raclopride appeared to be equipotent. The difference in the potency of SCH 23390 for 100% corn oil and 10% sucrose could have been

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due to two possibilities: First, different durations of food deprivation were used in the two experiments. Second, rats sham fed a greater volume of 10% sucrose than 100% corn oil such that the differential potency may have been due to volume-related factors rather to the specific nutrient. In the present experiment we measured the relative potency of both antagonists for 100% corn oil, 10% sucrose and 6% sucrose under identical experimental conditions. Hence, rats sham fed approximately equal volumes of 100% corn oil and 6% sucrose (4,19) in a 30-minute sham-feeding test, the third group, then (6% sucrose), was added to control for volume-related factors.

In addition to evaluating the role of deprivation and volume-related factors in the apparent difference in the potency of SCH 23390, these experiments also tested a prediction of the dopamine hypothesis of the positive reinforcing effect of orosensory stimulation by nutrients (17,21). The prediction is that the potency of the DA antagonists will be inversely related to the hedonic potency of the orosensory stimuli of the nutrients. This prediction is based on the assumption that the positive reinforcing effect (reward) of a range of concentrations of orosensory stimuli on the movements of licking and ingestion is dependent upon the concentration of DA at relevant receptor sites. We tested this prediction in the second experiment by determining the relative preference of the three liquids in 2-bottle, 30-min preference tests on the assumption that relative intake in a 2-bottle, sham-feeding test is a measure of the relative positive reinforcing effect (hedonic potency) of the orosensory stimuli of the two liquids tested (23).

## EXPERIMENT 1

This experiment compared the effects of the selective D-1 antagonist, SCH 23390 and the selective D-2 antagonist, (−)-raclopride, in rats sham feeding 100% corn oil, 10% and 6% sucrose under identical experimental conditions.

### METHOD

#### *Animals and Environment*

Twenty-five male Sprague-Dawley rats (Taconic Farms, Germantown, NY) weighing 210–278 g were used in this experiment. Rats were housed and tested in individual hanging plastic cages in a temperature-controlled environment (21 ± 1°C) with a 12:12 light/dark cycle (lights on 0800). Rats were maintained on Purina rat chow and tap water.

#### *Surgical Procedure*

All rats were implanted with chronic stainless steel gastric cannulas according to previously described methods (24). Briefly, after overnight food deprivation, rats were anesthetized with chloropent anesthesia (pentobarbital sodium, chloral hydrate and magnesium sulfate; 3 $ml \cdot kg^{-1}$, IP) and a midline incision was made to expose the abdominal viscera. The stomach was isolated and the cannula (11 mm long, with a 15 mm diameter flanged end) was inserted through a small incision (1 mm) in the nonglandular portion of the stomach. A purse string suture was made through the gastric wall around the shaft of the cannula, thus preventing leakage of gastric contents into the peritoneum. To promote adhesion of the gastric wall and peritoneum, a small piece of Marlex Mesh (Bard Implants Division, Billerica, MA) was stretched down over the shaft of the cannula so that it lay flush against the gastric wall. The cannula was then externalized through a stab wound in the left abdominal wall. A removable screw cap closed the cannula to prevent drainage of gastric contents while rats were not being tested.

#### *Testing Procedure*

Rats were allowed 2 weeks to recover from surgery, they were then trained to sham feed one of three liquids: 100% corn oil (n = 8), 6% sucrose (n = 8) or 10% sucrose (n = 9). All rats were placed on a 17-hr, overnight, food-deprivation schedule. At 0900 the screw cap occluding the cannula was removed and the stomach was gently lavaged with tap water until the gastric drainage was free of food particles. To facilitate drainage and collection of gastric contents, a silastic drainage tube surrounded by a flexible metal spring was threaded into the shaft of the cannula. Rats were returned to their cages and the drainage tube was passed through a longitudinal gap in the wire-mesh floor, thus allowing the rat free movement throughout the experimental period. An IP injection of 0.9% saline (2 $ml \cdot kg^{-1}$) was given, and a plastic tray was placed below the rats' cages to collect gastric drainage. Fifteen min later, rats were offered 100% corn oil (Mazola, Englewood Cliffs, NJ; blended with Tween-80; Sigma Chemical Co., St. Louis, MO; 0.75 ml Tween-80 per 100 ml corn oil) in a calibrated drinking tube (Wahman), 6% sucrose (Sigma Chemical Co., St. Louis, MO; w/v in distilled water) or 10% sucrose (w/v in distilled water). The corn oil and sucrose solutions were mixed the afternoon preceding the test and were presented at room temperature. Latency to initiate sham feeding was noted and sham intakes at 6-min intervals were recorded for a 30-min period. Following the 30-min test the drainage tube was removed and the screw cap was replaced. Pellets were returned immediately after the test and were available until the next deprivation period began. Tap water was available at all times except during the test.

After baseline intakes (intake after a saline injection) were established, drug testing was initiated. All rats received 4 doses of raclopride (Astra Lakemeda, Sodertalje, Sweden; 100, 200, 300, 400 $\mu g \cdot kg^{-1}$, in a volume of 2 $ml \cdot kg^{-1}$) in ascending order. A vehicle (0.9% saline) test always preceded and followed a raclopride test. After each rat received each dose of raclopride once, they were tested with 4 doses of SCH 23390 (Schering Corporation, Bloomfield, NJ; 12.5, 25, 50, 100, $\mu g \cdot kg^{-1}$ in a volume of 2 $ml \cdot kg^{-1}$) using the same protocol, with one exception: the vehicle was 1% acetic acid.

#### *Statistical Analyses*

Before data could be included in analysis, two criteria had to be met to insure complete collection of the sham-fed solutions (8): first, gastric contents had to begin draining from the tube by 15 seconds after the initiation of sham feeding; second, the gastric contents collected during the test session had to equal or exceed the volume consumed. Data from all rats met these criteria at all doses tested and each group was analyzed separately. Differences in drug-dose effects on 30-min intakes were analyzed with one-way, repeated measures analysis of variance (ANOVA) with dose of drug the repeated factor. Differences in intakes following vehicle were not found, therefore the pooled vehicle condition was used as a zero level dose. Significant differences in main effects were analyzed with post hoc Student-Newman-Keuls' tests. For each drug dose that was found to significantly inhibit 30-min intake, we analyzed the latency to the first 6-min interval during which a significant inhibition of sham feeding appeared. These data were then analyzed with a one-way repeated measures ANOVA (time in 6-min intervals being the repeated measure). Post hoc comparisons using Student-Newman-Keuls' tests were used to determine the earliest time point at which sham-fed intakes were significantly decreased relative to vehicle injection. Comparisons between nutrient groups were made using a two-way, repeated measures ANOVA (dose × group), with dose of drug the repeated factor. For this comparison, the percent inhibition from 30-min intakes (relative to vehicle) for each significant dose of antagonist were used. Significant differences between groups were

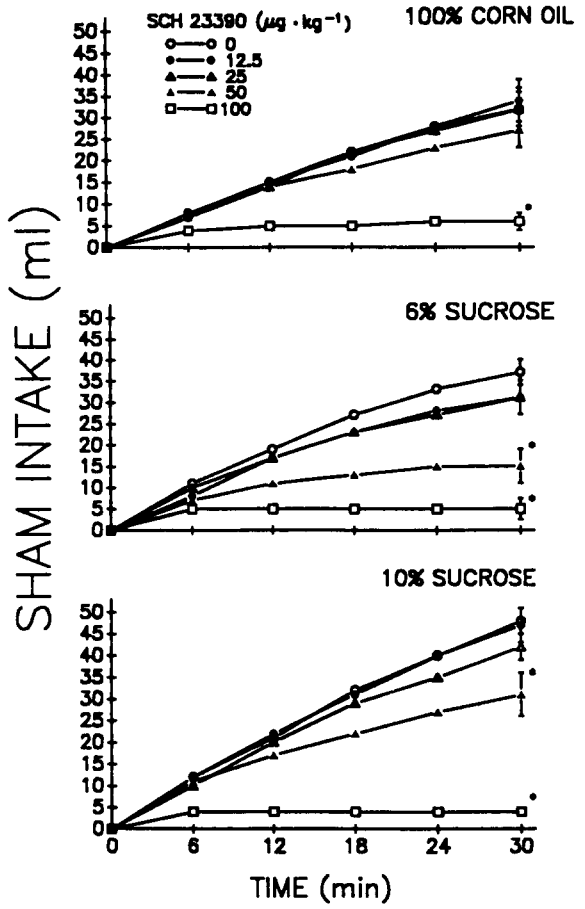


FIG. 1. Mean cumulative sham intake (ml) of 100% corn oil (top panel, n = 8), 6% sucrose (middle panel, n = 8) or 10% sucrose (bottom panel, n = 8) after injection (IP) of 1% acetic acid vehicle or one of four doses of SCH 23390. *$p<0.05$ SCH 23390 vs. vehicle by Student-Newman-Keul's test after a significant one-way ANOVA. For visual clarity, SE's are only shown at the 30-min intake.

determined with Student-Newman-Keuls' post hoc tests.

## RESULTS

SCH 23390 decreased sham feeding of 6% sucrose, $F(4,7) = 16.89$, $p<0.001$, and 10% sucrose, $F(4,7) = 18.68$, $p<0.001$, in a dose-related manner, but only the highest dose (100 $\mu g \cdot kg^{-1}$) decreased the sham intake of 100% corn oil, $F(4,7) = 15.85$, $p<0.001$ (Fig. 1). The minimal effective dose required to inhibit 6% and 10% sucrose-sham feeding was 50 $\mu g \cdot kg^{-1}$ ($p<0.05$) and for corn oil it was 100 $\mu g \cdot kg^{-1}$ ($p<0.05$). The rank order of potency for the inhibition of sham feeding for the 50 $\mu g \cdot kg^{-1}$ dose was: 6% sucrose > 10% sucrose > 100% corn oil ($p<0.05$, Fig. 2). The latency to the first significant inhibition by the 50 $\mu g \cdot kg^{-1}$ dose was 6 min for 6% sucrose and 12 min for 10% sucrose (Table 1). The latency to the first significant inhibition for the 100 $\mu g \cdot kg^{-1}$ dose was 6 min for all three groups (Table 1). The latency to initiate sham feeding was less than 1 min for all groups after all doses except after the 100 $\mu g \cdot kg^{-1}$ dose which produced a latency of $4 \pm 4$ min for all groups (Table 1).

In contrast to SCH 23390, raclopride not only produced a dose-related decrease in sham-fed 6% sucrose, $F(4,7) = 20.96$, $p<0.001$, and 10% sucrose, $F(4,8) = 34.66$, $p<0.001$, but raclopride also decreased 100% corn oil in a dose-related manner, $F(4,7) = 11.79$, $p<0.001$ (Fig. 3). The minimal effective dose for a significant inhibition was 200 $\mu g \cdot kg^{-1}$ for all groups ($p<0.05$, Figs. 3 and 4). The order of potency on sham feeding for the 200 and 300 $\mu g \cdot kg^{-1}$ doses was: 6% sucrose > 10% sucrose > 100% corn oil ($p<0.05$, Fig. 4). The latency to the first significant inhibition was 6 min for all groups and doses ($p<0.05$, Table 1). The latency to initiate sham feeding was <1 min for all doses in the three groups (Table 1).

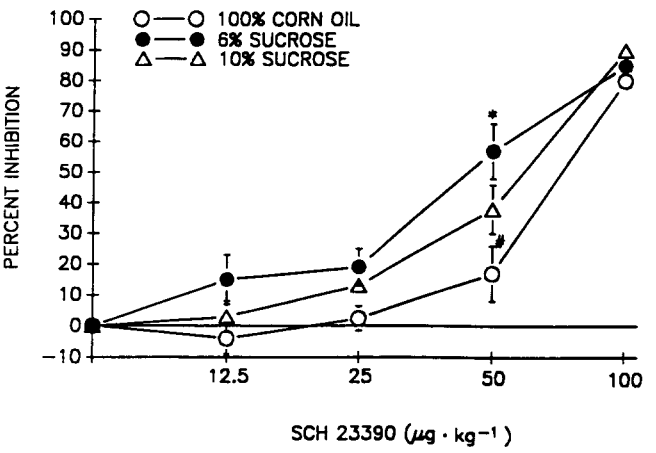


FIG. 2. Percent inhibition of 30-min sham intake after intraperitoneal injections of 4 doses of SCH 23390 in rats sham feeding 100% corn oil (open circles, n = 8), 6% sucrose (filled circles, n = 8) or 10% sucrose (open triangles, n = 8). *Indicates that the inhibitory effect of SCH 23390 was significantly ($p<0.05$) larger in rats sham feeding 6% sucrose than rats sham feeding 10% sucrose or corn oil. #Indicates that the inhibition produced by SCH 23390 in rats sham feeding corn oil was significantly smaller than in rats sham feeding 6% or 10% sucrose. For clarity, SE's were omitted for the 100 $\mu g \cdot kg^{-1}$ dose: SEM values were less than 3% for all groups. Percent inhibition was calculated from the following formula: intake after vehicle − intake after drug/intake after vehicle × 100.

## DISCUSSION

The D-1 antagonist SCH 23390 decreased sham feeding of both 6% and 10% sucrose in a dose-related manner. This is consistent with previous reports (11–13). The decrease in sucrose sham feeding appears to be a direct reduction in the sensory and/or hedonic effects of the sucrose because the effects were observed after doses of SCH 23390 that did not increase the latency to initiate sham feeding (Table 1) or produce overt motor incapacity (3). This same dose of SCH 23390, however, did not decrease the intake of corn oil during sham feeding. Since the motor movements for sham feeding sucrose and corn oil are similar, this provides further evidence that SCH 23390 reduced the sensory and/or hedonic qualities of sucrose and did not decrease intake by producing incapacitating sedation or motor side effects.

In contrast to sucrose, only the highest dose (100 $\mu g \cdot kg^{-1}$) of SCH 23390 decreased the sham-fed intake of 100% corn oil. This dose, however, also increased the latency for all groups to initiate sham feeding (Table 1) and produced apparent motor impairment in that rats maintained a stationary and rigid posture throughout most of the experimental period. Thus, it is not possible to attribute the effect of this dose to a specific reduction of the hedonic effect of the orosensory stimuli of corn oil. Since the experimental conditions were identical for all three solutions, these results strongly suggest that unlike sweet taste, activity at the

TABLE 1

EFFECTS OF SCH 23390 AND RACLOPRIDE ON LATENCIES TO SHAM FEED AND TO INHIBITION OF SHAM FEEDING

| | SCH 23390 | | | | | | Raclopride | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Latencies (min) to: | | | | | | Latencies (min) to: | | | | | | |
| | Sham Feed | | | Inhibition | | | Sham Feed | | | Inhibition | | | |
| Dose | Oil | Suc (6%) | Suc (10%) | Oil | Suc (6%) | Suc (10%) | Dose | Oil | Suc (6%) | Suc (10%) | Oil | Suc (6%) | Suc (10%) |
| 0.0 | <1 | <1 | <1 | — | — | — | 0 | <1 | <1 | <1 | — | — | — |
| 12.5 | <1 | <1 | <1 | — | — | — | 100 | <1 | <1 | <1 | — | — | — |
| 25.0 | <1 | <1 | <1 | — | — | — | 200 | <1 | <1 | <1 | 6* | 6* | 6* |
| 50.0 | <1 | <1 | <1 | — | 6* | 12* | 300 | <1 | <1 | <1 | 6* | 6* | 6* |
| 100.0 | 4 ± 4 | 4 ± 4 | 4 ± 4 | 6* | 6* | 6* | 400 | <1 | <1 | <1 | 6* | 6* | 6* |

Data are mean (± SEM) latencies to sham fed, and to inhibition of sham feeding. Doses are $\mu g \cdot kg^{-1}$.

*$p<0.05$ compared to vehicle by Student-Newman-Keul's test after a significant effect of a one-way ANOVA.

After SCH 23390, n = 8 for all groups after all doses. After raclopride, n = 8 for corn oil and 6% sucrose (all doses), n = 9 for 10% sucrose.

level of the D-1 receptor is not necessary or is certainly much less involved in the processing of the sensory and/or reward effects of sham-fed corn oil than of 6% or 10% sucrose.

In contrast to the differential effect of SCH 23390 on sucrose and corn oil, the D-2 antagonist, raclopride, produced a dose-related decrease in 6% sucrose, 10% sucrose, and 100% corn oil. The minimal effective dose (200 $\mu g \cdot kg^{-1}$) was the same for all three liquids, raclopride did not increase the latency to initiate sham feeding after any dose (Table 1), and rats did not appear sedated or incapacitated.

Although raclopride inhibited the sham intake of all three liquids, the inhibitory potency of raclopride differed depending on the solution that was sham fed. The rank order of inhibitory potency was 6% sucrose > 10% sucrose > 100% corn oil. This differential potency suggests that motor deficits alone cannot account for the decreased intake. The results with raclopride suggest that activity at D-2 receptors is necessary for the normal processing of the sensory and/or hedonic effects of the oral stimuli produced by corn oil and sucrose during sham feeding.

In this experiment the rank order of inhibitory potency of both antagonists was 6% sucrose > 10% sucrose > 100% corn oil. Based on the hypothesis that DA mediates the rewarding effect of the orosensory stimuli of nutrients (17), one would predict that DA release would be directly proportional to the relative reward value of orosensory stimuli of the nutrients. Thus, the potency of a competitive DA antagonist would be inversely proportional to the relative rewarding effect of the orosensory stimuli of nutrients. Since the hedonic potency of 10% sucrose is larger than 6% sucrose (23), the results in this experiment are consistent with that hypothesis. It is unclear, however, whether the potency of the antagonists is also inversely related to the reward value of corn oil since its hedonic potency relative to the two sucrose solutions under these conditions is not known.

## EXPERIMENT 2

The purpose of this experiment was to establish the relative hedonic potency of sham-fed corn oil by determining relative preferences of 100% corn oil, 10% sucrose and 6% sucrose in 2-bottle, 30-min, sham-feeding preference tests.

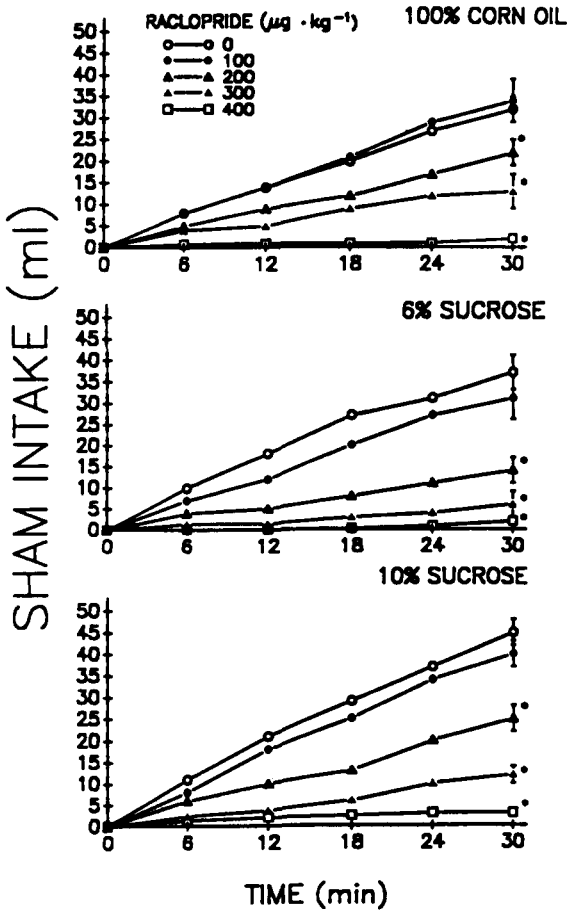


FIG. 3. Mean cumulative sham intake (ml) of 100% corn oil (top panel, n = 8), 6% sucrose (middle panel, n = 8) or 10% sucrose (bottom panel, n = 9) after injection (IP) of 0.9% saline or one of four doses of (−)-raclopride. *$p<0.05$ raclopride vs. 0.9% saline by Student-Newman-Keul's test after a significant one-way ANOVA.

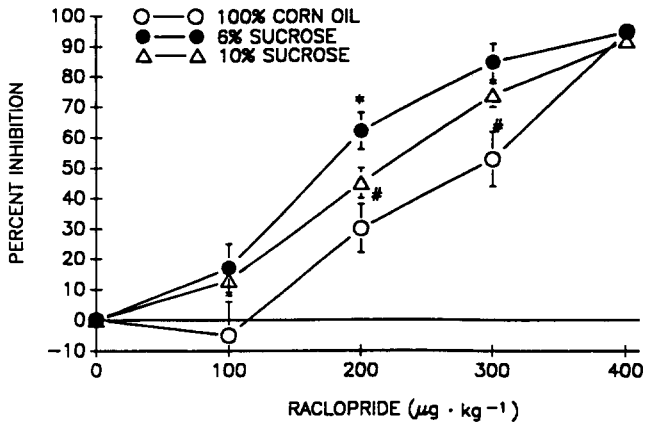


FIG. 4. Inhibition of 30-min sham intake after intraperitoneal injections of 4 doses of raclopride in rats sham feeding 100% corn oil (open circles, n=8), 6% sucrose (filled circles, n=8) or 10% sucrose (open triangles, n=8). *Indicates that the inhibitory effect of raclopride was significantly ($p<0.05$) larger in rats sham feeding 6% sucrose than rats sham feeding 10% sucrose or 100% corn oil. #Indicates that the inhibitory effect of raclopride was significantly ($p<0.05$) smaller in rats sham feeding 100% corn oil than in rats sham feeding 6% or 10% sucrose. For visual clarity the SEM's for the 400 $\mu g \cdot kg^{-1}$ were omitted: values were less than 4% for all groups. Percent inhibition was calculated from the following formula: intake after vehicle − intake after drug/intake after vehicle × 100.

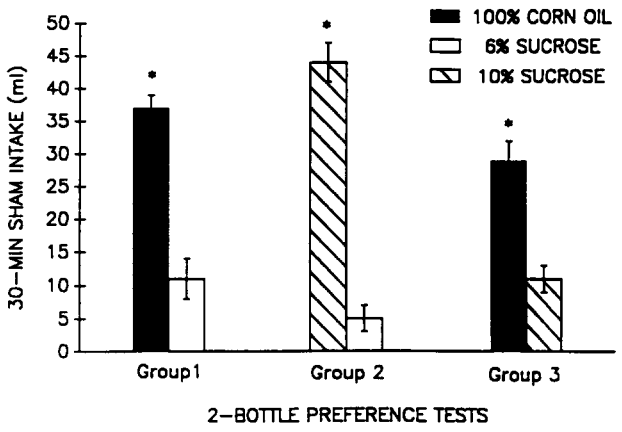


FIG. 5. Results from 2-bottle sham-feeding preference tests. Data are the average for the two preference tests, mean ± SEM sham intake (ml) for the 30-min test are shown. *$p<0.05$ after matched pairs Student's $t$-test.

## METHOD

### *Animals and Environment*

A new group of 24 male Sprague-Dawley rats (Taconic Farms, Germantown, NY) weighing 220–305 g were used in this experiment. Rats were housed, tested and maintained as described in Experiment 1. All rats were implanted with chronic gastric cannulas according to the method described above, with the exception that the anesthesia was methoxyflurane (Metofane, Pitman Moore).

### *Testing Procedure*

After a two-week postsurgical recovery period, rats were placed on a 17-hr, overnight food-deprivation schedule and trained to sham feed their respective solutions using the protocol described in Experiment 1.

Rats were randomly divided into three groups and trained to sham feed one of two solutions on alternate days. Group 1 (n=8) was trained to sham feed 100% corn oil (blended with Tween-80; 0.75 ml per 100 ml corn oil) and 6% sucrose (in distilled water, w/v), group 2 (n=9) was trained to sham feed 10% (in distilled water, w/v) and 6% sucrose, and group 3 (n=7) was trained to sham feed 100% corn oil and 10% sucrose. All solutions were prepared the afternoon preceding the test and were presented at room temperature.

During the 1-bottle training tests, rats were forced to sham feed equal volumes of each solution. This was accomplished in groups 1 and 3 by allowing each rat to consume only as much 6% sucrose and 10% sucrose, respectively, on day 2 as the 30-min intake of 100% corn oil on day 1. For example, if a rat in group 1 sham fed 5 ml of 100% corn oil on day 1, its drinking tube was removed on day two after it consumed 5 ml of 6% sucrose. In group 2, the 6% and 10% sucrose intakes were yoked to the mean volume of 6% sucrose ingested by group 1 (see Table 2).

Test solutions for all groups were offered on alternate sides of the front of the cage. For example, rats in group 1 were offered 100% corn oil and 6% sucrose on the left on days 1 and 2, respectively, and on days 3 and 4 the solutions were offered on the right side of the cage and so on. At the conclusion of each test session, the drainage tube was removed from the rat and the screw cap was replaced. Chow and water were returned immediately following the test.

Rats were trained to sham feed the solutions in 1-bottle tests until 100% corn oil intake stabilized. Thirty-min intakes of 100% corn oil stabilized at 31 ± 2 and 30 ± 2 ml which required a total of 16 training tests (i.e., 8 training tests per solution), for groups 1 and 3, respectively (see Table 2). At this time, two 2-bottle preference tests were conducted on successive days. Rats were simultaneously offered the two solutions that they had been trained with for 30 min of sham feeding. If the rat did not sample both solutions within 30 sec, it was forced to by removing the sampled solution until it sampled the other solution. The positions of the solutions were reversed on the second test day.

TABLE 2

ONE-BOTTLE TRAINING TESTS

| | Group 1 | | Group 2 | | Group 3 | |
|---|---|---|---|---|---|---|
| Test No. | Corn Oil | 6% Suc | 6% Suc | 10% Suc | Corn Oil | 10% Suc |
| 3,4 | 10 ± 3 | 8 ± 4 | 10 ± 2 | 11 ± 1 | 12 ± 2 | 10 ± 4 |
| 7,8 | 18 ± 1 | 14 ± 2 | 17 ± 1 | 20 ± 1 | 21 ± 1 | 18 ± 3 |
| 11,12 | 25 ± 0 | 19 ± 3 | 24 ± 1 | 25 ± 0 | 22 ± 1 | 20 ± 2 |
| 15,16 | 31 ± 2 | 27 ± 3 | 29 ± 2 | 31 ± 0 | 30 ± 2 | 29 ± 1 |

Data are mean ± SEM sham intake (ml) for representative 30-min 1-bottle training tests.

### *Statistical Analyses*

Criteria described in Experiment 1 for inclusion of sham feeding data in analysis were applied in this experiment also (8). Data for the two preference test days did not differ and were averaged. Mean 30-min sham intakes of the two solutions for each group were compared using a matched pairs $t$-test. The significance of the number of rats that ingested more of one solution over

the other was analyzed by the binomial test.

### RESULTS

The rank order of preference was 100% corn oil > 10% sucrose > 6% sucrose. Group 1 preferred 100% corn oil over 6% sucrose ($p<0.001$, Fig. 5), 8 out of 8 rats consumed more corn oil than sucrose ($p<0.007$). In group 2, 10% sucrose was preferred over 6% sucrose ($p<0.001$, Fig. 5), 9 out of 9 rats sham fed more 10% sucrose than 6% sucrose ($p<0.004$). The rats in group 3 preferred 100% corn oil over 10% sucrose ($p<0.01$, Fig. 5), 7 out of 7 rats sham fed more corn oil than 10% sucrose in 30 min ($p<0.01$).

### DISCUSSION

When sham feeding, rats prefer 100% corn oil over 10% and 6% sucrose and they prefer 10% sucrose over 6% sucrose. Because we used a yoked-intake design during the 1-bottle training sessions, the preferences observed in the 2-bottle, sham-feeding tests are not due to differing amounts of orosensory stimulation prior to the preference tests. Thus, under our experimental conditions, the relative hedonic potency of the three liquids was 100% corn oil > 10% sucrose > 6% sucrose. Since this rank order is the inverse of the rank order of inhibitory potency of the competitive DA antagonists in Experiment 1, the result is consistent with the hypothesis that central DA release is a direct function of the relative rewarding potency of the orosensory stimuli of nutrients.

## GENERAL DISCUSSION

The major result of these experiments is that the inhibitory potency of SCH 23390 and raclopride is inversely related to the hedonic potency of the orosensory stimulation produced by 6% sucrose, 10% sucrose and 100% corn oil during sham feeding. This fulfills one of the predictions of the hypothesis that DA mediates the positive reinforcing effects of the orosensory stimulation produced by sugar (4, 11–13, 15, 22) and corn oil (19): a larger positive reinforcing effect of the orosensory stimuli of a sugar or corn oil as measured by preference in 2-bottle tests, should be more difficult to antagonize because more DA would be released at central synapses.

Although this inverse correlation is consistent with the hypothesis, it cannot be considered strong evidence for the following reasons: 1) The correlation has been obtained with only three different liquids. A larger range of concentrations of both nutrients needs to be tested. 2) Relative hedonic potency has been estimated by only one measure, the 2-bottle preference test. Additional measures would be useful. 3) We have asserted that the motor requirements for sham feeding sucrose and corn oil are sufficiently similar to be ignored in the interpretation of the results; this may not be true. 4) In recent preliminary experiments there was no evidence that sham feeding these three liquids released different quantities of DA at central synapses as measured by regional DA metabolism (20). Results with more sensitive techniques, such as microdialysis, have not been reported.

Although the inverse correlation between hedonic potency of the orosensory stimulus and DA antagonist potency is of limited value for proving the DA hypothesis of orosensory reward, it may be quite useful in interpretation of the differential effects of D-1 and D-2 antagonists (18). For example, Experiment 1 showed that no dose of SCH 23390 that did not produce obvious motor impairment, decreased the sham intake of 100% corn oil, but at least two doses of raclopride did. This result could be interpreted that D-1 receptors are not involved in the processing of the orosensory stimuli of corn oil during sham feeding, but D-2 receptors are. Such a dissociation would be of considerable interest for the problem of the functional relationship of D-1 and D-2 receptors for food reward (18). But given the results of the preference test in Experiment 2 in which 100% corn oil was markedly preferred to 10% sucrose and 6% sucrose, the results may be more conservatively interpreted as due to quantitative differences in hedonic potency rather than to a categorical difference in types of DA receptors. Further experiments are required to distinguish between these two possibilities.

In summary, these experiments demonstrate that the rank order of potency of SCH 23390 and raclopride for inhibiting the sham-fed intake of 100% corn oil, 10% sucrose and 6% sucrose is inversely correlated with the hedonic potency of these liquids as measured by 2-bottle preference tests. This result is consistent with the hypothesis that central DA mediates the positive reinforcing effect of orosensory stimuli of sucrose and corn oil during sham feeding. The results also demonstrate that in interpreting the effect of DA antagonists on the positive reinforcing effect of orosensory stimuli of nutrients on ingestion, the relative hedonic potency of the nutrient stimuli must be controlled.

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