Pharmacology Biochemistry and Behavior, Vol. 59, No. 2, pp. 451–457, 1998
© 1998 Elsevier Science Inc.
Printed in the USA. All rights reserved
0091-3057/98 $19.00 + .00

ELSEVIER

PII S0091-3057(97)00439-5

Devazepide, a CCK_A Antagonist, Attenuates the Satiating but Not the Preference Conditioning Effects of Intestinal Carbohydrate Infusions in Rats

CATALINA PÉREZ, FRANÇOIS LUCAS AND ANTHONY SCLAFANI

Department of Psychology, Brooklyn College and the Graduate School, The City University of New York, Brooklyn, NY 11210

Received 31 January 1997; Revised 30 May 1997; Accepted 19 June 1997

PÉREZ, C., F. LUCAS AND A. SCLAFANI. *Devazepide, a CCK_A antagonist, attenuates the satiating but not the preference conditioning effects of intestinal carbohydrate infusions in rats.* PHARMACOL BIOCHEM BEHAV **59**(2) 451–457, 1998.—Endogenous cholecystokinin (CCK) is thought to participate in the satiating action of foods, and some data suggest that it may also mediate their postingestive reinforcing effects. This was investigated by determining if the CCK_A receptor antagonist, devazepide, attenuates flavor preference conditioning by intraduodenal (ID) carbohydrate infusions. In Experiment 1, food-restricted female rats were trained 30 min/day to associate a cue flavor (CS+) with ID infusions of 8% Polycose and a different flavor (CS−) with ID water infusions. Half of the rats (DEV group) were pretreated with devazepide (300 μg/kg body weight) and the other half (CON group) with vehicle, 30 min prior to CS training sessions and choice tests. Both groups displayed similar CS+ preferences (CON: 68%; DEV: 69%). In contrast, devazepide blocked the feeding inhibitory effects of ID Polycose infusion and cholecystokinin octapeptide injection in Experiment 2. A higher dose of devazepide (1200 μg/kg) also failed to inhibit preference conditioning by ID Polycose in Experiment 3. These results indicate that, although CCK_A mechanisms play a role in the satiating effect of ID carbohydrates, they do not mediate their reinforcing effect. The present study, along with other recent reports, indicate that different mechanisms mediate the satiating and reinforcing actions of nutrients. © 1998 Elsevier Science Inc.

Flavor Preference Conditioning Intraduodenal infusions Polycose CCK Satiation

THERE is extensive evidence implicating the gut hormone cholecystokinin (CCK) in the postingestive satiating action of food (20). This was first suggested by the findings that administration of exogenous CCK suppresses food intake in rats and a variety of other species. Compelling evidence for a physiological role of endogenous CCK in satiety comes from reports that injections of CCK_A receptor blockers increase food intake (15,21). Furthermore, CCK_A receptor antagonists block the feeding-inhibitory effects of intraduodenal (ID) nutrient infusions (26,27).

In addition to its involvement in postingestive satiety, CCK may mediate the reinforcing actions of nutrients in the gut. It is now well documented that rats learn to prefer flavors paired with intragastric (IG) or ID nutrient infusions (4,7,18). Little is known about the physiological signals generated by nutrients that mediate these conditioned preferences. Mehiel and Bolles (10,11) hypothesized that CCK released by nutrients in the gut was the feedback signal that reinforced flavor preferences. In support of this view, Mehiel (9) summarized data showing that preferences could be conditioned by pairing a flavor with injections of cholecystokinin octapeptide (CCK-8). In a more extensive report, Pérez and Sclafani (14) obtained conditioned preferences by pairing flavors with a low dose of CCK-8 (0.5 μg/kg) but not with higher doses. Conditioned odor preferences have also been produced in neonatal and weanling rats by associating a novel odor with low doses of

Requests for reprints should be addressed to Dr. Catalina Pérez, Department of Psychology, Brooklyn College of CUNY, 2900 Bedford Ave., Brooklyn, NY 11210-2889.

CCK-8 (0.25 or 0.5 μg/kg) (25). CCK-8 failed to condition odor preferences, however, in slightly older rats (28 days) (25). These findings demonstrate that exogenous CCK can, at least under some conditions, reinforce flavor or odor preferences but do not establish a role for endogenous CCK in postingestive preference learning. We addressed this issue in the present study by determining if pharmacological blockade of CCK_A receptors attenuates carbohydrate-conditioned flavor preferences in rats.

EXPERIMENT 1

Intestinal carbohydrate (maltose) infusions have been reported to suppress sham-feeding in rats and this suppression is reversed by treatment with the CCK_A receptor antagonist devazepide (27). ID carbohydrate infusions also condition flavor preferences; that is, rats learn to prefer a flavored solution paired with ID glucose or Polycose over a differently flavored solution paired with ID water infusions (4,7). In Experiment 1 we investigated whether devazepide would attenuate the flavor-conditioning effect of ID Polycose infusions.

METHOD

Subjects

Twenty-three adult female rats (CD stock, Charles River Laboratories, Wilmington, MA) with a mean weight of 266 g (range: 231–321 g) were used. Data from three rats were excluded because of problems with their ID catheters. The rats were individually housed in standard wire-mesh cages in a vivarium maintained at 21°C under a 12 L:12 D cycle (lights on 0800 h). The rats were given food rations (Purina Chow, No 5001) to maintain them at 90% of their ad lib body weight. Water was available ad lib 20 h/day. The food rations and water were given about 2 h after the daily sessions.

Surgery

The rats were surgically implanted with ID catheters according to a technique adapted from Davis and Campbell (3). Briefly, a silastic tube (0.025 i.d., 0.047 o.d.) was inserted 2–3 cm into the duodenum after entering the stomach. The tube was routed under the skin to the back of the neck and was connected to a Luer-Lok assembly fixed to the skull with dental cement and stainless steel screws.

Apparatus

The rats were trained and tested in plastic cages (23 × 24 × 31.5 cm high) with a slotted plastic top and stainless steel grid floor. Above the cage, Tygon tubing from a variable-speed syringe pump was connected to the input port of a swivel on a counterbalanced lever. Tygon tubing, protected by a stainless steel spring connected the swivel's output port to the rat's Luer-Lok assembly. The front wall of the cage contained holes, centered 32 mm apart, through which the rat had access to stainless steel drinking spouts [see (24)]. The spouts were attached to drinking tubes mounted on motorized holders that positioned the spouts at the front of the cage at the start of the test session and then retracted them at the end of the session. Licking behavior was monitored by an electronic lickometer interfaced to a microcomputer. On training trials, the rat's licking responses activated a syringe pump set at an infusion rate of 0.54 ml/min. The oral intake and ID infusion volumes were maintained at 1:1 by computer software.

Solutions

The conditioned stimuli (CS) consisted of 0.2% saccharin solutions (Sigma Chemical Co., St. Louis, MO) flavored with 0.05% grape or cherry unsweetened Kool-Aid (General Foods, White Plains, NY) prepared using tap water. The nutrient infusion contained 8% (w/v) Polycose (Ross Laboratories, Columbus, OH), which is a form of hydrolyzed corn starch. For half of the rats cherry-saccharin was the CS+ paired with ID Polycose infusions, and grape-saccharin was the CS− paired with ID water infusions; the flavor-infusion pairs were reversed for the remaining subjects.

Injections

Devazepide was injected intraperitoneally (IP) at a dose of 300 μg/kg. The drug was prepared at a concentration of 300 μg/ml by dissolving 3 mg into a mixture of 0.2 ml of dimethyl sulfoxide (DMSO) and 9.8 ml saline (0.15 M NaCl). The vehicle control contained DMSO and saline only. Rats were injected with devazepide or its vehicle (1 ml/kg) 30 min prior to the daily training and test sessions.

Procedure

After a postsurgery recovery period (6–12 days) the rats were familiarized with unflavored 0.2% saccharin by giving them unlimited access to the solution for 2 days. The next day the rats started on the feeding restriction schedule. During an 8-day pretraining phase the rats were accustomed to drink the saccharin solution in the test cages (30 min/day) and were progressively habituated to the experimental routine. For the first three sessions the rats were not connected to the infusion system; on sessions 4 and 5 they were connected to the infusion system but did not receive infusions; on sessions 6–8 they were infused with water as they drank saccharin. They were also injected with saline 30 min prior to sessions 7 and 8. The rats were then divided into two groups matched for saccharin intake and body weight: devazepide group (DEV, $n = 11$) and control group (CON, $n = 9$).

After the adaptation period, the rats were trained to associate the CS+ solution with ID infusions of 8% Polycose and the CS− solution with ID water infusions during alternate one-bottle sessions. The left–right position of the CS solutions varied following an ABBA sequence over the eight training sessions. Oral intakes and ID infusions were each limited to a maximum of 7 ml during the 30-min training sessions to reduce potential intake differences between the two groups; the DEV group would have been expected to consume more than the CON group. In sessions 9 and 10 the rats were given choice tests with unlimited access to the CS+ and CS− solutions but without ID infusions. The left–right position of the CS solutions was reversed between days. Thirty minutes prior to the training and test sessions, the rats were injected IP with devazepide (DEV group) or vehicle (CON group). In this and subsequent experiments the rats were trained and tested 6 days/week during the midportion of the day.

Statistical Analyses

Intakes were averaged over the four (CS+ and CS−) training and two test sessions. The training data of the two groups were compared using a nonparametric test (Mann–Whitney) since a maximum limit was imposed on the CS intakes. The two-bottle data were analyzed using repeated measures analysis of variance (ANOVA) followed by tests of simple main effects and post hoc comparisons (Newman–Keuls)

when appropriate. They were also expressed as percent CS+ intake ((CS+ intake/total intake) × 100).

RESULTS

In the training sessions most rats consumed less than the 7 ml of CS+ and CS− available to them. The DEV group drank somewhat more than the CON group of the CS+ (6.3 vs. 5.4 ml/30 min) and the CS− (6.6 vs. 5.3 ml/30 min), although the difference was significant only for the CS− ($U = 21$, $p < 0.05$).

Figure 1 shows the CS+ and CS− intakes during the two-bottle test. Both groups consumed reliably more CS+ than CS−, $F(1, 18) = 20.5$, $p < 0.001$, and did not differ in their intakes; the percent CS+ intakes of the CON and DEV groups were 68 and 69%, respectively.

EXPERIMENT 2

In Experiment 1, devazepide failed to block flavor conditioning by intestinal Polycose infusions. This suggests that carbohydrate-conditioned flavor preferences are not mediated by endogenous CCK acting at peripheral CCK_A receptors. Alternatively, it is possible that with repeated administration the devazepide injection lost its efficacy through behavioral and/or pharmacological tolerance. To test whether the DEV rats still responded to devazepide, and to demonstrate the drug's effectiveness in the control rats, two types of tests were conducted. We examined the ability of devazepide to block the feeding suppression produced by exogenous CCK-8 and the feeding suppression produced by intestinal Polycose.

In the CCK-8 test the rats drank the CS+ as they were infused ID with 8% Polycose, based on the finding that CCK-8 is more effective in suppressing CS+ intake than CS− intake (5). In the nutrient satiation test the rats were given a highly palatable mixture of 2% Polycose and 0.2% saccharin to drink. This solution promotes greater intake than the CS training solutions and thus is more effective in evaluating the satiating effects of the nutrient co-infusions. Note that, unlike in Experiment 1, the DEV and CON rats were given identical drug treatments in this experiment.

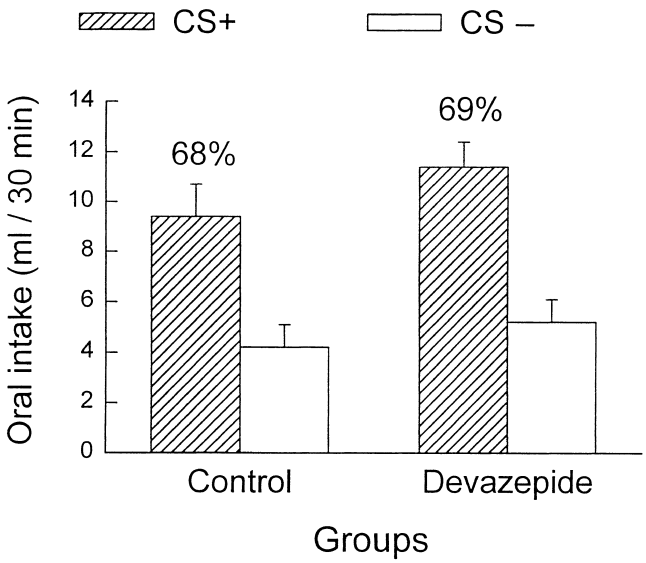

FIG. 1. Mean (+SE) intakes of the CS+ and CS− solutions during the 30-min two-bottle preference test of Experiment 1. The CS+ and CS− had previously been paired with ID infusions of Polycose (8%) and water, respectively. In training and testing, the Devazepide Group was pretreated with devazepide (300 μg/kg), and the control group with vehicle. Numbers atop bars represent mean percentage intakes of the CS+.

METHOD

Subjects

The DEV and CON rats of Experiment 1 were used. Data were lost from some animals due to technical problems as indicated below.

Drugs

Devazepide (300 μg/kg) was prepared as in Experiment 1. CCK-8 was prepared using isotonic saline at a concentration of 4 μg/ml. Rats were injected IP with 1 ml/kg. Devazepide or its vehicle was injected 30 min prior to, and CCK-8 or its vehicle (saline) was injected 2 min prior to, the test sessions.

Procedure

In daily 30-min sessions, which began the day after the last test session of Experiment 1, the rats were given access to the CS+ paired with ID infusions of 8% Polycose. The ID infusion (but not oral intake) was limited to 7 ml to avoid gross differences between the CON and DEV groups in the amounts of nutrient infused. On days 1, 3, and 5, all rats received vehicle injections at −30 and −2 min. On day 2, half the rats in each group were given devazepide and CCK-8 injections and the other half received vehicle and CCK-8. On day 4 the rats received the reverse treatment. On day 6 all the rats were treated with devazepide and vehicle injections. Data were collected from 9 CON rats and 10 DEV rats.

Three days after the end of the CCK-8 test, during which the rats did not receive any treatment, the nutrient satiation test began. The rats were offered unlimited access to the 2% Polycose + 0.2% saccharin (P+s) solution paired with ID infusions that were also unlimited. For the first 6 days all the rats were injected with devazepide vehicle and were infused with water (days 1 and 2), 8% Polycose (days 3 and 4), and 16% Polycose (days 5 and 6). On days 7 and 8 the rats were pretreated with devazepide and infused with 16% Polycose. The ID infusion of Polycose was increased to 16% to enhance the carbohydrate's feeding suppressive effect. Data were collected from eight CON rats and nine DEV rats.

RESULTS

The results of the CCK-8 test are displayed in Fig. 2. Relative to vehicle control, CCK-8 treatment depressed CS+ intake by 53% in the CON group and by 31% in the DEV group. When devazepide was injected prior to CCK-8, it blocked the CCK-8-induced intake suppression; the CON group consumed 2% less and the DEV group 30% more CS+ following the devazepide + CCK-8 treatment relative to the vehicle control. Statistical analyses of CS+ intakes after vehicle, CCK-8, and devazepide + CCK-8 administration revealed a significant treatment effect, $F(2, 34) = 27.9$, $p < 0.001$, with intakes under the three treatments different from each other ($ps < 0.05$). There was no significant effect of group or group by treatment interaction. Devazepide treatment on day 6 increased CS+ intake relative to vehicle control on day 5, $F(1, 17) = 55.1$, $p < 0.001$ (see Fig. 2). This ef-

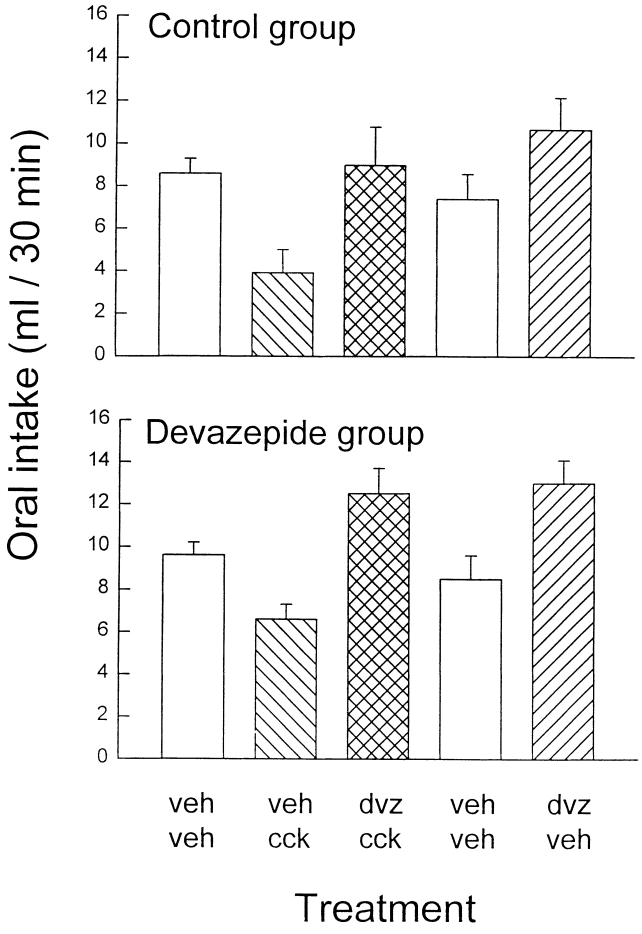

FIG. 2. Mean (+SE) intakes of the CS+ solution, paired with ID infusions of Polycose (8%), during 30-min, one-bottle sessions in Experiment 2. The control and Devazepide groups received the same injections 30 min (vehicle (veh) or 300 μg/kg devazepide (dvz)) and 2 min (vehicle or 4 μg/kg CCK-8) prior to the test sessions. From left to right the bars represent intakes after the following injections: vehicle vehicle; vehicle CCK-8; devazepide CCK-8; vehicle vehicle; devazepide vehicle.

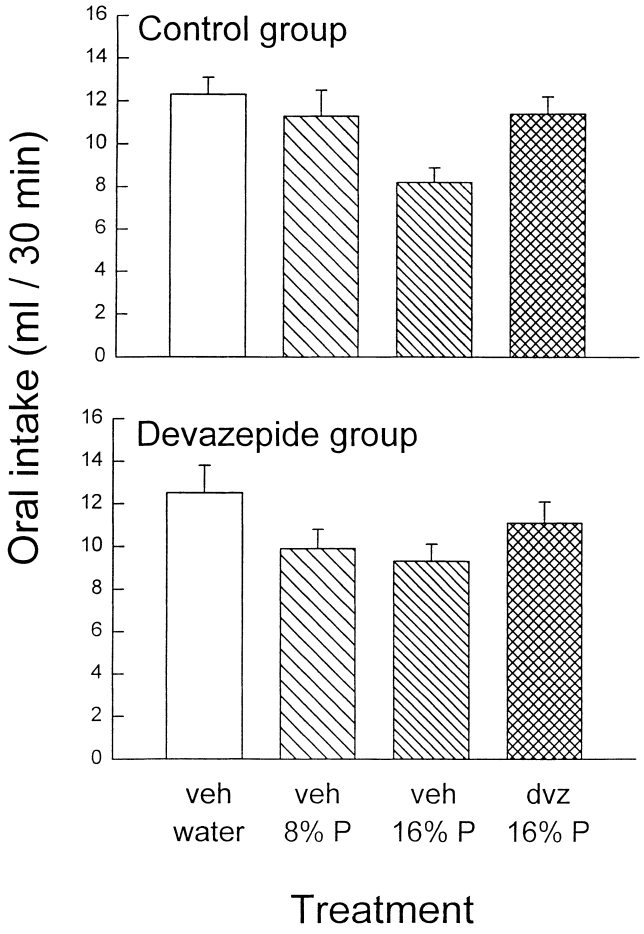

FIG. 3. Mean (+SE) intakes of Polycose + saccharin solution during 30-min satiation test of Experiment 2. The rats in the Control and Devazepide groups received ID infusions of water, 8% Polycose (8% P), or 16% Polycose (16% P) as they drank the solution. All rats were injected 30 min prior to the session with vehicle (veh) or devazepide (dvz, 300 μg/kg).

fect did not differ significantly between the groups (39 and 65% increase in the CON and DEV groups, respectively).

In the nutrient satiation test (Fig. 3), ID Polycose infusions inhibited intake of the P+s solution in a concentration dependent manner, $F(2, 30) = 16.8$, $p < 0.001$; overall, 8% Polycose infusion suppressed intake relative to water infusion, and 16% infusion suppressed intake relative to 8% infusion ($ps < 0.01$). A separate analysis of the intakes under the ID water, ID 16% Polycose, and ID 16% Polycose + devazepide conditions revealed a significant treatment effect, $F(2, 30) = 19.4$, $p < 0.001$, but no group by treatment interaction. In particular, devazepide injection increased solution intake, relative to the vehicle control ($p < 0.001$), and intakes in the ID Polycose + devazepide condition did not differ from those in the ID water + vehicle condition.

EXPERIMENT 3

In Experiment 2 devazepide was effective in blocking the feeding inhibitory effects of IP CCK-8 injection and ID carbohydrate infusions in both the CON and DEV groups. Yet, the drug failed to prevent the acquisition and expression of a carbohydrate-conditioned flavor preference in Experiment 1. Conceivably, blocking preference conditioning may require a higher drug dose than that required to attenuate feeding suppression. To test this possibility, the rats were retrained with new CS flavors paired with ID Polycose and water infusions but the DEV group was treated with devazepide at a high dose of 1200 μg/kg body weight.

METHOD

Procedure

After the intestinal satiation test of Experiment 2, the rats were offered plain 0.2% saccharin solution to drink and were infused with water for two 30 min/day sessions. The rats were then trained (eight sessions) and tested (two sessions) as in Experiment 1, except for the following differences. First, new CS flavors were used (0.05% orange or strawberry unsweet-

ened Kool Aid in 0.2% saccharin); the CS+/CS− flavor assignments were counterbalanced across the two groups and the flavor pairs used in Experiment 1. Second, CS intakes and ID infusions were limited to maximum volumes of 10 ml. Third, the DEV group was treated with devazepide at a dose of 1200 μg/kg. The drug injections were prepared at 1200 μg/ml by adding 12 mg of devazepide to a mixture of 0.2 ml DMSO, 50 mg carboxymethylcellulose, and 9.8 ml saline. The vehicle injections were similarly prepared but without the drug. Fourth, for reasons explained below, additional preference tests were conducted. After the first choice test (sessions 9 and 10), the rats were given a second choice test (sessions 11 and 12) without injections and a third test (sessions 13 and 14), in which half of the rats in each group were injected with the vehicle and the other half not injected.

RESULTS

During training the DEV group drank somewhat more than the CON group of the CS+ (9.9 vs. 8.2 ml/30 min) and the CS− (9.4 vs. 8.2 ml/30 min), although the difference was significant only for the CS+ ($U = 10, p < 0.05$).

Figure 4 shows the results of the two-bottle preference tests. In test 1, in which the DEV and CON groups were injected with devazepide and vehicle, respectively, both groups consumed reliably more CS+ than CS−, $F(1, 17) = 43.2$, $p < 0.001$. Their CS+ preferences were similar (CON 68%, DEV 69%) and identical to those of Experiment 1.

Although significant, the CS+ preferences were weaker than those obtained in a prior study using ID Polycose infusions but without daily IP injections (7). We, therefore, determined if the present rats would show stronger preferences if given an additional two-choice test without injections. In test 2, the CON and DEV groups consumed more CS+ and less CS− than they did in test 1 [Fig. 4, CS by test interaction; $F(1, 17) = 8.3$, $p < 0.01$]. The CON and DEV groups' CS+ preferences were now 78 and 81%, respectively, and did not reliably differ. The test 2 results would appear to suggest that the injection procedure interfered with the expression of the CS+ preference. However, we have previously observed that CS+ preferences may increase with repeated testing (12). Thus, to isolate the effect of the IP injection per se, an additional choice test was conducted in which half of the rats in each group ($n = 9$) were given a vehicle injection and the other half ($n = 10$) were given no injection before the daily sessions. The CON and DEV groups were combined because they did not differ in the prior preference tests. Both treatment groups consumed more CS+ than CS− [13.4 vs. 3.7; $F(1,17) = 84.2$, $p < 0.001$] and their intakes did not reliably differ, although the noninjected rats tended to show stronger preferences than the injected rats (82 vs. 76%). These results suggest that the CS+ preferences increased from test 1 to 2 primarily due to repeated testing, although a detrimental effect of the injection procedure cannot be completely ruled out. Despite these variations, the DEV rats did not differ from the CON rats in their CS+ preferences.

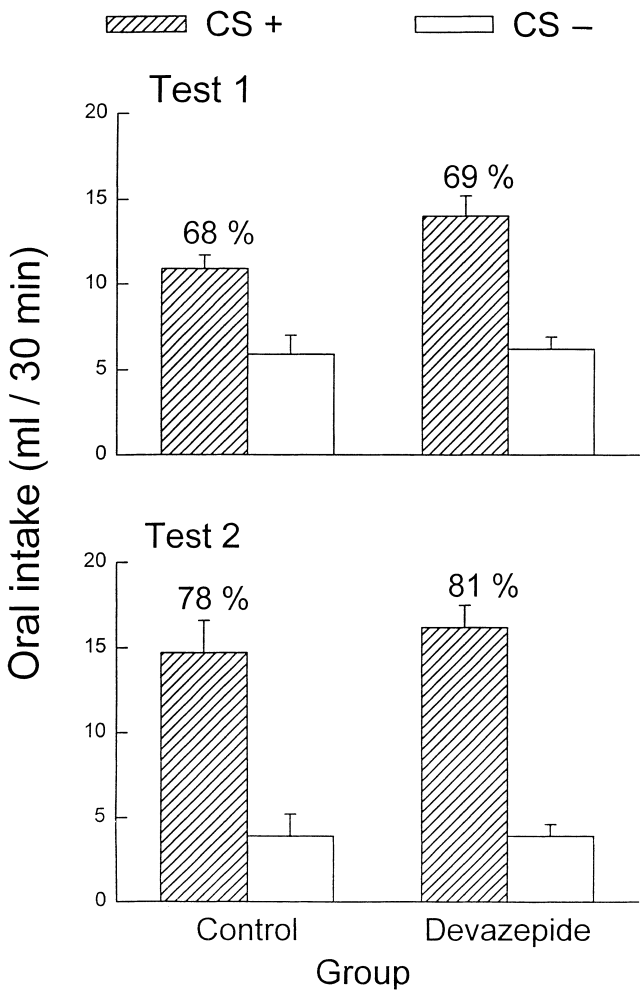

FIG. 4. Mean (+SE) intakes of the CS+ and CS− solutions during the 30-min two-bottle preference tests of Experiment 3. The CS+ and CS− had previously been paired with ID infusions of Polycose (8%) and water, respectively. In training and test 1, the Devazepide group was pretreated with devazepide (1,200 μg/kg), and the control group with vehicle. The rats received no injections in test 2. Numbers atop bars represent mean percentage intakes of the CS+.

GENERAL DISCUSSION

In confirmation of other recent findings (7), the present results demonstrate that ID infusions of Polycose condition flavor preferences in rats. The new finding here is that blocking CCK_A receptors with devazepide failed to attenuate preference conditioning, even at a high dose of 1200 μg/kg. This suggests that endogenous CCK acting on CCK_A receptors contributes little, if anything, to the postingestive reinforcing effects of carbohydrate. The total lack of effect of devazepide was somewhat surprising in view of earlier reports of modest flavor preferences conditioned by exogenous CCK (9,14,25). Perhaps endogenous CCK has a reinforcing action that is redundant to other postingestive reinforcing effects of carbohydrates.

Although devazepide did not attenuate carbohydrate conditioning in Experiment 1, it did block the feeding suppression produced by Polycose infusions as well as exogenous CCK in Experiment 2. The DEV and CON rats did not differ in their response to devazepide in the second experiment, which indicates that the DEV rats' repeated devazepide treatments in the first experiment did not cause them to be insensitive to the drug. The results of Experiment 2 are consistent with the previous report that devazepide blocks the feeding inhibition produced by intestinal maltose infusions (27). Note also that the DEV rats tended to consume more than did the CON rats during the one-bottle training sessions of Experi-

ments 1 and 3 even though CS intakes were limited during training. Taken together, these findings indicate a role for CCK_A receptors in carbohydrate satiety but not reinforcement. Carbohydrate satiety and reinforcement were also dissociated in a study of rats with partial visceral deafferentation produced by capsaicin (7). The capsaicin treatment substantially reduced the feeding suppression produced by ID Polycose infusions, but did not reduce the flavor preferences conditioned by the infusions. This is particularly relevant to the present results because capsaicin treatment also blocks CCK-8 feeding suppression (17). Thus, two quite different pharmacological agents, devazepide and capsaicin, have similar inhibitory effects on carbohydrate satiety and no effect on carbohydrate reinforcement.

The present results fail to support the idea that nutrient-stimulated CCK release is an important mediator of nutrient conditioned flavor preferences (9,14). A role for CCK in nutrient reinforcement is not completely excluded, however. Conceivably, endogenous CCK may mediate the postingestive reinforcing actions of fat and/or protein, although preliminary findings indicate that devazepide treatment does not block fat-conditioned flavor preferences (13). Also, CCK_B receptor antagonists were not studied, although there is little evidence implicating this CCK receptor subtype in ingestive behavior (2,16).

To date, attempts to identify the reinforcement pathway by which IG or ID nutrient infusions reinforce flavor preferences have not been successful. As noted above, capsaicin-induced visceral deafferentation fails to block preference conditioning, as does abdominal vagotomy, although vagotomy may attenuate conditioning somewhat (19). Both of these treatments are incomplete and spare visceral afferent inputs to the brain so that a neural pathway for nutrient reinforcement cannot be excluded. In addition to CCK, pancreatic insulin has been hypothesized to have a role in flavor preference conditioning (23), although the recent finding of glucose-conditioned preferences in diabetic rats fails to support this idea (1). The involvement of other gut hormones in nutrient reinforcement has yet to be examined. It is also possible that carbohydrate-conditioned flavor preferences are mediated by glucose sensors in the brain responding to the increased plasma glucose levels produced by IG or ID carbohydrate infusions. However, there is only limited evidence that nutrient infusions that bypass the gastrointestinal tract or hepatic-portal system are effective in conditioning flavor preferences (6,8,22). The identification of the interoceptor mechanisms that mediate nutrient-conditioned preferences requires further investigation.

Whereas devazepide, capsaicin, and abdominal vagotomy all fail to block ID nutrient reinforcement they attenuate the feeding inhibition produced by ID nutrient (7,27,28). Taken together, these findings indicate that the satiating and reinforcing actions of nutrients involve different physiological mechanisms.

ACKNOWLEDGEMENTS

This research was supported by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (DK-31135) and a NIMH Research Scientist Award (MH-00983) to Anthony Sclafani. Polycose was generously donated by Ross Laboratories and devazepide by Merck, Sharp and Dohme Research Laboratories. The authors thank Dr. Karen Ackroff for helpful comments on this paper.

REFERENCES

1. Ackroff, K.; Sclafani, A.; Axen, K. V.: Diabetic rats prefer glucose-paired flavors over fructose-paired flavors. Appetite 28:73–83; 1997.
2. Corwin, R. L.; Gibbs, J.; Smith, G. P.: Increased food intake after type A but not type B cholecystokinin receptor blockade. Physiol. Behav. 50:255–258; 1991.
3. Davis, J. D.; Campbell, C. S.: Chronic, intrajugular, intraportal, gastric, and duodenal cannulae for the rat. In: Singh, D.; Avery, D. D., eds. Physiological techniques in behavioral research. Monterey: Brooks/Cole Publishing Company; 1975:163–177.
4. Drucker, D. B.; Sclafani, A.: The role of gastric and postgastric sites in glucose-conditioned flavor preferences in rats. Physiol. Behav. 61:351–358; 1997.
5. Fedorchak, P. M.; Bolles, R. C.: Nutritive expectancies mediate cholecystokinin's suppression-of-intake effect. Behav. Neurosci. 102:451–455; 1988.
6. Gowans, S. E.; Weingarten, H. P.: Elevations of plasma glucose do not support taste-to-postingestive consequence learning. Am. J. Physiol. 261:R1409–R1417; 1991.
7. Lucas, F.; Sclafani, A.: Capsaicin attenuates feeding suppression but not reinforcement by intestinal nutrients. Am. J. Physiol. 270:R1059–R1064; 1996.
8. Mather, P.; Nicolaidis, S.; Booth, D. A.: Compensatory and conditioned feeding responses to scheduled glucose infusions in the rat. Nature 273:461–463; 1978.
9. Mehiel, R.: Hedonic-shift conditioning with calories. In: Bolles, R. C., ed. The hedonics of taste. Hillsdale, NJ: Lawrence Erlbaum Associates; 1991:107–126.
10. Mehiel, R.; Bolles, R. C.: Hedonic shift learning based on calories. Bull. Psychon. Soc. 26:459–462; 1988.
11. Mehiel, R.; Bolles, R. C.: Learned flavor preferences based on calories are independent of initial hedonic value. Anim. Learn. Behav. 16:383–387; 1988.
12. Pérez, C.; Lucas, F.; Sclafani, A.: Carbohydrate, fat and protein condition similar flavor preferences in rats using an oral-delay conditioning procedure. Physiol. Behav. 57:549–554; 1995.
13. Pérez, C.; Lucas, F.; Sclafani, A.: Devazepide, a CCK_A antagonist, blocks feeding suppression but not reinforcement by intestinal nutrients (Abstract). Appetite 27:297; 1996.
14. Pérez, C.; Sclafani, A.: Cholecystokinin conditions flavor preferences in rats. Am. J. Physiol. 260:R179–R185; 1991.
15. Reidelberger, R. D.; O'Rourke, M. F.: Potent cholecystokinin antagonist L 364718 stimulates food intake in rats. Am. J. Physiol. 257:R1512–R1518; 1989.
16. Reidelberger, R. D.; Varga, G.; Solomon, T. E.: Effects of selective cholecystokinin antagonists L364,718 and L365,260 on food intake in rats. Peptides 12:1215–1221; 1991.
17. Ritter, R. C.; Ladenheim, E. E.: Capsaicin pretreatment attenuates suppression of food intake by cholecystokinin. Am. J. Physiol. 248:R501–R504; 1985.
18. Sclafani, A.: Conditioned food preferences. Bull. Psychon. Soc. 29:256–260; 1991.
19. Sclafani, A.; Lucas, F.: Abdominal vagotomy does not block carbohydrate-conditioned flavor preferences in rats. Physiol. Behav. 60:447–453; 1996.
20. Smith, G. P.: The satiating effect of cholecystokinin and bombesin-like peptides. In: Smith, G. P., ed. The structure and mechanisms of satiation. New York: Oxford University Press; 1997:
21. Strohmayer, A. J.; Greenberg, D.: Devazepide alters meal patterns in lean, but not obese, male Zucker Rats. Physiol. Behav. 56:1037–1039; 1994.
22. Tordoff, M. G.; Friedman, M. I.: Hepatic-portal glucose infusions decrease food intake and increase food preference. Am. J. Physiol. 251:R192–R196; 1986.
23. Vanderweele, D. A.; Oetting Deems, R.: Insulin, sham feeding, real feeding, glucostasis, and flavor preferences in the rat. Ann. NY Acad. Sci. 575:582–584; 1989.

24. Weijnen, J. A. W. M.: Lick sensors as tools in behavioral and neuroscience research. Physiol. Behav. 46:923–928; 1989.
25. Weller, A.; Blass, E. M.: Cholecystokinin conditioning in rats: Ontogenetic determinants. Behav. Neurosci. 104:199–206; 1990.
26. Woltman, T.; Castellanos, D. A.; Reidelberger, R. D.: Role of cholecystokinin in the anorexia produced by duodenal delivery of oleic acid in rats. Am. J. Physiol. 269:R1420–R1433; 1995.
27. Yox, D. P.; Brenner, L.; Ritter, R. C.: CCK-receptor antagonists attenuate suppression of sham feeding by intestinal nutrients. Am. J. Physiol. 262:R554–R561; 1992.
28. Yox, D. P.; Stokesberry, H.; Ritter, R. C.: Vagotomy attenuates suppression of sham feeding induced by intestinal nutrients. Am. J. Physiol. 260:R503–R508; 1991.