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Norepinephrine-Facilitated Eating: Reduction in Saccharin Preference and Conditioned Flavor Preferences With Increase in Quinine Aversion

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MATTHEWS, J. W., E. L. GIBSON AND D. A. BOOTH. *Norepinephrine-facilitated eating: reduction in saccharin preference and conditioned flavor preferences with increase in quinine aversion.* PHARMACOL BIOCHEM BEHAV 22(6) 1045–1052, 1985.—Paraventricular (PVN) hypothalamic norepinephrine (NE) injections which facilitated feeding were nonetheless found to reduce both the unconditioned preference for saccharin and starch-conditioned preferences for almond odor and lemon taste, as well as enhancing aversion to quinine. These results add to the evidence that PVN NE elicits eating by attenuating a satiety signal.

Feeding Norepinephrine Paraventricular nucleus Saccharin preference Conditioned preference Odor preference Taste preference Carbohydrate appetite Quinine aversion

INTRAHYPOTHALAMIC administration of norepinephrine (NE) has been shown many times to elicit feeding [14,18]. Yet the behavioral processes controlling feeding that are altered by NE in this stimulation of food intake remain to be characterised.

The most effective injection site is in the region of the paraventricular nucleus (PVN) [16,19] and recent experiments [18,26] have investigated the effects of noradrenergic activation of the PVN region on nutrient self-selection. Norepinephrine, the alpha-adrenergic agonist clonidine, and the tricyclic antidepressant amitriptyline produced selective increases in the consumption of foods rich in carbohydrate and yet NE failed to elicit the increased consumption of a saccharin solution. Furthermore, the NE feeding effect is readily blocked by addition of quinine to the test food [11,24]. These results suggest that NE is not facilitating intake by either a general increase in the incentive value of all ingestive stimuli or a specific increase in the palatability of sweetness. Another possibility that had yet to be tested was that NE facilitates the intake of carbohydrate-rich foods by increasing specifically the incentive value that the stimuli of such test diets are likely to acquire during adaptation, as the result of preference conditioning by the postingestional effects of dietary starch (e.g., satiety) [7, 8, 9, 10]. Alternatively, NE may block the satiation conditioned by the food starch to food stimuli and repletion cues [4, 5, 7, 9] or some other carbohydrate-specific satiation which may not necessarily be learned.

The present experiments investigate the effects of NE on some of these behavioral controls of feeding. For the first time, the roles of a variety of different conditioned food incentives in noradrenergic feeding are examined. Feeding preferences classically conditioned by the effects of starch (unconditioned stimulus, US) [5, 9, 10] are acquired rapidly using odors and tastes as conditioned stimuli (CSs). Associations are more difficult to establish using visual stimuli but have been demonstrated in a conditioned aversion paradigm where the visual stimulus was localised to the food source [2, 12, 23]. We paired a potential CS, the odor, taste of container-appearance of liquid food, with the US, the effects of starch on mild hunger. The effects of NE injection into the PVN region on the rat's preferences for these conditioned stimuli were then examined. We also studied the effects of PVN NE on the rat's preference for a sweet non-nutritive saccharin solution and on its aversion to a bitter quinine solution. The results demonstrate a reduction of both unlearned and learned hedonic effects during the NE feeding effect and provide incidental evidence for an attenuation of learned satiation which could explain the feeding effect.

GENERAL METHOD

Animals

The subjects were 24 male hooded rats (bred at the Department of Psychology, University of Birmingham). Prior to the experiments, the rats were adapted to a 12 hr:12 hr light-dark cycle and maintained on powdered laboratory rat chow with water available at all times.

Surgery

Guide cannulae of 0.51-mm outer diameter were implanted into the left side of the brain under pentobarbitone

anaesthesia (Nembutal, 50 mg/kg) using a Kopf stereotaxic instrument. The cannulae were aimed at the PVN site [19], using in Experiment 1 the co-ordinates anterior 6.2 mm, medial 0.7 mm and ventral 1.7 mm following the atlas of Pellegrino and Cushman [24], and in Experiment 2 anterior 5.8 mm, medial 0.4 mm and ventral 2.0 mm, following the atlas of König and Klippel [15].

Conditioning and Testing

The rats were accustomed to liquid meals and their sensory preferences were conditioned by giving them access to a variety of aqueous solutions containing partly hydrolysed starch (Snowflake, CPC Ltd, Manchester) whilst mildly deprived of food [4, 5, 9]. All solution concentrations are given in g per 100 ml of solution (%). The rats' conditioned preferences were tested under extinction conditions (starch and its US effects absent). The effects of PVN NE on unconditioned and conditioned ingestive responses were tested by comparison of intakes after administration of 0.44 μl of 65 mM (−) norepinephrine bitartrate (Sigma) in 90 mM NaCl (4.8 μg of NE base [3,20]) through the intracranial cannula with intakes after intracranial injection of the same volume of 155 mM NaCl.

EXPERIMENT 1: EFFECTS OF NE ON UNCONDITIONED PREFERENCE AND AVERSION AND STARCH-CONDITIONED PREFERENCES

In the first Experiment, sensory preferences and aversions were measured by their effects on the total intake of a single test solution. Visual, olfactory and gustatory cues were provided in turn for preference conditioning by association with the effects of ingesting meals of 10% starch solution.

METHOD

Feeding Schedule

Each day, maintenance chow was removed 2 hr into the light period. Two and a half hours later the rats were given 0.5-hr access to that day's solution, the intakes recorded, and the chow replaced 2 hr later.

Initial Adaptation and Preference Conditioning

For the first three days of pre-surgical adaptation, 16 rats were given access to a 0.1% sodium saccharin solution (Fisons, Loughborough). Since hungry rats consume saccharin as though it were food [21], for each rat the saccharin intake on the final day was used as a criterion for evaluating the effectiveness of the subsequent preference-conditioning procedures.

The first opportunity to condition a preference was provided with visual cues. Each rat was given 10% starch solution from striped tubes for at least two days and then until it reached an intake equal to or exceeding its saccharin intake criterion.

The 16 rats were then given 10% starch with an almond scent, i.e., 2% almond essence (Rayner, London), for two days or until the saccharin criterion was reached. The final conditioning procedure was daily presentation of lemon-flavored, i.e., 2 mM citric acid (BDH Laboratory Chemicals, Poole), 10%-starch for two days or until criterion.

Pre-surgical adaptation was completed by two days of presentation of bitter glucose, i.e., 0.005 g quinine sulphate (BDH) per 100 ml of 1% D-glucose (Fisons), followed by a day with tap water.

Testing of PVN NE

A cannula, aimed at the PVN region, was then implanted in each rat and five days allowed for recovery before intake tests were resumed. To test the effects of NE injections under ad lib conditions, the rats were deprived of food or water for only the 0.5-hr period, 4.5 hr into the light period, when they were presented with one of a variety of fluids. Rats were randomly assigned to two groups: group 1 (n=8) received the saline test before the NE test and group 2 (n=8) the NE test before the saline test throughout the rest of the experiment.

To assess how effective the intracranial placements were in guiding NE to sites producing feeding, the first solution given post-surgically was milk (50 ml Nestlé sweetened condensed milk + 50 ml water). Milk was given for two adaptation days followed by the two PVN injection test days.

A succession of 4-day test periods was then administered in the same sequence as in the pre-surgical part of training (Table 1), i.e., first saccharin, then striped, almond-scented, lemon-flavored, and finally quinine solutions. In each period, there were two re-adaptation or retraining days followed by the two PVN injection test days (Fig. 2).

For tests of conditioned responses to cues, the 10% starch was not included in the test solution but, in order to minimise any consequent change in taste, 1% glucose was included in all solutions not containing starch, since the partly hydrolysed starch contained approximately 10% of free maltose and glucose. To assess the effects of flavors, the rats were finally given a single day with a test on plain 1% glucose solution from ordinary spouts without PVN injection.

Histology

Following testing, the rats were decapitated under pentobarbitone anaesthesia and the brains fixed in formol saline. The brains were cut into 50-μm sections close to the plane of the stereotaxic atlas of König and Klippel [15]. Placements of the cannula tips were recorded on diagrams from König and Klippel.

Data Analysis

The results were analysed using non-parametric statistical tests [25]. All the Wilcoxon Matched-Pairs Signed-Ranks tests were two-tailed.

RESULTS

Placement Anatomy

Figure 1 presents the histologically determined placements for 12 of the 16 rats used in the Experiment. Histological data were unavailable for the other 4 rats. For each condition where NE injections were shown to have significant group effects on intake, there were substantial effects in individual rats with placements in the vicinity of the paraventricular nucleus.

Pre-Surgical Adaptation and Training Intakes

The rats were first adapted to 0.1% saccharin. On the first day of presentation, they showed a typical neophobia (Table 1): intakes were significantly lower than the final water intakes (Wilcoxon, $T=18$, $N=14$, $p<0.05$). Four rats drank no

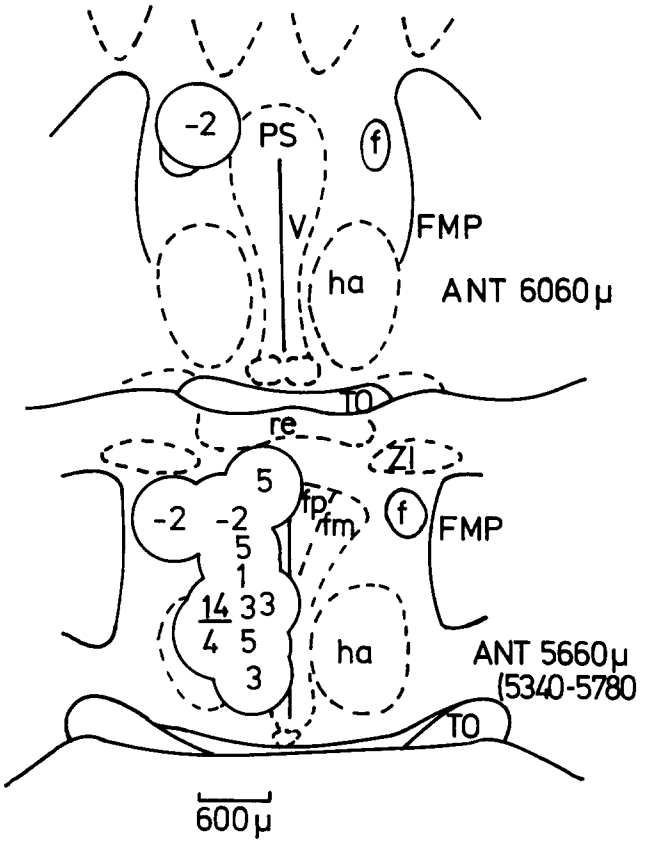

FIG. 1. Two hypothalamic sections are shown, from the atlas of König and Klippel; anterior-posterior co-ordinates are given for each section with the spread of the placements shown in brackets. Each circle denotes the site at which a rat's injections were made. The number within each circle gives the noradrenergic facilitation of milk intake to the nearest ml. PS, periventricular system; fp, nucleus paraventricularis pars parvocellularis; f, fornix; fm, nucleus paraventricularis pars magnocellularis; V, third ventricle; ha, anterior hypothalamic nucleus; re, nucleus reuniens; TO, optic tract; ZI, zona incerta; FMP, medial forebrain bundle.

measurable amount of saccharin on that day; they were given five days of saccharin adaptation. The other 12 rats were given three days of adaptation. Intake increased on the second day (Table 1). On the final day of saccharin adaptation, intakes were significantly higher than the final water intakes ($T=24$, $N=16$, $p<0.05$).

With striped tubes, 15 rats required two trials and one required three trials to reach the criterion of equalling or exceeding their last day's saccharin intake. For almond and lemon flavors, no rat required more than two days to reach the saccharin intake criterion.

The intakes for all three conditioned stimuli on their very first test days were higher than the water intake on its test day (Table 1). Moreover, whilst the initial intakes of striped starch and almond starch did not differ significantly from each other ($T=58$, $N=15$, $p>0.05$), both were significantly lower than the initial intakes of lemon starch ($T=0$, $N=16$, $p<0.01$; $T=9$, $N=16$, $p<0.01$). Thus across the first four conditions there may have been a reduction in the tendency for novel cues to suppress drinking.

Intakes of bitter glucose on both the first ($T=5$, $N=16$, $p<0.01$) and second ($T=24$, $N=16$, $p<0.05$) trials were

TABLE 1

FLUID INTAKES (ml) DURING ADAPTATION AND TRAINING PRIOR TO SURGERY

	First Presentation		Second Presentation	
Condition	Mean	SD	Mean	SD
Saccharin	1.5	1.7	5.4*	3.3
Stripes	7.0	3.9	10.7*	3.7
Almond	7.3	4.2	11.7*	5.3
Lemon	13.5	4.1	13.7	3.7
Quinine	0.6	0.4	0.8	0.8
Water	3.1	2.7		

*$p<0.05$, by Wilcoxon Matched-Pairs Signed-Ranks test, compared with the first presentation ($N=16$).

below those of water (Table 1), showing that the quinine solution was aversive initially and remained aversive.

Postsurgical Retraining and Control Intakes

Two rats failed to complete all test conditions following surgery because of cannula blockages. For the milk and saccharin conditions, intakes increased over successive readaptation or retraining tests (Table 2).

The intakes of the conditioned stimuli also increased over the training tests. However, when control intracranial injections of saline were given subsequently, with the stripes, almond and lemon stimuli being tested with 1% glucose instead of 10% starch, there were significant decreases in drinking in all three conditions (Table 2). This indicates stimulus differences between 1% glucose and 10% starch.

The decrease was greatest for striped glucose, intermediate for lemon glucose and least for almond glucose, suggesting that the starch had conditioned appreciable incentive to lemon and to almond but not to stripes.

In the case of the lemon flavor only, inspection of the intake data suggests that the fall of 1% glucose consumption under saline-injection conditions was greater in group 2, receiving NE injections first, than in group 1, receiving saline injections first. This would be expected if a day on 1% glucose partly extinguished the starch-conditioned lemon preference.

The PVN saline-injected intakes for the saccharin ($T=0$, $N=14$, $p<0.01$), almond glucose ($T=0$, $N=14$, $p<0.01$) and lemon glucose ($T=0$, $N=14$, $p<0.01$) conditions (Table 2) were all significantly greater than the final plain glucose intakes (Fig. 2). This is evidence that these cues did indeed have a facilitatory effect on the consumption of fluid. However, for the striped starch, there was no significant difference between the final glucose intake and the intake following saline injection ($T=25$, $N=14$, $p>0.05$). This indicates that the visual cue did not affect glucose intake, possibly because this cue had not been conditioned by starch whereas the olfactory and gustatory cues had been.

There was a small increase in postsurgical intakes of bitter glucose across training tests but the saline-injected intakes of bitter glucose were significantly lower than the plain glucose intakes ($T=6$, $N=14$, $p<0.01$), further confirming that this concentration of quinine had an inhibitory effect on drinking.

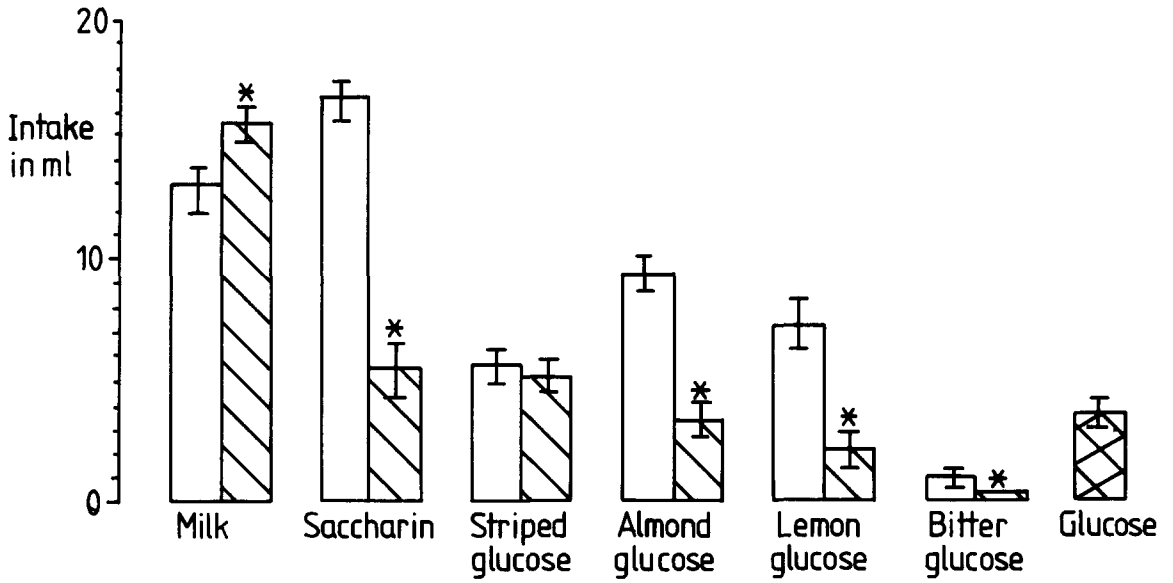

FIG. 2. Mean intakes following norepinephrine injection (hatched columns), saline injection (open columns), or with no injection (cross hatched column) for each condition in Experiment 1. An asterisk indicates a set of intakes which differs significantly from the corresponding intakes following saline injection (Wilcoxon, $p<0.05$).

Effects of PVN NE Injection on Feeding, Aversion and Preference

Compared to saline injections (Fig. 2), NE injections into the PVN significantly facilitated milk drinking ($T=28.5$, $N=16$, $p<0.05$), confirming that the cannula implantation sites were effective for NE-facilitated food consumption.

There was a significant negative correlation between the NE-induced feeding effect (milk intake following saline injection subtracted from milk intake following NE injection) and the intakes of milk following saline injection (Spearman Rank Correlation Coefficient, $r=-0.77$, $N=16$, $p<0.01$). This suggests that there was a 'ceiling effect' on NE-elicited intakes, i.e., the immediate satiating effects of high saline-injected intakes tended to reduce the facilitatory effects of NE injections on food intake.

Relative to saline injections, injections of NE caused a significant suppression of bitter glucose drinking ($T=4.5$, $N=12$, $p<0.01$). This indicates that PVN NE injection enhanced the aversiveness of quinine taste (Fig. 2).

Relative to intakes after saline injections, NE injections into the PVN region caused significant suppressions of the intake of saccharin ($T=2$, $N=16$, $p<0.01$), almond glucose ($T=1$, $N=15$, $p<0.01$) and lemon glucose ($T=4$, $N=14$, $p<0.01$) solutions (Fig. 2). Indeed, there were no significant differences between the intakes following NE injection and the uninjected plain glucose intakes for any of these conditions (Wilcoxon, $p>0.05$). These results suggest that the drug eliminated the unconditioned and conditioned facilitatory effects of these stimuli on consumption.

For the striped glucose test, however, there was no significant difference between the intakes following NE and saline injection ($T=51$, $N=16$, $p>0.05$) or between the intakes following NE and the final unstriped glucose intakes ($T=28.5$, $N=14$, $p>0.05$). There had been no evidence that the visual cue had been conditioned by starch, and so this result is consistent with the above interpretation that the suppressive effects of NE on intake arise from the neurotransmitter's action on the incentive from oral cues. Furthermore, this lack of effect of NE on striped glucose intake excludes the possibility that the suppression of intake with preference or aversion cues present was a general suppression of the intake of water or of virtually non-nutritive fluids (1% glucose).

There were significant correlations between the extent to which NE suppressed intakes and the intakes following saline injection, in the cases of saccharin ($r=0.71$, $N=16$, $p<0.01$), almond glucose ($r=0.64$, $N=15$, $p<0.01$), lemon glucose ($r=0.58$, $N=14$, $p<0.05$) and quinine glucose ($r=0.82$, $N=14$, $p<0.01$) but not striped glucose ($r=0.33$, $N=16$, $p>0.05$). That is, for each preference or aversion condition, the NE-induced decrement in intake was greater the higher that the intake had been following saline injection. This indicates that the incentive-reduction effect of PVN NE was larger for strong incentives.

DISCUSSION

Effects of Training Procedures

The finding that the rats' intakes under uninjected and saline-injected conditions increased across sessions is consistent with the expectation from past experiments [6, 9, 10] that the pairing of an odor or a taste with the effects of dilute starch in mildly hungry animals would condition a preference to the oral CS. Furthermore, when the rats were injected with saline, drops in intakes of almond odor and lemon taste were less than for striped tubes, suggesting that incentive was conditioned to the oral cues but not to the visual cue. Visual cues are thought to be hard to condition by visceral USs in the rat [13] and as a result we were precluded from testing here the effect of PVN NE on a conditioned visual food incentive.

The decrease in CS intake in saline-injection extinction tests, compared to retraining intakes, suggests that the

TABLE 2

FLUID INTAKES (ml) IN POST-SURGERY RETRAINING AND SALINE TESTING IN RATS TESTED WITH INTRACRANIAL SALINE FIRST (GROUP 1) OR SECOND (GROUP 2)

			First retraining day		Second retraining day		Saline-injected	
Condition	Group	N	Mean	SD	Mean	SD	Mean	SD
Milk	1	8	5.7	1.8	12.2*	2.4	12.3	4.0
	2	8	6.0	3.4	10.8*	3.8	13.3*	4.4
Saccharin	1	8	11.0	4.5	12.0	5.5	16.0*	4.3
	2	8	14.3	4.5	11.4	4.6	16.8*	3.2
Stripes	1	8	13.4	4.1	15.8	4.0	5.4*	3.5
	2	8	13.3	4.5	17.0*	6.5	5.8*	1.7
Almond	1	8	12.5	2.7	17.6*	2.4	9.5*	2.2
	2	7	10.6	4.3	14.7*	2.7	9.1*	3.3
Lemon	1	7	15.5	1.6	17.3	2.6	8.9*	4.5
	2	7	14.4	3.7	16.7	3.4	5.4*	2.0
Quinine	1	7	0.4	0.2	1.3*	1.0	1.4	1.8
	2	7	0.8	0.5	0.7	0.8	0.6	0.5

*$p<0.05$, by Wilcoxon Matched-Pairs Signed-Ranks test, compared with the immediately preceding intake value for any particular condition.

change from 10% starch to 1% glucose was discriminable by the rat. The decrease seems unlikely to have been partial extinction of a conditioned preference, as it was at least sometimes no greater in the group injected with saline after NE than in the group injected with saline first. This intake decrement, and the steady increase in the initial intake of fluids even for the visually cued starch, are explicable if conditioning was occurring to cues in addition to the odor and taste stimuli. If the 10% starch solution was at all discriminable from the 1% glucose solution (e.g., in texture cp. [4]), these discriminable cues could have become conditioned by the post-ingestional effects of starch. Then their absence in extinction tests would attenuate incentive to that conditioned to the lemon and almond stimuli only.

The quinine flavoring was intended to function as an unconditioned aversive stimulus. Aravich and Sclafani [1] have suggested that quinine might suppress feeding through the conditioning of the bitter taste to aversive post-ingestional pharmacological effects of quinine, in addition to initially suppressing feeding through bitterness. The slightly increasing quinine intake over successive control trials suggests that the lower quinine concentrations and the briefer periods of access used in this study suppressed intake through bitter taste alone.

Effects of Norepinephrine

The observation that NE injected into the region of the PVN facilitated milk drinking is in agreement with previous findings [16,19].

The intensification by NE of the intake-suppressant effect of quinine taste extends the findings of Booth and Quartermain [11] and Sclafani and Toris [24]. The latter authors demonstrated that quinine eliminated the chow intake-facilitating actions of NE injection. Our observation indicates that this blockade of the NE-feeding effect may involve an NE-induced increase in the aversiveness of a bitter taste.

Leibowitz [18] and Tretter and Leibowitz [26] have reported that NE injections fail to elicit consumption of a saccharin solution. The results of this experiment show that NE injection does not just fail to elicit extra incentive in sweetness but actually reduces or eliminates the facilitating effects of saccharin on intake.

This experiment investigated for the first time the effects of NE on ingestive responses to cues that have been preference-conditioned by the effects of starch. PVN NE injection reduced or removed the facilitating effects of carbohydrate-conditioned cues on intakes of 1% glucose solution. This view is supported by the fact that the NE-induced reductions in intake were greater in those rats whose intakes had been more facilitated by these incentives.

PVN NE facilitates the consumption of foods rich in carbohydrate, including unsweetened starch [18,26]. During adaptation to a diet, the rat may well learn to eat it according to its carbohydrate content by the processes of conditioning of (dis)incentive and (de)satiation [4, 6, 7, 10]. Yet we find here that PVN NE attenuates incentive conditioned to flavors by previous experience of the flavors in a starch diet. The starch solution used to condition incentive in these experiments was, however, very dilute. Thus, one explanation of the various findings could be that NE facilitates the consumption of foods rich in carbohydrate while attenuating food consumption incentive conditioned by dilute carbohydrate. To test this, Experiment 2 used high rather than low starch concentrations for flavor conditioning, to see whether NE facilitated rich-conditioned incentive rather than suppressed it as it had suppressed dilute-conditioned incentive.

EXPERIMENT 2: EFFECT OF NE ON PREFERENCE CONDITIONED BY CONCENTRATED STARCH

Concentrated starch conditions a preference in the mildly hungry animal and indeed a stronger hungry preference than

does dilute starch [4, 5, 6, 7, 8, 9]. So Experiment 2 studied the effect of PVN NE on flavor preference conditioned by concentrated starch (at a caloric density approximately that of chow) to see whether the reduction in conditioned incentive in Experiment 1 was peculiar to a dilute US.

The single-solution test for preference, used in Experiment 1, confounds the cue of interest with other oronasal cues and internal cues. The attenuation by NE of saccharin incentive and incentive conditioned by dilute starch might be peculiar to tests of incentives in virtually or absolutely non-nutritive fluids (like 1% glucose). Consequently, we carried out a second experiment in which the non-nutritive test solution was formulated to have sensory characteristics very similar to those of the concentrated starch used in training. Furthermore, we tested conditioned incentive strength in extinction by means of two-solution choice tests, which disconfound preference for the conditioned cue from reactions to the background oronasal and internal cues. Attenuation of conditioned preference by NE in such a design would strongly support the deductions made from the pattern of results in Experiment 1, namely that the NE feeding effect occurs despite attenuation of incentives.

METHOD

Conditioning and Testing

Eight PVN-implanted rats were fully adapted to a mild food-deprivation schedule, and to drinking sweet, thick solutions from glass tubes. Maintenance food was removed 4 hr into the light period and the animals were given training and test meals 4 hr later.

The rats were first tested for the effectiveness of their cannulae in producing feeding following PVN NE injections. After the 4-hr deprivation, the rats were satiated by access for 15 min to a highly palatable mixture of diluted (1:4 with water) sweetened condensed milk (Nestlé) and powdered chow (4:3 v/v). Fifteen minutes later, half the rats were injected intracranially with NE and half with saline. The injections were reversed on the second test day. Immediately following injections, each rat was presented with two chow pellets (about 3 g each). Intake of the pellets was recorded after 30 and 60 min.

On conditioning days, the rats were satiated using the procedure above. At the end of the 15-min interval each rat was given ad lib access to a solution of 60% (w/v) starch flavored with 2% w/v almond essence. The starch was removed after 25 min.

Following conditioning, the rats were tested for a preference to the 60% starch-paired odor under extinction conditions, and the effect of PVN NE on this conditioned preference was determined at the same time, as follows.

The pre-satiation and intracranial injection procedures were the same as those used in the PVN NE-induced chow-feeding test above. Immediately after injection, the rats were given a choice of two test fluids. Both were solutions of 0.7% cellulose gum (7HF sodium carboxymethylcellulose, Hercules Ltd) and 0.01% sodium saccharin dissolved in distilled water, i.e., the solutions were closely matched to 60% starch in both sweetness and texture, but were non-nutritive. However, one solution was flavored with 2% almond, while the other had no additional flavor. This allowed a sensitive measure of preference for an almond-flavored solution over an unflavored solution, unaffected by total intake. Each rat was forced to sample both solutions at the start of the test meal, and the position of the tubes was reversed at frequent intervals during the meal to prevent the measure of almond preference being biased by a side preference.

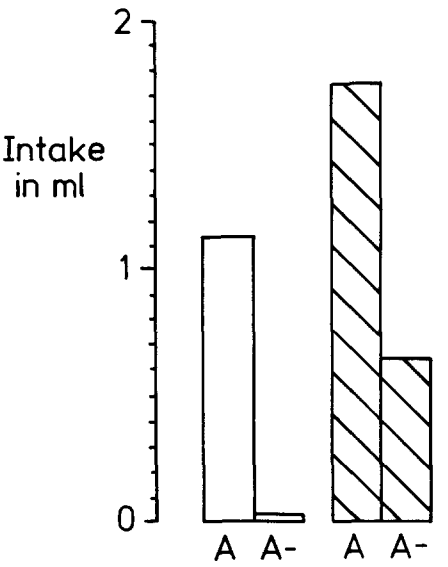

FIG. 3. Mean intakes following norepinephrine injection (hatched columns) or saline injection (open columns), for almond-flavored solutions (A) or unflavored solutions (A^-) in Experiment 2. Both test solutions contained 0.7% cellulose gum and 0.01% saccharin in distilled water.

After 25-min access, the final intakes were recorded to the nearest 0.1 ml and the tubes removed. The almond-preference ratio for each rat was calculated as the intake of almond-flavored solution divided by the total intake of both solutions.

The rats were tested in this manner over two days in a balanced design. All rats therefore had an equal number of exposures to the odorised and non-odorised test solutions. One rat lost its cannula after the first test day and so its data were discarded.

Data Analysis

The effect of NE on the starch-conditioned almond-preference was analysed by the Wilcoxon Matched-Pairs Signed-Ranks test.

The total intakes under NE and saline injections approximated to a normal distribution and so these were compared using a correlated t-test.

RESULTS

The 7 rats tested for effects of NE on conditioned incentive ate 0.76 g (SE=0.39) of chow after injection of saline into the PVN region and 1.47 g (SE=0.35) after PVN NE injection—thus demonstrating a reliable NE feeding effect ($t(6)=2.03$, $p<0.05$).

The mean preference ratio for almond flavor, previously paired with concentrated starch, was 0.98 (SE=0.01) after injection of saline into the PVN. This mean ratio was highly significantly greater than 0.5, i.e., indifference ($t(6)=37.2$, $p<0.001$). This starch-conditioned odor preference was significantly less following injection of NE compared to saline injection (T=0, N=6, $p<0.025$, 1-tail), the mean ratio after NE being 0.72 (SE=0.11).

However, even though the almond preference was attenuated in PVN NE eaters, the total intake of the sweet,

thick test solution was significantly greater after NE injection than after saline injection (Fig 3; $t(6)=2.67$, $p<0.025$, 1-tail), indicating a facilitation of the intake of this starch-like non-nutritive fluid by PVN NE in satiated rats.

DISCUSSION

Injections of NE into the PVN area produced an increase in total sweetened gum intake whilst at the same time producing a reduction of the flavor preference conditioned by concentrated starch.

One explanation of these findings is that NE attenuates satiation. The component of satiation attenuated could well be the learned reaction to the combination of dietary and postingestional cues that in the past predicted oversatiation or the avoidance of undersatiation, i.e., has predicted the effects of ingesting concentrated starch when already almost replete [4, 5, 9]. If this NE-attenuated satiation (or NE-augmented desatiation) is normally specific to carbohydrate-conditioned cue-combinations (not fat or protein conditioned), as the results of Booth [4] suggest, then the present results demonstrate that the NE feeding effect is indeed a carbohydrate-specific appetite, and a learned one.

Alternatively, NE may facilitate appetite. This could not be facilitation of sweetness preference (Experiment 1, [18,26]) nor of conditioned olfactory and gustatory incentive (Experiment 1, [18,26]) but could be facilitation of textural incentive. The solutions used in extinction conditions in the two experiments differed only in texture. Following NE injection, the solution used in Experiment 1 was associated with a suppression of intake and the solution used in Experiment 2 was associated with a facilitation of intake. It may be that NE makes the animal particularly sensitive to the texture of a solution, facilitating the intake of highly viscous "thick" solutions but suppressing the intake of "thin" solutions. This possibility could be examined by studying the effects of NE on the unconditioned intakes of the test solutions used in Experiments 1 and 2.

CONCLUSION

These experiments have demonstrated that the facilitation of feeding by NE is allied with a decrease in the incentive value of food stimuli.

If PVN NE elicits feeding by disrupting some interoceptively based satiety [18], this satiety blockade must be sufficient to release feeding despite concurrent reduction in food incentive. Also, the satiety blockade may be specific to one post-ingestional satiety signal whilst other satiety cues are unaffected: the 'ceiling effect' on elicited milk intake observed in Experiment 1 indicates that sufficiently high intakes generate a satiety that is not overriden by NE. This might be an unlearned satiating effect of strong distension, whereas the NE effect operates on a learned postingestional satiation. This possibly NE-blocked postingestional satiety also might be food-cue dependent, like the disrupted incentives. Conditioned satiation is learned behavior that has indeed been shown to be a flavor-dependent response to a replete internal state [4, 5, 7, 8]. Therefore, injection of NE into the PVN may elicit eating by blocking influential carbohydrate-conditioned aspects of satiation based on combinations of visceral and dietary cues, i.e., by augmenting learned carbohydrate appetite.

Alternatively, NE may make the rat particularly sensitive to one sort of unconditioned stimulus—the texture of the solution. It is unclear, however, how this hypothesis (unlike the satiety blockade hypothesis) can explain the appetite for sweet as well as non-sweet carbohydrate shown by animals following NE injection [18,26].

Whichever of these explanations is supported by experiments currently taking place at this laboratory, the experiments reported here indicate, for the first time, a selective interference by PVN NE with normal behavioral controls of feeding which limits the range of mechanisms by which the noradrenergic feeding effect can be considered to be mediated.

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