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Morphine Enhancement of Sucrose Palatability: Analysis by the Taste Reactivity Test

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RIDEOUT, H. J. AND L. A. PARKER. *Morphine enhancement of sucrose palatability: Analysis by the taste reactivity test.* PHARMACOL BIOCHEM BEHAV 53(3) 731-734, 1996.—The ability of morphine to modify sucrose palatability was assessed by the taste reactivity test. In Experiment 1, rats were injected with morphine (0.0, 0.5, 2.0, and 10.0 mg/kg, subcutaneously), 30 min before receiving a 10-min intraoral infusion of 2% or 20% sucrose solution. A dose of 2.0 mg/kg morphine enhanced ingestive reactions elicited by both concentrations of sucrose solution. In Experiment 2, the interval between morphine pretreatment and the taste reactivity test was manipulated. Rats given 2.0 mg/kg morphine 30 or 120 min before testing displayed enhanced ingestive reactions elicited by 20% sucrose solution during the first 5 min of a 10-min test. The results support the hypothesis that morphine enhances the hedonic assessment of sucrose solution.

Morphine Palatability Sucrose Taste Taste reactivity Ingestion Reward

OPIOIDS play a role in the modulation of feeding in rats (1,6,14). At low doses, morphine enhances feeding (12,13,17); furthermore, it has been suggested that this enhancement of feeding is specifically the result of morphine-induced enhancement of palatability (5,10,13).

The measure of pharmacologic modulation of palatability used by most investigators has been consumption. However, a more direct test of the palatability of a solution than that of consumption is the taste reactivity test devised by Grill and Norgren (7). In the taste reactivity (TR) test, flavoured solutions are intraorally infused through chronically implanted cannulae. An infusion of a sweet-tasting solution (e.g., sucrose) typically elicits ingestive reactions consisting of tongue protrusions, paw licking, and mouth movements; an infusion of a bitter substance (e.g., quinine) elicits aversive reactions, such as chin rubs, gapes, and paw treading.

Parker et al. (15) used the TR test to investigate the ability of morphine to modify the palatability of sucrose and quinine solutions. If morphine enhances feeding by directly modifying the palatability of food, then it should enhance ingestive reactions elicited by sucrose solution and attenuate aversive reactions elicited by quinine solution. In fact, rats displayed attenuated aversion of quinine, but not enhanced ingestion of sucrose, during a 10-min intraoral infusion that began 30 min after a subcutaneous (SC) injection of 2 mg/kg morphine.

On the other hand, Doyle et al. (4) reported that rats that were administered 4 mg/kg morphine, SC, 1.5-2 h before a 1-min TR test with a sucrose-quinine mixture (7% sucrose and 0.01% quinine) displayed enhanced ingestive reactions but no change in aversive reactions during the infusion. These data suggest that morphine directly enhanced the positive hedonic properties of the sucrose-quinine tastant. Doyle et al. suggested that the difference in the pattern of results from that reported by Parker et al. (16) may be due to a difference in the dose of morphine employed or the morphine–TR test interval. In fact, morphine enhancement of feeding has been reported to be evident only 1-3 h postinjection, preceded by a 1-h period of suppressed intake (9). The present series of experiments attempted to resolve the discrepancies between the findings of Parker et al. (16) and Doyle et al. (4) with respect to the effects of morphine on sucrose palatability.

EXPERIMENT 1

Experiment 1 examined the effect of several doses of morphine (0.0, 0.5, 2.0, and 10.0 mg/kg, SC) on the palatability

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of 2% and 20% sucrose solution. If morphine enhances palatability by directly increasing the positive hedonic properties of sucrose solution, then the level of ingestive reactions would be expected to be greater in morphine-pretreated rats compared with saline controls; however, such an effect may be dose-specific.

Method

Subjects. The subjects were 83 male Sprague-Dawley rats weighing 289-392 g on the day of testing. The rats were housed individually in suspended stainless-steel cages and maintained ad lib on Purina rat chow ((Bioserv, Frenchtown, NJ) and water throughout the experiment. The housing room was illuminated on a 12 L : 12 D schedule.

Procedure.

Surgery. One week after arriving in the laboratory and being handled, the rats were implanted with intraoral cannulae. After being water deprived for a 24-h period, each rat received an initial injection of atropine [0.5 ml, intraperitoneally (IP)] 15 min before being anaesthetized with ketamine (100 mg/kg, IP) and rompun (10 mg/kg, IP). A 15-ga, thin-walled, stainless-steel needle was inserted through the skin in the dorsal midneck region. The needle was advanced SC behind the ear along the inside of the cheek, where it exited into the mouth behind the first molar through the soft part of the cheek. The skin at both the entry and exit sites was swabbed with iodine. A 10-cm length of polyethylene (PE 90) tubing was inserted through the barrel of the needle. The needle was then removed, leaving the tubing in its place, where it was secured at the entry site at the neck by a 20-ga intramedic adapter, and at the exit site in the mouth by a 5-mm rubber O-ring.

Taste reactivity testing. After a 1-week recovery period, each rat was given three 10-min adaptation trials. On each of the adaptation trials, the rat was placed in the glass TR test chamber (22.5 × 26 × 20 cm) and its cannula attached to the infusion pump (Model 22; Harvard Apparatus, Cambridge, MA) by a 35-cm-length of the same polyethylene tubing used in the surgery. The test area was illuminated by four 100-W lightbulbs, with two on either side of the chamber and two aimed at a mirror hung at an angle below the floor of the chamber. After a 1-min habituation period in the chamber, the rats received 10 min intraoral infusion of water at a rate of 1 ml/min.

Testing began on the day following the final adaptation trial. The rats were treated in an identical manner to the adaptation trials, except that they received an SC injection of 0, 0.5, 2.0, or 10.0 mg/kg morphine 30 min before receiving a 10-min intraoral infusion of either 2% or 20% sucrose solution at a rate of 1 ml/min. There were 10–12 rats per group. To facilitate recording of the orofacial and somatic reactions of the rats, a Panasonic (Yokohama, Japan) videocamera was focused at the mirror hung below the floor of the chamber.

Behavioural categories. The videotapes of the TR test were scored in real time by raters blinded to the experimental assignments and using an event recorder software package for an IBM personal computer (The Observer; Noldus Inc., Netherlands, NL). The ingestive TR reactions were recorded as the total amount of time during the 10-min test to the nearest 0.1 s. Ingestive reactions included tongue protrusions (forward or lateral extensions of the tongue), paw licking (licking the solution from the front paws), and the mildly ingestive/neutral mouth movements (forward or lateral movement of the lower mandible without opening the mouth). Each of the ingestive reactions was combined to produce a composite score. The interrater reliability coeficient for this method of scoring has been described previously (15). The data were blocked into two 5-min periods for analysis.

Results and Discussion

Fig. 1 presents the mean (±SEM) duration (s) of ingestive reactions elicited by 2% and 20% sucrose solution during each of two 5-min blocks of testing in Experiment 1. A 2 × 4 × 2 mixed-factor analysis of variance (ANOVA), with the between-groups factors of sucrose concentration and pretreatment dose and the within-groups factor of block of 5 min, was conducted. The analysis revealed a significant main effect of concentration [$F(1, 75) = 24.37$; $p < 0.001$]. Rats spent more time displaying ingestive reactions during an infusion of 20% sucrose than 2% sucrose solution, suggesting that the 20% sucrose is more palatable than 2% sucrose. However, the analysis revealed no Concentration × Pretreatment Dose interaction. A significant main effect of pretreatment dose was also obtained [$F(3, 75) = 6.11$; $p < 0.01$]. Subsequent Newman-Keuls tests revealed that rats administered 2.0 mg/kg spent significantly more time displaying ingestive reactions than did rats in each of the other pretreatment groups (each $p < 0.05$). Finally, there was a significant Dose × Block of 5-min interaction [$F(3, 75) = 10.42$; $p < 0.001$]. For each block of 5 min, a one-way ANOVA was conducted collapsed across sucrose concentrations with the between-group factor of morphine pretreatment dose. In Block 1, a significant dose effect was obtained [$F(3, 79) = 2.96$; $p < 0.05$]; subsequent Newman-Keuls tests revealed that rats administered 2.0 mg/kg morphine spent more time displaying ingestive reactions than did rats administered any other dose of morphine (each $p < 0.05$). In Block 2, a significant dose effect was also obtained [$F(3, 79) = 8.23$; $p < 0.001$]; however, Newman-Keuls tests revealed that ingestive reactions were suppressed in rats administered 10.0 mg/kg compared with all other dose conditions (each $p < 0.05$).

EXPERIMENT 2

Experiment 2 assessed the effect of the variable of pretreatment interval on morphine-induced modification of sucrose palatability. If the changes in morphine-induced feeding that occur with the passage of time, as previously reported (9), are representative of palatability shifts, then the strength of ingestive reactions elicited by sucrose solution should depend on the interval between morphine administration and the TR test. Because Experiment 1 revealed that a dose of 2 mg/kg, SC, produced maximal enhancement of sucrose palatability under the conditions in which the test was conducted, Experiment 2 attempted to replicate this effect and extend it to an interval of 120 min, similar to the method employed by Doyle et al. (4).

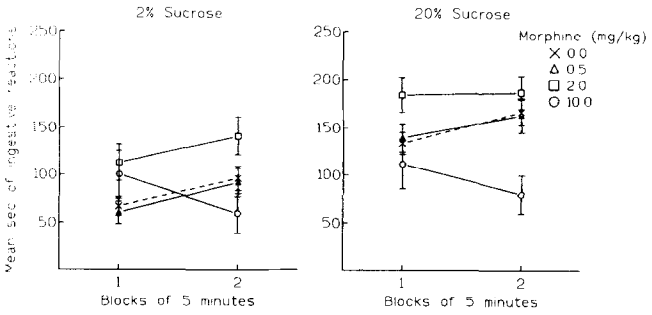

FIG. 1. The mean duration (s) of ingestive reactions displayed during the 10-min intraoral infusion of 2% and 20% sucrose solution by rats administered 0.0, 0.5, 2.0, or 10.0 mg/kg of morphine 30 min before testing in Experiment 1.

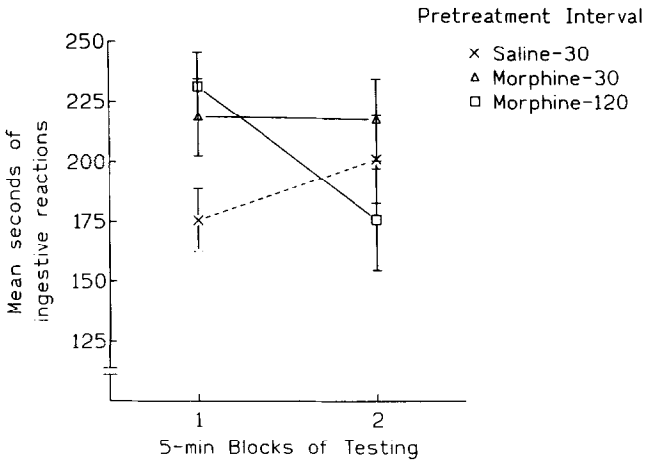

FIG. 2. The mean duration (s) of ingestive reactions displayed by rats administered saline or 2.0 mg/kg morphine 30 or 120 min before a 10-min intraoral infusion of 20% sucrose solution in Experiment 2.

Method

Subjects. The subjects were 27 male Sprague-Dawley rats, weighing 267–351 g on the day of testing. They were housed individually in suspended stainless-steel cages and maintained ad lib on Purina rat chow and water throughout the experiment. The housing room was illuminated on a 12 L : 12 D schedule. The rats were treated in a manner identical to that of Experiment 1, except where noted.

Procedure. On the day following the final adaptation trial, the rats received the TR test. The rats were treated in a manner identical to the adaptation trials except that they were given SC injections of 2.0 mg/kg morphine, 30 min (n = 10) or 120 min (n = 9) before receiving a 10-min intraoral infusion with 20% sucrose solution at a rate of 1 ml/min. A control group (n = 8) received SC injections of saline 30 min before receiving the TR test.

Results and Discussion

Figure 2 presents the mean duration (s) of ingestive reactions displayed by the various groups during each 5-min block of the 10-min TR test in Experiment 2. The data were analyzed as a 3 × 2 mixed-factor ANOVA with the between-group factor of pretreatment group, and the within-group factor of blocks of 5 min. The analysis revealed no significant group effects; however, there was a significant Group × Block interaction [$F(2, 24) = 3.35$; $p < 0.05$]. During the first 5-min block, a single-factor ANOVA revealed a significant pretreatment effect [$F(2, 24) = 3.64$; $p < 0.05$]. Newman-Keuls tests revealed that ingestive reactions were significantly enhanced only in those rats that were administered morphine 120 min before the TR test, compared with saline controls ($p < 0.05$). By a less conservative one-tailed t-test, the 30-min morphine pretreatment group also displayed more ingestive reactions than did controls during the first 5-min block of testing [$t(16) = 1.99$; $p < 0.05$]. Because this finding replicates the results of Experiment 1, it is probably a reliable effect. However, during the second 5-min block, the pretreatment effect was not significant.

GENERAL DISCUSSION

At a dose of 2.0 mg/kg, morphine produced enhancement of sucrose palatability. This effect was apparent whether morphine was administered 30 or 120 min before the TR test, and was most prominent during the first 5 min of the 10-min test. It is conceivable that a higher dose of morphine would have enhanced sucrose palatability over a longer temporal interval. The present findings support the assertion that morphine enhances feeding by directly enhancing the positive hedonic properties of a tastant (4,5,11,18). The failure of Parker et al. (16) to detect morphine-induced enhancement of ingestive reactions may have been the result of animals receiving only a single adaptation trial before TR testing. In the present investigation, the animals were well adapted to the test chamber, which may have provided for more stable responding during the TR test.

Our results support the findings reported by Doyle et al. (4) that morphine pretreatment enhances the ingestive component of taste reactivity. However, in contrast to their report that morphine pretreatment did not modify the aversive component of reactivity to a sucrose-quinine mixture, other reports from our laboratory (2,16) have demonstrated that morphine also attenuates quinine-elicited aversive reactions. This effect has been demonstrated following one (16) or three (2) adaptation trials preceding the TR test trial. It should be noted that the concentration of quinine (0.05%) employed in our experiments was much higher than that used by Doyle et al. (0.01%) and the duration of the test was longer (5–10 min) in our laboratory than theirs (1 min). These factors would be expected to facilitate the demonstration of a suppression of responding, as floor effects in the report by Doyle et al. may have precluded the demonstration of attenuated aversive reactions.

It is apparent, then, from the present data and from earlier investigations (4,5), that activation of endogenous opioid receptors by the administration of the opiate agonist morphine may modify feeding by acting on a palatability mechanism. Consumption tests have shown that morphine is effective at increasing intake of highly palatable foods (5), and the taste reactivity test suggests that morphine directly enhances the positive hedonic properties of highly palatable tastes (4).

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REFERENCES

1. Capuano, C. A.; Liebowitz, S. F.; Barr, G. A. The ontogeny of opioid receptors mediating opiate-induced feeding in rats. Neuropharmacology 29:433–437; 1990.
2. Clarke, S.; Parker, L. A. Morphine-induced modification of quinine palatability: Effects of multiple morphine-quinine trials. Pharmacol. Biochem. Behav. 51:505–508; 1995.
3. Cooper, S. J. Palatability-induced drinking after administration of morphine, naltrexone, and diazepam in the nondeprived rat. Substance Alcohol Actions Misuse 3:259–265; 1982.
4. Doyle, T. G.; Berridge, K. C.; Gosnell, B. A. Morphine enhances hedonic taste palatability in rats. Pharmacol. Biochem. Behav. 46:745–749; 1993.

5. Evans, K. R.; Vaccarino, F. J. Amphetamine- and morphine-induced feeding: Evidence for involvement of reward mechanisms. Neurosci. Biobehav. Rev. 14:9–22; 1990.
6. Gosnell, B. A.; Krahn, D. D.; Majchrzak, M. J. The effects of morphine on diet selection are dependent upon baseline diet preferences. Pharmacol. Biochem. Behav. 37:207–212; 1990.
7. Grill, H. J.; Norgren, R. The taste reactivity test: I. Mimetic responses to gustatory stimuli in neurologically normal rats. Brain Res. 143:263–279; 1978.
8. Leeb, K.; Parker, L. A; Eikelboom, R. Effects of pimozide on the hedonic properties of sucrose: Analysis by the taste reactivity test. Pharmacol. Biochem. Behav. 39:895–901; 1991.
9. Leshem, M. Morphine induces delayed anorexia in rats. Psychopharmacology 94:254–258; 1988.
10. Linseman, M. A. Central vs. peripheral mediation of opioid effects on alcohol consumption in free-feeding rats. Pharmacol. Biochem. Behav. 33:407–413; 1989.
11. Lynch, W. C.; Burns, G. Opioid effects on intake of sweet solutions depend both on prior drug experience and on prior ingestive experience. Appetite 15:23–32; 1990.
12. Lynch, W. C.; Libby, L. Naloxone suppresses intake of highly preferred saccharin solutions in food deprived and sated rats. Life Sci. 33:1909–1914; 1983.
13. Milano, W. C.; Wild, K. D.; Hui, Y.; Hubbell, C. L.; Reid, L. D. PCP, THC, ethanol, and morphine and consumption of palatable solutions. Pharmacol. Biochem. Behav. 31:893–897; 1989.
14. Morley, J. E.; Levine, A. S.; Kneip, J.; Grace, H.; Zeugner, H.; Sherman, G. T. The opioid receptor and food intake. Eur. J. Pharmacol. 112:17–25; 1985.
15. Parker, L.; Carvell, T. Orofacial and somatic responses elicited by lithium-, nicotine-, and amphetamine-paired sucrose solution. Pharmacol. Biochem. Behav. 24:883–887; 1986.
16. Parker, L. A.; Maier, S.; Rennie, M.; Crebolder, J. Morphine- and naltrexone-induced modification of palatability: Analysis by the taste reactivity test. Behav. Neurosci. 106:999–1010; 1992.
17. Sanger, D. J.; McCarthy, P. S. Differential effects of morphine on food and water intake in food deprived and freely feeding rats. Psychopharmacology 72:103–106; 1991.
18. Touzani, K.; Akarid, K.; Velley, L. Modulation of saccharin preference by morphine and naloxone: Inversion of drug effects as a function of saccharin concentration. Pharmacol. Biochem. Behav. 38:37–41; 1991.