CENTRAL ENHANCEMENT OF TASTE PLEASURE BY INTRAVENTRICULAR MORPHINE

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Do centrally-administered opioid agonists stimulate feeding by enhancing the palatability of foods? This hypothesis has been supported by several lines of evidence, including previous 'taste reactivity' studies of the influence of systemic morphine on affective (hedonic and aversive) behavioral reactions to taste palatability. The present study examined whether opioid agonists enhance palatability by acting centrally on brain palatability systems. Here we report the effect of intraventricular microinjections of morphine (0, 12, 25, 50 nmols) on hedonic taste reactions to a 0.12 M sucrose solution. The effect on feeding was also assessed in order to determine whether feeding and palatability enhancement are linked, as would be required by the hypothesis that feeding is due to enhanced palatability. Both hedonic taste reactivity patterns and feeding were significantly increased together by morphine administration into the lateral ventricle. We conclude that opioid-induced enhancement of the hedonic palatability of food is a centrally mediated effect. Enhancement of food palatability may be an important psychological route by which intracranial administration of opioid agonists induce feeding.

Key Words: Feeding; Food Intake; Palatability; Taste reactivity; Lateral ventricle; Opioid; Morphine

INTRODUCTION

Opioid neural systems have long been implicated in the mediation of feeding behavior. For example, ingestion of palatable food naturally activates endogenous opioid brain systems [Blass et al., 1993; Blass & Hoffmeyer, 1991; Gosnell, 1987; Lieblich et al., 1983]. Further, both systemic and intracranial administration of opioid agonists stimulate feeding in animals [for reviews see Cooper et al., 1988; Gosnell, 1987; Levine et al., 1985; Morley et al., 1983; Reid, 1985]. Conversely, opioid antagonists suppress intake of palatable foods [Apfelbaum & Mandenoff, 1981; Calcagnetti et al., 1990; Cooper, et al., 1988; Gosnell, 1987; Gosnell & Majchrzak, 1990; Levine et al., 1982; Morley, et al., 1983; Reid, 1985; Rockwood & Reid, 1982; Rowland et

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al., 1980b; Stapleton et al., 1979]. Thus the degree of activation of brain opioid systems appears correlated with behavioral feeding under a variety of circumstances.

What is the *psychological process* by which opioid agonists stimulate feeding? Opioid agonists might increase food intake by increasing the perceived palatability of food [Cooper & Gilbert, 1984; Cooper & Kirkham, 1993; Cooper & Turkish, 1981; Evans & Vaccarino, 1990; Gosnell & Majchrzak, 1990; Oomura et al., 1986; Wise & Raptis, 1986], by inhibiting caloric satiety [Kirkham & Cooper, 1988], by reducing neophobia [Gosnell, 1987], or by acting on other processes involved in feeding. These hypotheses are not mutually exclusive, and it is likely that opioids enhance feeding by activating more than one psychological process.

In particular, the hypothesis that opioid-induced feeding is mediated at least in part by enhanced taste pleasure is supported by findings in animal studies that opioid agonists selectively increase the intake of palatable food or saccharin over that of ordinary food or water [Evans & Vaccarino, 1990; Milano et al., 1989; Shor-Posner et al., 1986], and by findings that opioid antagonists attenuate the preference for palatable foods or liquids [Apfelbaum & Mandenoff, 1981; Calcagnetti, et al., 1990; Gosnell & Majchrzak, 1990; Levine, et al., 1982; Rockwood & Reid, 1982; Rowland et al., 1980a; Stapleton, et al., 1979]. In this vein, studies of subjective reports of palatability in humans have produced suppression of subjective food pleasantness in some studies [Drewnowski et al., 1992; Fantino et al., 1986], but not in others [Hetherington et al., 1991]. Such discrepancies in findings from studies of human reports are difficult to interpret. They might result in part because human subjective reports of affect may sometimes be distorted by the cognitive processes of interpretation required for their generation [Nisbett & Wilson, 1978]. Under at least some conditions, subjective reports concerning taste pleasantness may fail to accurately reflect basic underlying affective events [Berridge, in press; Mook & Votaw, 1992; Wilson & Schooler, 1991]. For this reason, it is helpful to 'double-check' putative changes in taste palatability induced by opioid agents using a measure, such as affective reactions, that can be applied to animals.

Affective reactions elicited by taste palatability can be measured in animals using the taste-reactivity paradigm developed by Grill and Norgren [Grill & Norgren, 1978b]. The taste reactivity test measures species-typical hedonic and aversive reactions. Hedonic reactions, such as tongue protrusions, paw-licks, etc., are emitted by rats in response to preferred sweet tastes. Aversive reactions, such as gapes, head-shakes, etc., are emitted to bitter tastes. Many manipulations that alter feeding, such as caloric hunger or satiety, sodium hunger, benzodiazepine administration, conditioned taste aversions, brain lesion-induced aphagia, etc., change rat hedonic and aversive reaction patterns in the appropriate direction [Berridge, 1991; Berridge et al., 1984; Berridge & Peciña, 1995; Cabanac & Lafrance, 1990; Grill & Norgren, 1978a; Pelchat et al., 1983; Pfaffmann et

al., 1977]. These manipulations appear to control feeding in part by altering the affective perception of food palatability. A few manipulations change feeding without altering affective reaction patterns, such as electrical stimulation of the lateral hypothalamus and mesotelencephalic dopamine depletion [Berridge & Valenstein, 1991; Berridge et al., 1989]. These manipulations appear to control feeding by acting on a process that is separate from basic affective perceptions of palatability [Berridge, in press]. Thus, the taste reactivity paradigm can be used to discover whether a particular brain system mediates food pleasure and aversion, versus whether it controls feeding by some alternative psychological process [Berridge & Peciña, 1995; Berridge, in press; Grill & Berridge, 1985].

Using the taste reactivity measure of affective reactions, Parker and colleagues found that systemic morphine suppressed aversive reactions to a bitter quinine taste [Parker et al., 1992], and suggested that opioid activation reduced the aversiveness of the bitter taste. To further determine whether opioid activation actually enhances *hedonic* taste palatability, Doyle et al. examined the effect of systemic morphine (2 mg/kg), a dose that stimulates feeding, upon affective reactions to a sucrose-quinine solution directly infused into the mouth [Doyle et al., 1993]. Doyle et al. [1993] found that morphine selectively enhanced positive hedonic reactions to the bittersweet taste, without enhancing aversive reactions, at a time when the feeding increase would be maximal. The authors concluded from their results that opioid-induced feeding is at least partly mediated by an increase in the hedonic palatability of food.

Do opioid agonists enhance hedonic reactions by acting directly on brain systems that process food palatability? All taste-reactivity studies of opioid agents so far have used only systemic administration. By contrast, elicitation of feeding has been shown to result from central, as well as systemic, administration of opioid agonists. In order to determine whether palatability enhancement is produced by central administration, we investigated whether intraventricular opioid microinjections into the forebrain lateral ventricle, which have been shown to elicit feeding [Gosnell, 1987; Imura et al., 1986; Morley, et al., 1983; Robert et al., 1989], also are sufficient to enhance hedonic reactions to a sweet taste.

METHODS

Subjects

Seven Sprague-Dawley male rats (from the breeding colony in our laboratory) weighing 300 to 350 grams at the beginning of the experiment were housed in pairs on a 14-10 LD cycle and tested in individual cages. Rats had free access to food and water. All surgery and testing was performed during the light phase of the cycle. Experiments were conducted between 9:00 a.m. and 5:00 p.m.

Cannulae Implantation

Rats were pretreated with Atropine (1 mg/kg) and anesthetized with Ketamine (100 mg/kg) and Rompun (5 mg/kg). Each animal was surgically implanted with a unilateral intracranial cannula (22 gauge) aimed at either the right or the left lateral ventricle. With Bregma and Lambda in the same horizontal plane, skull holes were drilled and the dura was opened. A 22-gauge stainless steel guide cannula was placed using the stereotaxic coordinates from the atlas of Paxinos and Watson [Paxinos & Watson, 1982]. The coordinates used were A-P= -0.8 mm from bregma, L= ± 1.5 mm, and V=3.5 mm from skull surface. Following surgery, a dummy cannula was placed in the guide cannula to prevent occlusion. Rats were allowed to recover for at least one week before testing.
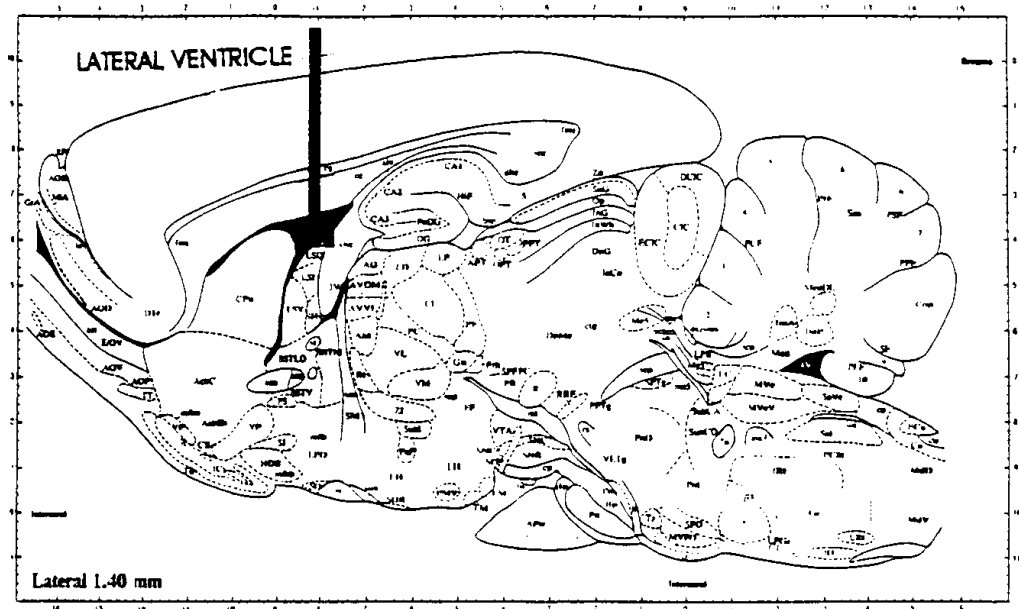

Fig. 1: Lateral ventricle targets. Adapted from Paxinos and Watson [Paxinos and Watson, 1982]

Each rat was also implanted with two bilateral chronic oral cannulae. The cannulae (heat-flared PE 100 tubing) entered the mouth just lateral to the first maxillary molar, ascended lateral to the skull, and exited the head at the dorsal part of the skull, where they were attached to a 19 gauge steel tubing. These cannulae do not interfere with the normal eating behavior of the animal, and they allow the direct infusion of solutions into the mouth. All cannulae were anchored with skull screws and acrylic cement.

Morphine doses and stimuli

Morphine sulfate (Sigma) was dissolved in bacteriostatic physiological saline. The order of drug administration (0, 12, 25, 50 nmols) was randomized across animals except for the first and the last injections which were always vehicle alone (0 nmols morphine). Morphine doses were administrated in a volume of 1.0 µl, and were chosen from the existing literature on morphine-induced stimulation of feeding and from pilot studies performed in our laboratory. The taste stimulus used for oral infusions was a 0.12 M sucrose solution, given in a 1 ml volume. The palatable food used for the feeding test was a cereal mash (1g commercial baby cereal/3 ml of water) given ad lib throughout the intake test.

Habituation

During the 10-day recovery period after surgery, rats were supplied with cereal mash in their home cages to reduce neophobia. In addition, during the last five days of this period, rats were mock-injected each day and exposed to the exact sequence of events that would later be exposed to during the real experiment. The purpose of this initial habituation phase was to familiarize animals with the experimental paradigm and ensure that stable baseline levels for both feeding and taste reactivity would be attained by the time microinjections began.

Feeding Tests

Testing began 10 days after surgery and continue every other day for 10 days. Rats were taken in individual cages to the testing room and food pellets were removed from the top of the cages. Rats were intracranially injected with either morphine sulfate or the saline vehicle, and left undisturbed for three hours. On each test day, a rat received either morphine or vehicle in a counterbalanced order. Since previous reports on opioid-induced feeding suggested that stimulation of feeding is greatest around two to three hours after the drug injection [Stanley, Lanthier, and Leibowitz, 1989; Woods and Leibowitz, 1985], both taste reactivity and feeding tests were administrated in that order beginning three hours after the microinjection.

Taste reactivity test

Three hours after administration of the drug, one of the rat's oral cannulae was connected to a stimulus delivery tube, consisting of PE 50 tubing attached to PE 10 fine tubing. The rat was then placed in a cylindrical test chamber. After a ten minute habituation period, a 1 ml volume of the 0.12 M sucrose solution was infused into the mouth of the animal at a constant rate (1 ml/min) during one minute. The behavior of the rat was videotaped during testing via a mirror mounted beneath the transparent floor, which allowed the camera to zoom up so that the face and the mouth of the rat filled the entire screen. The entire taste reactivity procedure took approximately 12 minutes.

Videoanalysis of taste reactivity records

The videotaped behavior of each rat was scored (frame-by-frame to 1/10 speed) for the occurrence of hedonic, aversive, and neutral reactivity components (see, [Berridge and Peciña, 1995; Grill and Berridge, 1985] for a discussion of taste reactivity analysis and taste reactivity components and classification). Hedonic actions were *paw licking; lateral tongue protrusions*, non-rhythmic protrusion past the lip followed by forward extension, lasting about 160 ms; and tongue protrusions, *rhythmic tongue protrusion* along the midline, with a cycle length of roughly 160 ms. Neutral components were *rhythmic mouth movements* at the same or lower frequency as rhythmic tongue protrusion; and *passive dripping,* the passive leaking of fluid from the mouth. Aversive actions were *gapes*, large openings of the mandible and retraction of the lower lips lasting about 125 ms; *chin rubbing,* bringing the mouth in direct contact with the floor and projecting the body forward; *face washing,* either a single wipe over the face with the paws or a bout of several wipes: *forelimb flails*, shaking of the forelimb with a frequency of greater than 60 HZ; head shaking, at greater than 60 HZ; and *paw treading*, planting of the limbs on the floor and alternating forceful strikes forward and back; and rapid locomotion around the chamber.

Videotapes were scored by an observer who was blind to microinjection condition in a slow motion analysis at 1/30 to 1/10 normal speed. For the purpose of quantifying the number of responses emitted, discrete actions such as lateral tongue protrusions, gapes, chin rubs, forelimb flails and head shaking, and bouts of face washing, paw treading, and locomotion were counted each time they occurred. Continuous actions that typically persist for relatively long periods were counted as folfows: paw licks, mouth movements, passive dripping, face washing and locomotion were counted in 5 sec. bins (any occurrence of these behaviors up to 5 sec. in duration was counted as a single occurrence). Rhythmic tongue protrusions were scored in the same way in 2 sec. bins.

Verification of the cannulae placement

At the completion of the experiment, rats were deeply anesthetized with sodium pentobarbital (5 mg/kg). India ink was microinjected into the lateral ventricle, using the same procedure as for morphine. Th rats were perfused intracardially ten minutes later. The brains were removed and cut midsagitally. Th presence of ink in the lateral ventricle verified the correct location of the ventricular cannulae.

Statistical Analysis

The results were evaluated for statistical significance by a one-way ANOVA for repeated measures with dose of morphine sulfate as the main factor, and by post hoc Newman-Keuls tests for paired comparisons.

RESULTS

Feeding

Microinjections of morphine sulfate administration into the lateral ventricle significantly stimulater feeding, $F_{(3, 24)}= 3.02$, $p<0.05$ (Fig.2). Individual post-hoc comparisons of the average amount of baby cerea ingested showed that morphine sulfate significantly stimulated feeding at all the doses tested: 12 nmols ($p<0.05$ Newman-Keuls), 25 nmols ($p<0.01$) and 50 nmols ($p<0.05$). The intermediate dose used, 25 nmols, proved t be the most effective one for increasing intake. Under the effects of this dose, animals ingested nearly twice a much cereal mash as they did after the vehicle alone.

Taste Reactivity

Microinjections of morphine into the lateral ventricle significantly enhanced the number of hedonic responses elicited by the 0.12 M sucrose solution, $F_{(3,18)}=3.24$, $p<0.05$; (Fig.3). Although morphine appeared to increase the number of hedonic reactions at all the doses tested, a Newman-Keuls comparison indicated that only the intermediate dose, 25 nmols, significantly increased the number of hedonic reactions over baseline levels.
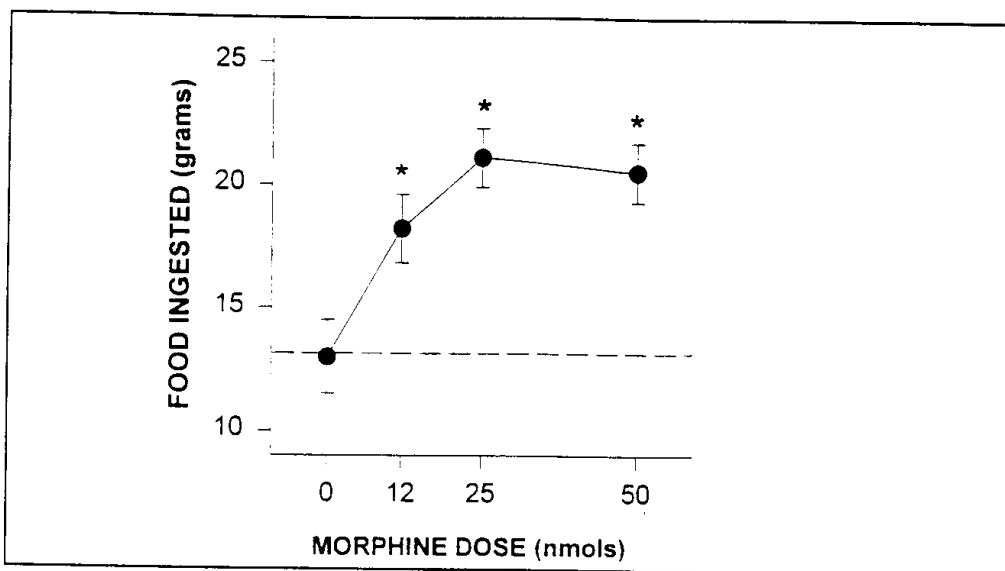
Fig. 2: Lateral ventricle microinjections of morphine enhance feeding. Consumption in a 1-h voluntary intake test of cereal mash after intraventricular morphine (ANOVA, $p < 0.05$)
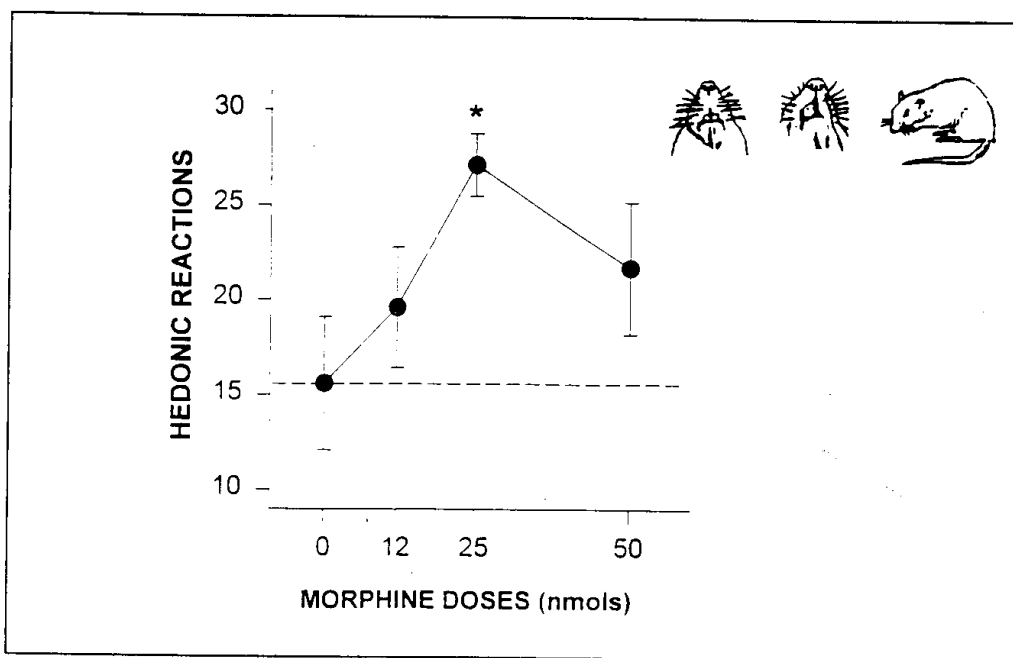

Fig. 3: Lateral ventricle microinjections of morphine enhance hedonic taste reactions. Hedonic taste reactions elicited by a 0.12 M sucrose solution after intraventricular morphine (ANOVA, $p < 0.05$)

DISCUSSION

Microinjections of morphine into the lateral ventricle stimulated intake of a cereal mash and simultaneously enhanced hedonic affective reactions emitted in response to a 0.12 M sucrose solution. These results support the hypothesis that opioid agonists stimulate feeding behavior by enhancing the hedonic perception of food palatability. These results provide the first direct evidence that opioid enhancement of hedonic taste reactivity is a central effect of the drug on brain systems. Morphine appears to activate brain systems that process hedonic taste palatability. The relative contribution of particular opioid receptor subtypes to palatability enhancement remains to be determined.

Of the doses tested (12, 25 and 50 nmols), the most effective dose for feeding enhancement was 25 nmols. Rats ingested almost twice the amount of cereal mash after this dose as they did after vehicle control microinjections. The same 25 nmol dose also produced the strongest enhancement of taste pleasure, as assessed by hedonic reaction patterns. Hedonic reactions to 0.12 M sucrose were nearly doubled by this dose compared to vehicle control levels. The similar magnitude of the effects on intake and on hedonic taste reactivity potentiation suggests that palatability enhancement may mediate the stimulation of feeding.

The anatomical site responsible for opioid-induced enhancement of taste pleasure is an important question that remains to be answered by future studies. Many different brain sites have been shown to be able to support opioid-induced feeding. For example, food intake is increased by opioid microinjections into the ventral tegmentum, the paraventricular and ventromedial nuclei of the hypothalamus, the nucleus accumbens, and the amygdala [Badiani et al., 1995; Bakshi & Kelley, 1993a; Bakshi & Kelley, 1993b; Evans & Vaccarino, 1990; Gosnell, 1988; Hamilton & Bozartz, 1988; Jenck et al., 1986; Leibowitz & Hor, 1982; Majeed et al., 1986; McLean & Hoebel, 1983; Mucha & Iversen, 1986; Nencini & Stewart, 1990; Noel & Wise, 1993; Stanley et al., 1989]. Whether all of these structures are responsible for palatability enhancement, or only some of them, remains to be seen. Although it is possible that all sites which support feeding would also enhance hedonic palatability, it is equally possible that some sites stimulate feeding via other functions. For example, opioid agents have been reported to modulate hypothalamic neuronal responsiveness to glucose [Aou et al., 1984; Karadi et al., 1992; Nishino et al., 1987; Ono et al., 1982; Ono et al., 1985; Oomura et al., 1974]. Such an effect might or might not alter hedonic reactions to taste, since at least some brain manipulations that stimulate feeding increase intake without enhancing palatability [Berridge, in press; Berridge & Valenstein, 1991].

Although anatomical sites that support opioid-induced feeding provide the most likely candidates for the opioid substrates of palatability, it is also possible that opioid modulation of palatability might occur earlier in the processing of the taste signal itself. Opioid systems do exist in the primary gustatory pathway: for example, in the nucleus of the solitary tract (first relay nucleus) and in the pontine parabrachial nucleus (second relay nucleus) [Carr et al., 1991; Herman & Novin, 1980; Mansour et al.,1987]. Benzodiazepine-induced hedonic

nhancement, which acts via $GABA_A$ neurotransmitter systems, has already been shown to act via brainstem ystems [Berridge, 1988; Peciña & Berridge, 1992; Peciña & Berridge, submitted]. Although this may not be irectly relevant to opioid-induced hedonic enhancement, it at least lends plausibility to the hypothesis that rainstem substrates are capable of mediating changes in palatability induced by pharmacological agents.

Future studies, which combine cannulae mapping with taste reactivity tests, will be needed in order to iscover which among these various candidate brain structures contains the site(s) responsible for the central nhancement of hedonic taste palatability by opioid agonists. In any case, we can conclude from the present esults that opioid agonists may stimulate feeding by enhancing the perceived palatability of food, and that alatability enhancement results directly from the action of opioid agonists on central brain systems.

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REFERENCES

ou, S., Oomura, Y., Lenard, L., Inokuchi, A. and Minami, T. (1984) Behavioral significance of monkey hypothalamic glucose-sensitive neurons. Brain Res. 302, 69-74.

ofelbaum, M. and Mandenoff, A. (1981) Naltrexone suppresses hyperphagia induced in the rat by a highly palatable diet. Pharmacol. Biochem. & Behav. 15, 89-91.

idiani, A., Leone, P., Noel, M. B. and Steward, J. (1995) Ventral tegmental area opioid mechanisms and modulation of ingestive behavior. Brain Res. 670, 264-276.

ikshi, V. P. and Kelley, A. E. (1993a) Feeding induced by opioid stimulation of the ventral striatum: role of opiate receptor subtypes. J. Pharmacol. Exp. Ther. 265, 1253-1260.

ikshi, V. P. and Kelley, A. E. (1993b) Striatal regulation of morphine-induced hyperphagia: an anatomical mapping study. Psychopharmacology 111, 207-214.

erridge, K. C. (1988) Brainstem systems mediate the enhancement of palatability by chlordiazepoxide. Brain Res.447, 262-268.

erridge, K. C. (1991) Modulation of taste affect by hunger, caloric satiety, and sensory- specific satiety in the rat. Appetite 16, 103-120.

erridge, K. C. (in press) Neural systems of wanting and liking in food reward: a taste reactivity analysis of process and brain substrates. Neurosci. Biobeh. Rev.

erridge, K. C., Flynn, F. W., Schulkin, J. and Grill, H. J. (1984) Sodium depletion enhances salt palatability in rats. Behav. Neurosci. 98, 652-660.

erridge, K. C. and Peciña, S. (1995) Benzodiazepines, appetite, and taste palatability. Neurosci. Biobehav. Rev.19, 121-131.

erridge, K. C. and Valenstein, E. S. (1991) What psychological process mediates feeding evoked by electrical stimulation of the lateral hypothalamus? Behav. Neurosci. 105, 3-14.

erridge, K. C., Venier, I. L. and Robinson, T. E. (1989) Taste reactivity analysis of 6-hydroxydopamine-induced aphagia: implications for arousal and anhedonia hypotheses of dopamine function. Behav. Neurosci. 103, 36-45.

ass, E. M., Cramer, C. P. and Fanselow, M. S. (1993) The development of morphine-induced antinociception in neonatal rats: a comparison of forepaw, hindpaw, and tail retraction from a thermal stimulus. Pharm. Biochem. Behav.44, 643-649.

Blass, E. M. and Hoffmeyer, L. B. (1991) Sucrose as an analgesic for newborn infants. Pediatrics 87, 215-218.

Cabanac, M. and Lafrance, L. (1990) Postingestive alliesthesia: the rat tells the same story. Physiol. Behav. 47, 539-543.

Calcagnetti, D. J., Calcagnetti, R. L. and Fanselow, M. S. (1990) Centrally administered opioid antagonists, norbinaltorphimine, 16-methyl cyprenorphine and MR2266, suppress intake of a sweet solution. Pharmacol. Biochem. Behav. 35, 69-73.

Carr, K. D. (1991) Effects of parabrachial opioid antagonism on stimulation-induced feeding. Behav. Neurosci.545, 283-286.

Cooper, S. J. and Gilbert, D. B. (1984) Naloxone suppresses fluid consumption in tests of choice between sodium chloride solutions and water in male and female water-deprived rats. Psychopharmacology (Berlin) 84, 362-367.

Cooper, S. J., Jackson, A., Kirkham, T. C. and Turkish, S. (1988) Endorphins, opiates and food intake. In: Endorphins, opiates and behavioral processes (Eds.), pp. 143-186. Willey, Chichester.

Cooper, S. J. and Kirkham, T. C. (1993) Opioid mechanisms in the control of food consumption and taste preferences. In: Opioids, part I and II (Eds.), pp. 239-262. Springer-Verlag, Berlin.

Cooper, S. J. and Turkish. S. (1981) Food and water intake in the non-deprived pigeon after morphine and naloxone administration. Neuropharmacology 20, 877-883.

Doyle, T. G., Berridge, K. C. and Gosnell, B. A. (1993) Morphine enhances hedonic taste palatability in rats. Pharmacol. Biochem. Behav. 46, 745-749.

Drewnowski, A., Krahn, D. D., Demitrack, M. A., Nairn, K. and Gosnell, B. A. (1992) Taste responses and preferences for sweet high-fat foods: evidence for opioid involvement. Physiol. Behav. 51, 371-379.

Evans, K. R. and Vaccarino, F. J. (1990) Amphetamine- and morphine-induced feeding: evidence for involvement of reward mechanisms. Neurosci. Biobehav. Rev. 14, 9-22.

Fantino, M., Hosotte, J. and Apfelbaum, M. (1986) An opioid antagonist, naltrexone, reduces preference for sucrose in humans. Am. J. Physiol. 251, R91-96.

Gosnell, B. A. (1987) Central structures involved in opioid-induced feeding. Fed. Proc. 46, 163-167.

Gosnell, B. A. (1988) Involvement of mu opioid receptors in the amygdala in the control of feeding. Neuropharmacology 27, 319-326.

Gosnell, B. A. and Majchrzak, M. J. (1990) Centrally administered opioid peptides stimulate saccharin intake in nondeprived rats. Pharmacol. Biochem. Beh. 33, 805-810.

Grill, H. J. and Berridge, K. C. (1985) Taste reactivity as a measure of the neural control of palatability. In: Progress in Psychobiology and Physiological Psychology (Eds.), pp. 1-61. Academic Press, Orlando.

Grill, H. J. and Norgren, R. (1978a) The taste reactivity test. I. Mimetic responses to gustatory stimuli in neurological normal rats. Brain Res. 143, 263-279.

Grill, H. J. and Norgren, R. (1978b) The taste reactivity test. II. Mimetic responses to gustatory stimuli in chronic thalamic and chronic decerebrate rats. Brain Res. 143, 281-297.

Hamilton, M. E. and Bozartz, M. A. (1988) Feeding elicited by dinorphin (1-13) microinjections into the ventral tegmenta area in rats. Life Sci. 43, 941-946.

Hetherington, M. M., Vervaet, N., Blass, E. and Rolls, B. J. (1991) Failure of naltrexone to affect the pleasantness or intake of food. Pharmacol. Biochem. Behav. 40, 185-190.

Herman, B. H., Leslier, F. and Goldstein, A. (1980) Behavioral effects and in vivo degradation of intraventricularly administered dynorphin-(1-13) and D-Ala^2 dynorphin-(11) in rats. Life Sci. 42, 1705-1712.

Imura, H., Nakao, K., Yanaihara, N., Katsuura, G. and Nakamura, M. (1986) Potent action of leumorphine on consummatory behaviors in rats: comparison with other opioid peptides. Neuroendocrinology 44, 142-148.

Jenck, F., Gratton, A. and Wise, R. A. (1986) Effects of pimozide and naloxone on latency for hypothalamically induced eating. Brain Res. 375, 329-337.

Karadi, Z., Oomura, Y., Nishino, H., Scott, T. R., Lenard, L. and Aou, S. (1992) Responses of lateral hypothalamic glucose-sensitive and glucose-insensitive neurons to chemical stimuli in behaving rhesus monkeys. J. Neurophysiol.67, 389-400.

Kirkham, T. C. and Cooper, S. J. (1988) Attenuation of sham feeding by naloxone is stereospecific: Evidence for opioid mediation of oro-sensory reward. Physiol. Behav. 43, 845-847.

Leibowitz, S. F. and Hor, L. (1982) Endorphinergic and alpha-noradrenergic systems in the paraventricular nucleus: effects on eating behavior. Peptides 3, 421-428.

Levine, A. S., Morley, J. E., Gosnell, B. A., Billington, C. L. and Bartness, T. J. (1985) Opioids and consummatory behavior. Brain Res. Bull. 14, 663-672.

Levine, A. S., Murray, S. S., Kneip, J., Grace, M. and Morley, J. E. (1982) Flavour enhances the antidipsogenic effect of naloxone. Physiol. & Behav. 28, 23-25.

Lieblich, I., Cohen, E., Ganchrow, J. R., Blass, E. M. and Bergmann, F. (1983) Morphine tolerance in genetically selected rats induced by chronically elevated saccharin intake. Science 221, 871-873.

Majeed, N. H., Przewlocka, B., Wedzony, K. and Przewlocka, R. (1986) Stimulation of food intake following opioid microinjection into the nucleus accumbens septi in rats. Peptides 7, 711-716.

Mansour, A., Khachaturian, H., Lewis, M. E., Akil, H. and Watson, S. J. (1987) Autoradiographic differentiation of mu, delta, and kappa opioid receptors in the rat forebrain and midbrain. J. Neurosci. 7, 2445-2464.

McLean, S. and Hoebel, B. G. (1983) Feeding induced by opiates injected into the paraventricular hypothalamus. Peptides 4, 287-292.

Milano, W. C., Wild, K. D., Hui, Y., Hubbell, C. L. and Reid, L. D. (1989) PCP, THC, ethanol and morphine and consumption of palatable solutions. Pharmacol. Biochem. Behav. 31, 893-897.

Mook, D. G. and Votaw, M. C. (1992) How important is hedonism? Reasons given by college students for ending a meal. Appetite 18, 69-75.

Morley, J. E., Levine, A. S., Yim, G. K. and Lowy, M. T. (1983) Opioid modulation of appetite. Neurosci. Biobehav. Rev. 7, 281-305.

Mucha, R. F. and Iversen, S. D. (1986) Increased food intake after opioid microinjections into nucleus accumbens and ventral tegmental area of rat. Brain Res. 397, 214-224.

Nencini, P. and Stewart, J. (1990) Chronic systemic administration of amphetamine increases food intake to morphine, but not to U50-488H, microinjected into the ventral tegmental area in rats. Brain Res. 527, 254-258.

Nisbett, R. W. and Wilson, T. D. (1978) Telling more than we can know: verbal reports on mental processes. Psychological Rev. 84, 231-259.

Nishino, H., Oomura, Y., Plata-Salaman, C. R. and Morimoto, M. (1987) Catecholaminergic mechanisms of feeding-related lateral hypothalamic activity in the monkey. Brain Res. 405, 56-67.

Noel, M. B. and Wise, R. A. (1993) Ventral tegmental injections of morphine but not U-50,488H enhance feeding in food-deprived rats. Brain Res. 632, 68-73.

Ono, T., Nishino, H., Fukuda, M., Sasaki, K., Muramoto, K. and Oomura, Y. (1982) Glucoresponsive neurons in rat ventromedial hypothalamic tissue slices in vitro. Brain Res. 232, 494-499.

Ono, T., Sasaki, K., Nakamura, K. and Norgren, R. (1985) Integrated lateral hypothalamic neural responses to natural and artificial rewards and cue signals in the rat. Brain Res. 327, 303-306.

Oomura, Y., Nishino, H., Aou, S. and Lenard, L. (1986) Opiate mechanisms in reward-related responses during operant feeding behavior of the monkey. Brain Res. 365, 335-339.

Oomura, Y., Ooyama, H., Sugimori, M., Nakamura, T. and Yamada, Y. (1974) Glucose inhibition of the glucose-sensitive neuron in the rat lateral hypothalamus. Nature 247, 284-286.

Parker, L. A., Maier, S., Rennie, M. and Crebolder, J. (1992) Morphine- and naltrexone-induced modification of palatability: analysis by the taste reactivity test. Behav. Neurosci. 106, 999-1010.

Paxinos, G. and Watson, C. (1982) The rat brain in stereotaxic coordinates. Academic Press, New York.

Peciña, S. and Berridge, K. C. (1992) Fourth ventricle microinjections of diazepam enhance hedonic reactions to taste. Soc. Neurosci. Abstr. 18, 1231.

Peciña, S. and Berridge, K. C. (submitted) Brainstem mediates benzodiazepine enhancement of taste palatability: comparison of diazepam microinjections into fourth versus lateral ventricles. Brain Res.

Pelchat, M. L., Grill, H. J., Rozin, P. and Jacobs, J. (1983) Quality of acquired responses to tastes by Rattus Norvegicus depends on type of associated discomfort. J. Comp. Psycho. 97, 140-153.

Pfaffmann, C., Norgren, R. and Grill, H. J. (1977) Sensory affect and motivation. Ann. N. Y. Acad. Sci. 290, 18-34.

Reid, L. D. (1985) Endogenous opioid peptides and regulation of drinking and feeding. Am. J. Cline. Nut. 42, 1099-1132.

Robert, J., Orosco, M., Rouch, C., Jacquot, C. and Cohen, Y. (1989) Effects of opiate agonists and antagonists on food intake and brain neurotransmitters in normophagic and obese "cafeteria" rats. Pharmacol. Biochem. Behav. 34, 577-583.

Rockwood, G. A. and Reid, L. D. (1982) Naloxone modifies sugar-water intake in rats drinking with open gastric fistulas. Physiol. Behav. 29, 1175-1178.

Rowland, D. L., Perrings, T. S. and Thommes, J. A. (1980a) Comparison of androgenic effects on food intake and body weight in adult rats. Physiol. Behav. 24, 205-209.

Rowland, N., Marques, D. M. and Fisher, A. E. (1980b) Comparison of the effects of brain dopamine-depleting lesions upon oral behaviors elicited by tail pinch and electrical brain stimulation. Physiol. Behav. 24, 273-281.

Shor-Posner, G., Azar, A. P., Filart, R., Tempel, D. and Leibowitz, S. F. (1986) Morphine-stimulated feeding: Analysis of macronutrient selection and PVN lesions. Pharmacol. Biochem. & Behav. 24, 931-936.

Stanley, B. G., Lanthier, D. and Leibowitz, S. F. (1989) Multiple brain sites sensitive to feeding stimulation by opioid agonists: a cannula mapping study. Pharmacol. Biochem. Behav. 31, 825-832.

Stapleton, J. M., Lind, M. D., Merriman, V. J. and Reid, L. D. (1979) Naloxone inhibits diazepam-induced feeding in rats. Life Sci. 24, 2421-2425.

Wilson, T. D. and Schooler, J. W. (1991) Thinking too much: introspection can reduce the quality of preferences and decisions. J. Pers. Soc. Psychol. 60, 181-192.

Wise, R. A. and Raptis, L. (1986) Effects of naloxone and pimozide on initiation and maintenance measures of free feeding. Brain Res. 368, 62-68.

Woods, J. S. and Leibowitz, S. F. (1985) Hypothalamic sites sensitive to morphine and naloxone: effects on feeding behavior. Pharmacol. Biochem. Behav. 23, 431-438.