Available online at www.sciencedirect.com
SCIENCE DIRECT®
European Journal of Pharmacology 478 (2003) 105–110
www.elsevier.com/locate/ejphar

Effect of morphine, naloxone and histamine system on water intake in adult male rats

Maryam Eidi[a], Shahrbanoo Oryan[b,*], Akram Eidi[c], Leili Sepehrara[b]

[a] Department of Biology, Varamin Unit, Islamic Azad University, Varamin, Iran
[b] Department of Biology, Science Faculty, Teacher Training University, Shahid Mofateh Street, P.O. Box 15815-1455, Tehran, Iran
[c] Department of Biology, Science and Research Unit, Islamic Azad University, Tehran, Iran

Received 6 January 2003; received in revised form 16 July 2003; accepted 22 July 2003

Abstract

The present study investigated the interaction between histamine and opioid systems on water intake in adult male rats. Intracerebroventricular (i.c.v.) injections were carried out in all experiments. Water intake was measured 1 h after drug injections. Administration of histamine (40–80 μg/rat) and naloxone (0.5–1 μg/rat) increased, while morphine (2.5 μg/rat), pyrilamine (25–50 μg/rat), the histamine H_1 receptor antagonist, and ranitidine (10–20 μg/rat), the histamine H_2 receptor antagonist, decreased water intake in isolated rats. Blockade of histamine H_1 and H_2 receptors attenuated the histamine-induced response. Pyrilamine, but not ranitidine, increased the inhibitory effect induced by morphine. Also, pharmacological blockade of histamine H_1 and H_2 receptors decreased the naloxone-induced effect on water intake. It is concluded that the histaminergic system may have a close interaction with morphine and naloxone on drinking behavior.

Keywords: Water intake; Drinking; Histamine system; Morphine; Naloxone; (rat)

1. Introduction

Histamine can be found in a restricted population of neurons originating from the tuberomammillary nucleus and projecting diffusely to several brain areas. The three subtypes of histamine receptors (H_1, H_2, H_3) are distributed in almost all parts of the brain of mammalian species (Schwartz et al., 1991; Wada et al., 1991). Central histaminergic neurons have been implicated in many physiological processes, such as circadian rhythms, thermoregulation, learning and memory and cardiovascular and neuroendocrine regulation (Onodera et al., 1994; Schwartz et al., 1991; Wada et al., 1991).

Several lines of evidence also suggest that neuronal histamine may be involved in the control of water intake (Onodera et al., 1994; Schwartz et al., 1991). Histamine is a potent dipsogen when injected into the anterior, lateral, preoptic or anterior–lateral hypothalamus (Leibowitz, 1973). Inhibition of histamine catabolism with metoprine increases water intake and induces diuresis (Lecklin and Tuomisto, 1995). It has been suggested that peripheral mechanisms may also be involved in the dipsogenic effect of histamine, because the amine elicits drinking even after its systemic administration (Clapham and Kilpatrick, 1993; Houpt et al., 1986; Kraly and Arias, 1990; Specht and Spear, 1989). However, a decreased tone in the endogenous histaminergic system after α-fluoromethylhistidine (α-FMH) administration does not cause any change in water intake (Ookuma et al., 1989; Orthon-Gambill and Salamon, 1992; Tuomisto et al., 1994); therefore, it is unclear whether endogenous histamine is involved in the regulation of water balance. Furthermore, in addition to its well-documented modulation of food intake, the endogenous opioid system also plays a role in water intake (Cooper et al., 1988; Levine et al., 1985).

To study the roles of postsynaptic histamine H_1 and H_2 receptors and their interactions with the opioid system in the regulation of water intake, the present experiment compared the effects of i.c.v.-administered histamine, histamine H_1 and H_2 receptor antagonists alone or in combination with opioid agents on water intake in rats.

* Corresponding author. Tel.: +98-21-2712499; fax: +98-21-2705836.
E-mail address: sh-oryan@saba.tmu.ac.ir (S. Oryan).

0014-2999/$ - see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/j.ejphar.2003.07.001

2. Materials and methods

2.1. Animals

Male Wistar rats weighing 200–250 g were housed individually in cages at 22–24 °C under a 12-h light/12-h dark cycle and with a relative air humidity of 40–60%. Rats had continuous access to food and tap water through a stainless steel spout attached to a glass-graduated cylinder mounted on the wall of the cage. All experiments were performed in accordance with institutional guidelines for animal use.

2.2. Cannula guide implantation

For central administration of drugs, the rats were implanted with a 21-gauge (0.8 mm) stainless steel guide cannula aimed at the lateral ventricle (David Kopf Instruments, USA). Implantation was done under ketamine-xylizine (100 mg/kg ketamine-5 mg/kg xylizine) anesthesia using stereotaxic coordinates taken from the atlas of Paxinos and Watson (1986), and was performed at least 5–7 days before testing. The coordinates used were 0.8 mm posterior to bregma, 1.6 mm lateral to the midline and 3.4 mm below the top of the skull. The cannula was fixed to the skull using one screw and dental acrylic. A stylet was inserted into the cannula to keep it patent prior to injections.

2.3. Intracerebroventricular (i.c.v.) injections

The rats were gently restrained by hand, the stylet was withdrawn from the guide cannula and a 27-gauge injection needle (0.5 mm beyond the tip of the implanted guide cannula) was inserted. The injection needle was attached to a 5-μl Hamilton syringe by a polyethylene tube. The injection solutions were administered in a total volume of 2 μl. The injection needle was retained in the guide cannula for an additional 30 s after injection to facilitate diffusion of the drugs.

2.4. Drugs

The drugs included histamine dihydrochloride (Merck, Germany), pyrilamine maleate, the histamine H_1 receptor antagonist (Sigma, Poole, UK), ranitidine, the histamine H_2 receptor antagonist (Roemmers, Argentina), morphine sulphate, the opioid receptor agonist (Temad, Iran), and naloxone dihydrochloride, the opioid receptor antagonist (Akzonobel, Netherlands). All the drugs were dissolved in saline. The drugs were used (i.c.v.) in a volume of 2 μl/rat.

2.5. Experimental procedure

The experiments were performed in conscious freely moving isolated rats 5–7 days after brain surgery. All rats were deprived of water for 24 h before each test day. After 24 h of water deprivation, the drugs were injected (i.c.v.) and the water bottles were returned to the cages. All rats received two injections: either a control saline injection followed 20 min later by injection of a drug, or drug injection followed 20 min later by another to determine the effect of first drug on the response to the second. In the control group, saline was injected 20 min before a second administration of saline. Immediately after drug administration, water intake was recorded for 1 h by reading from the graduated glass cylinder mounted on the wall of the cages.

2.6. Data analysis

Overall treatment effects of the experiments were examined using a repeated-measures two-way analysis of variance (ANOVA) and post hoc comparisons. The criterion for statistical significance was $P<0.05$.

2.7. Histology

Immediately after the water intake test, all rats were given 2 μl of methylene blue in a lateral ventricle, anesthetized with a high dose of ether and perfused transcardically with a phosphate-buffered saline solution (pH = 7.4). The brains were removed and placed in formaldehyde (4%). After 3 days, the brains were sliced into 60-μm-thin slices. Data from rats with incorrect placement were excluded from the analysis.

3. Results

Fig. 1 shows the effect of histamine alone or in combination with pyrilamine and ranitidine on water intake. Two-way ANOVA indicated that histamine (80 μg/rat) interacted with pyrilamine (25 and 50 μg/rat) and ranitidine (10 and 20 μg/rat) [pyrilamine, $F(2,42)=18.0$, $P<0.0001$; histamine, $F(1,42)=29.28$, $P<0.0001$; pyrilamine × histamine, $F(2,42)=3.24$, $P<0.05$ and ranitidine, $F(2,42)=25.06$, $P<0.0001$; histamine, $F(1,42)=40.44$, $P<0.0001$; ranitidine × histamine, $F(2,42)=3.66$, $P<0.05$]. Further analysis showed that injection of pyrilamine or ranitidine decreased water intake, while histamine increased this response. Blockade of both histamine H_1 and H_2 receptors attenuated the histamine-induced response.

Fig. 2 shows the effect of morphine alone or in combination with histamine on water intake. Two-way ANOVA indicated that the different doses of histamine (40 and 80 μg/rat) interacted with morphine (2.5 μg/rat) [histamine, $F(2,42)=6.39$, $P<0.01$; morphine, $F(1,42)=37.79$, $P<0.0001$; histamine × morphine, $F(2,42)=10.56$, $P<0.001$]. Further analysis showed that histamine increased, while morphine decreased, water intake. Histamine (40 μg/rat) increased the inhibitory effect of morphine on water consumption.

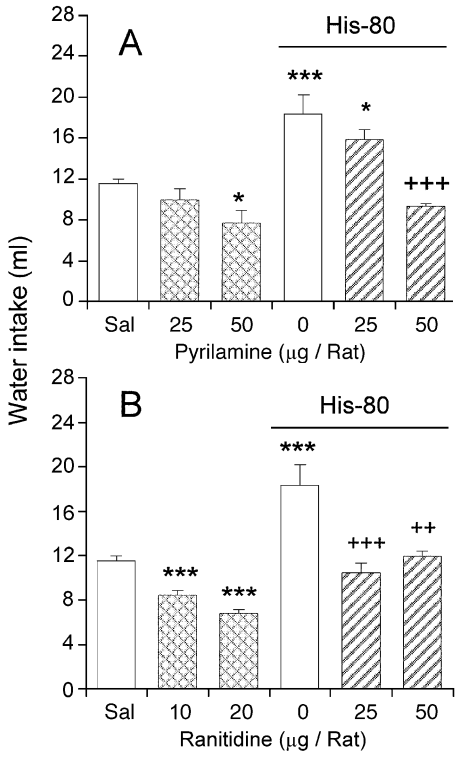

Fig. 1. Effect of pyrilamine (A) or ranitidine (B) in the presence or absence of histamine on water intake. Rats were injected (i.c.v.) either with saline (2 μg/rat) or different doses of pyrilamine (25 and 50 μg/rat) or ranitidine (10 and 20 μg/rat). Histamine (80 μg/rat) was administered 15 min after injections of pyrilamine or ranitidine, and water intake was measured for 1 h. Each column represents the mean ± S.E.M. for eight rats. $*P<0.05$, $***P<0.001$ different from saline group. $++P<0.01$, $+++<0.001$ different from histamine control group.

Fig. 3 shows the effect of morphine alone or in combination with pyrilamine and ranitidine on water intake. Two-way ANOVA indicated that morphine (2.5 μg/rat) interacted with pyrilamine (25 and 50 μg/rat) and ranitidine (10 and 20 μg/rat) [pyrilamine, $F(2,42)=0.32$, $P>0.05$; morphine, $F(1,42)=2.11$, $P>0.05$; pyrilamine × morphine, $F(2,42)=10.5$, $P<0.001$ and ranitidine, $F(2,42)=5.38$, $P<0.01$; morphine, $F(1,42)=16.32$, $P<0.001$; ranitidine × morphine, $F(2,42)=4.14$, $P<0.05$]. Further analysis showed that in-

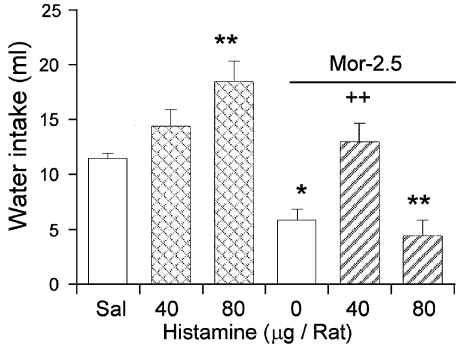

Fig. 2. Effect of histamine in the presence or absence of morphine on water intake. Rats were injected (i.c.v.) with either saline (2 μg/rat) or different doses of histamine (40 and 80 μg/rat). Morphine (2.5 μg/rat) was administered 15 min after injection of histamine, and water intake was measured for 1 h. Each column represents the mean ± S.E.M. for eight rats. $*P<0.05$, $**P<0.01$ different from saline group. $++P<0.01$ different from morphine control group.

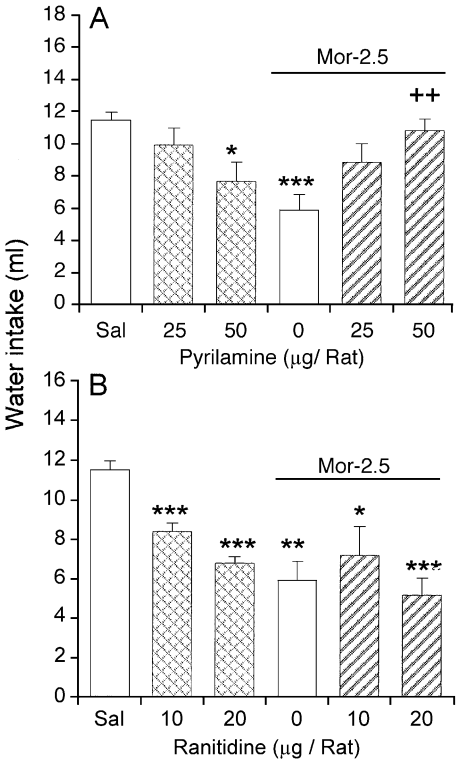

Fig. 3. Effect of pyrilamine (A) or ranitidine (B) in the presence or absence of morphine on water intake. Rats were injected (i.c.v.) with either saline (2 μg/rat) or different doses of pyrilamine (25 and 50 μg/rat) or ranitidine (10 and 20 μg/rat). Morphine (2.5 μg/rat) was administered 15 min after injection of pyrilamine or ranitidine, and water intake was measured for 1 h. Each column represents the mean ± S.E.M. for eight rats. $*P<0.05$, $**P<0.01$, $***P<0.001$ different from saline group. $++P<0.01$ different from morphine control group.

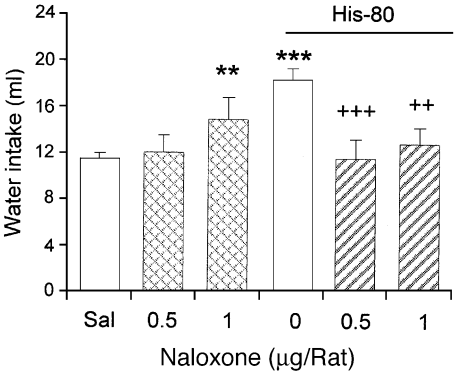

Fig. 4. Effect of naloxone in the presence or absence of histamine on water intake. Rats were injected (i.c.v.) with either saline (2 μg/rat) or different doses of naloxone (0.5 and 1 μg/rat). Histamine (80 μg/rat) was administered 15 min after injection of naloxone and water intake was measured for 1 h. Each column represents the mean ± S.E.M. for eight rats. $**P<0.01$, $***P<0.001$ different from saline group. $++P<0.01$, $+++P<0.001$ different from histamine control group.

jection of pyrilamine, ranitidine and morphine decreased water intake. Blockade of histamine H_1 receptors attenuated the morphine-induced response, while ranitidine did not change the morphine-induced inhibitory response.

Fig. 4 shows the effect of histamine alone or in combination with naloxone on water intake. Two-way ANOVA indicated that the different doses of naloxone (0.5 and 1 μg/rat) interacted with histamine (80 μg/rat) [naloxone, $F(2,42)=4.98$, $P<0.05$; histamine, $F(1,42)=4.29$, $P<0.05$; naloxone × histamine, $F(2,42)=8.44$, $P<0.001$]. Further analysis showed that histamine and naloxone increased water intake. Blockade of opioid receptors by naloxone decreased the histamine-induced response.

Fig. 5 shows the effect of naloxone alone or in combination with pyrilamine and ranitidine on water intake. Two-way ANOVA indicated that naloxone (1 μg/rat) interacted with pyrilamine (25 and 50 μg/rat) and ranitidine (10 and 20 μg/rat) [pyrilamine, $F(2,42)=15.03$, $P<0.0001$; naloxone, $F(1,42)=7.4$, $P<0.01$; pyrilamine × naloxone, $F(2,42)=0.97$, $P>0.05$ and ranitidine, $F(2,42)=12.8$, $P<0.0001$; naloxone, $F(1,42)=53.69$, $P<0.0001$; ranitidine × naloxone, $F(2,42)=3.32$, $P<0.05$]. Further analysis showed that pyrilamine and ranitidine decreased, while naloxone increased,

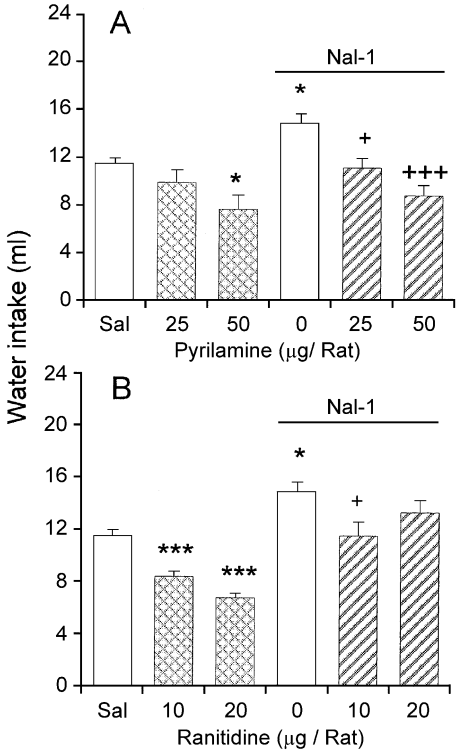

Fig. 5. Effect of pyrilamine (A) or ranitidine (B) in the presence or absence of naloxone on water intake. Rats were injected (i.c.v.) with either saline (2 μg/rat) or different doses of pyrilamine (25 and 50 μg/rat) or ranitidine (10 and 20 μg/rat). Naloxone (1 μg/rat) was administered 15 min after injection of pyrilamine or ranitidine, and water intake was measured for 1 h. Each column represents the mean ± S.E.M. for eight rats. *$P<0.05$, ***$P<0.001$ different from saline group. +$P<0.05$, +++$P<0.001$ different from naloxone control group.

water intake. Blockade of histamine H_1 receptors by pyrilamine (25 and 50 μg/rat) and ranitidine (10 μg/rat) decreased the naloxone-induced response.

4. Discussion

Our results show that i.c.v. administration of histamine increased water intake in isolated rats, while pharmacological blockade of histamine H_1 and H_2 receptors by pyrilamine or ranitidine, respectively, decreased this response. Blockade of histamine H_1 and H_2 receptors inhibited the histamine-induced response. The results show that both histamine H_1 and H_2 receptors are involved in water intake. It has been reported that elevation of the neuronal histamine level, by inhibition of the catabolism of histamine by metoprine, increases water intake and induces diuresis (Lecklin and Tuomisto, 1995), and that systemically administered H_1 and H_2 receptor blockers antagonize metoprine-induced changes in water intake (Lecklin and Tuomisto, 1998). Previously, it has been shown that histamine H_1 and H_2 receptor antagonists attenuate the drinking response to subcutaneous histamine in rats (Kraly and Arias, 1990; Specht and Spear, 1989). Furthermore, cimetidine, the histamine H_2 receptor antagonist, alone was able to inhibit the increase in water intake seen after histamine treatment (Houpt et al., 1986). Also, large doses of histamine administered peripherally may elicit drinking and possibly induce changes in urine flow indirectly by producing vasodilation and hypotension, and typically the effects of histamine on the vascular bed can be completely blocked only by a combination of H_1 and H_2 blockers (Lecklin and Tuomisto, 1998). In contrast to the present results, it has been reported that histamine acts within the central nervous system to decrease food intake, while having no direct effect on water intake (Meade and Denbow, 2001). There is much evidence that i.c.v. injection of histamine suppresses feeding (food and water intake) in cats, rats and goats (Machidori et al., 1992; Tuomisto and Eriksson, 1979). Furthermore, it has been reported that histamine after its infusion into the rat third ventricle does not increase water intake (Kraly and Arias, 1990).

In several animal species, central administration of histamine causes an antidiuretic response (Bennet and Pert, 1974; Bhargava et al., 1973), which results from increased vasopressin secretion (Tuomisto et al., 1980, 1984). Therefore, it has been suggested that hypothalamic histamine plays a role in the regulation of vasopressin secretion in response to dehydration. The effects of antagonists indicated that this action is mediated by both histamine H_1 and H_2 receptors (Kjaer et al., 1994).

Results showed that i.c.v. injection of morphine decreased, while that of naloxone increased, water intake in isolated rats. In addition to its well-documented modulation of food intake (Cooper et al., 1988; Levine et al., 1985; Morley et al., 1983), the endogenous opioid system also

plays a role in water intake (Yu and Bodnar, 1997). Many reports suggested that centrally administered opioid-selective agonists inhibit drinking in rats (Spencer et al., 1986). The role of opioids in the regulation of drinking has been correlated with the release of antidiuretic hormone. Morphine could conserve water by stimulating the release of antidiuretic hormone, which regulates water balance in the rat (Spencer et al., 1986; Vaswani et al., 1983). The effects of opioid peptides on the drinking behavior have been shown to be inconsistent, both inhibitory and stimulatory (Czech et al., 1984; Spencer et al., 1986; Sanger, 1981).

In the present experiment, the interaction between histaminergic and opioid systems on water intake was studied. The results show that the histamine H_1 receptor antagonist pyrilamine may interact with morphine or naloxone-induced water intake. Pyrilamine attenuated the inhibitory effect induced by morphine. Also, pretreatment with pyrilamine and ranitidine decreased the naloxone-induced response. However, blockade of opioid receptors by naloxone reduced the stimulatory effect induced by histamine. The results indicated that histamine and opioid systems possibly interact, which is supported by reports showing that other behaviors induced by morphine result in increase histamine release in the rat central gray (Brake and Hough, 1992), and that opioids enhance the brain turnover of histamine, an effect that can be blocked by naloxone (Itoh et al., 1988). It should also be considered that histamine H_2 receptor antagonists block morphine-induced locomotor hyperactivity in mice (Mickley, 1986). It has been reported that histamine potentiates morphine-induced learning behavior and that histamine receptor antagonists reduce morphine response in the passive avoidance task (Zarrindast et al., 2002). Moreover, several histamine H_1 receptor antagonists have been shown to have potentiating effects when administered together (Wauquier and Niemegeers, 1981; Zimmermann et al., 1997) and in combination with other opioids and even tend to augment the pleasurable effects of the latter (Shannon and Su, 1982; Suzuki et al., 1995).

Acknowledgements

We would like to thank Deputy Research of the Teacher Training University for financial support of the project.

References

Bennet, C.T., Pert, A., 1974. Antidiuresis produced by injections of histamine into the cat supraoptic nucleus. Brain Res. 78, 151–156.

Bhargava, K.P., Kulshrestha, V.K., Santhakumari, G., Srivastava, Y.P., 1973. Mechanism of histamine-induced antidiuretic response. Br. J. Pharmacol. 47, 700–706.

Brake, K.E., Hough, L.B., 1992. Morphine-induced increases of extracellular histamine levels in the periaqueductal gray in vivo; a microdialysis study. Brain Res. 572, 146–153.

Clapham, J., Kilpatrick, G.J., 1993. Histamine H_3 receptors—mediated modulation of water consumption in the rat. Eur. J. Pharmacol. 232, 99–103.

Cooper, S.J, Jackson, A., Kirkham, T.C., Turkish, S., 1988. Endorphins, opiates and food intake. In: Rodgers, R.J., Cooper, S.J. (Eds.), Endorphins, Opiates and Behavioral Processes. Wiley, New York, pp. 143–186.

Czech, D.A., Blake, M.J., Stein, E.A., 1984. Drinking behavior is modulated by CNS administration of opioids in the rat. Appetite 5, 15–24.

Houpt, T.R., Weixler, L.C., Troy, D.W., 1986. Water drinking induced by gastric secretagogues in pigs. Am. J. Physiol. 251, R157–R164.

Itoh, Y., Oishi, R., Nishibori, M., Saeki, K., 1988. Involvement of mu receptors in the opioid-induced increase in the turnover of mouse brain histamine. J. Pharmacol. Exp. Ther. 244, 1021–1026.

Kjaer, K., Knigge, U., Rouleau, A., Garbarg, M., Warberg, J., 1994. Dehydration-induced release of vasopressin involves activation of hypothalamic histaminergic neurons. Endocrinology 135, 675–681.

Kraly, F.S., Arias, R.L., 1990. Histamine in brain may have no role for histaminergic control of food-related drinking in the rat. Physiol. Behav. 47, 5–9.

Lecklin, A., Tuomisto, L., 1995. Fluid balance in rats of three different strains after inhibition of histamine catabolism. Physiol. Behav. 58, 861–867.

Lecklin, A., Tuomisto, L., 1998. The blockade of H_1 receptors attenuates the suppression of feeding and diuresis induced by inhibition of histamine catabolism. Pharm. Biol. Behav. 59, 753–758.

Leibowitz, S.F., 1973. Histamine: a stimulatory effect on drinking behavior in the rat. Brain Res. 63, 440–444.

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

Machidori, H., Sakata, T., Yoshimatsu, H., Ookuma, K., Fujimoto, K., Kurokawa, M., Yamatodani, A., Wada, H., 1992. Zucker obese rats: defect in brain histamine control on feeding. Brain Res. 590, 180–186.

Meade, S., Denbow, D.M., 2001. Feeding, drinking and temperature responses of chickens to intracerebroventricular histamine. Physiol. Behav. 73, 65–73.

Mickley, G.A., 1986. Histamine H_2 receptors mediate morphine-induced locomotor hyperactivity of the C57BL/6J mouse. Behav. Neurosci. 100, 79–84.

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

Onodera, K., Yamatodani, A., Watanabe, T., Wada, H., 1994. Neuropharmacology of the histaminergic neuron system in the brain and its relationships with behavioral disorder. Prog. Neurobiol. 42, 685–702.

Ookuma, K., Yoshimatsu, H., Sakata, T., Fujimoto, K., Fukagawa, K., 1989. Hypothalamic sites of neuronal histamine action on food intake by rats. Brain Res. 490, 268–275.

Orthon-Gambill, N., Salamon, M., 1992. FMH-induced decrease in central histamine levels produces increased feeding and body weight in rats. Physiol. Behav. 51, 891–893.

Paxinos, G., Watson, C., 1986. The Rat Brain in Stereotaxic Coordinates. Press, Sydney.

Sanger, D.J., 1981. Endorphinonergic mechanisms in the control of food and water intake. Appetite. J. Int. Res. 2, 193–208.

Schwartz, J.M., Arrang, J.M., Garbarg, M., Pollard, H., Ruat, M., 1991. Histaminergic transmission in the mammalian brain. Physiol. Rev. 71, 1–51.

Shannon, H.E., Su, T.P., 1982. Effects of the combination of tripelennamina and pentazocine at the behavioral and molecular levels. Pharmacol. Biochem. Behav. 17, 789–795.

Specht, S.M., Spear, L.P., 1989. Histamine-elicited drinking in weanling and adult rats. Physiol. Behav. 45, 63–70.

Spencer, R.L., Deupree, D., Hsiao, S., Mosberg, H.I., Hruby, V., Burks, T.F., Porreca, F., 1986. Centrally-administered opioid selective agonists inhibit drinking in the rat. Pharmacol. Biochem. Behav. 25, 77–82.

Suzuki, T., Takamori, K., Misawa, M., Onodera, K., 1995. Effects of the histaminergic system on the morphine-induced conditions place preference in mice. Brain Res. 675, 195–202.

Tuomisto, L., Eriksson, L., 1979. Antidiuresis induced by infusions of histamine into the brain ventricles of conscious hydrated goats. Eur. J. Pharmacol. 54, 191–201.

Tuomisto, L., Eriksson, L., Fyhrquist, F., 1980. Vasopressin release by histamine in the conscious goat. Eur. J. Pharmacol. 63, 15–24.

Tuomisto, L., Eriksson, L., Fyhrquist, F., 1984. Plasma vasopressin levels after I.C.V. infusion of histamine agonists in the conscious goat. Agents Actions 14, 558–560.

Tuomisto, L., Yamatodani, A., Jolkkonen, J., Sainio, E.L., Airaksinen, M.M., 1994. Inhibition of brain histamine synthesis increased food intake and attenuated vasopressin response to salt loading in rats. Methods Find. Exp. Clin. Pharmacol. 16, 355–359.

Vaswani, K., Tejwani, G.A., Muosa, S., 1983. Stress induced differential intake of various diets and water by rat: The role of the opiate system. Life Sci. 32, 1983–1996.

Wada, H., Inagaki, N., Yamatodani, A., Watanabe, T., 1991. Is the histaminergic neuron system a regulatory center for whole-brain activity? TINS 14, 415–418.

Wauquier, A., Niemegeers, C.J.E., 1981. Effects of chlorpheniramine, pyrilamine and astemizole on intracranial self-stimulation in rats. Eur. J. Pharmacol. 72, 245–248.

Yu, W.Z., Bodnar, R.J., 1997. Interactions between angiotensin-II and delta opioid receptor subtype agonists upon water intake in rats. Peptides 18, 241–245.

Zarrindast, M.R., Eidi, M., Eidi, A., Oryan, S., 2002. Effects of histamine and opioid systems on memory retention of passive avoidance learning in rats. Eur. J. Pharmacol. 452, 193–197.

Zimmermann, P., Wagner, U., Krauth, J., Huston, J.P., 1997. Unilateral lesion of dorsal hippocampus enhances reinforcing lateral hypothalamic stimulation in the contralateral hemisphere. Brain Res. Bull. 44, 256–271.