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Research report

Hypothalamic histamine release by taste stimuli in freely moving rats: Possible implication of palatability

Yada Treesukosol [a,1], Tomoko Ishizuka [a,b,*], Chizuko Yamamoto [a], Kanae Senda [b], Shintaro Tsutsumi [b], Atsushi Yamatodani [b], Takashi Yamamoto [a]

[a] *Department of Behavioral Physiology, Graduate School of Human Sciences, Osaka University, 1-2 Yamadaoka, Suita, Osaka, Japan*
[b] *Department of Medical Physics and Engineering, Graduate School of Allied Health Sciences, Faculty of Medicine, Osaka University, 1-7 Yamadaoka, Suita, Osaka, Japan*

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Abstract

Our previous study indicated that taste information via the chorda tympani (CT) activates the central histaminergic system in anesthetized rats. However, the physiological roles of taste-induced histamine release remain unknown, thus to further investigate the relationship between histamine release and gustatory information, in the present study we investigated the effect of taste stimuli infused intraorally on histamine release using in vivo microdialysis in free moving rats. Consistent with findings from our previous study, application of NaCl and HCl caused significant increases in histamine levels further supporting the suggestion that this phenomenon is attributed to the excitation of the CT. When rats were intraorally infused with quinine HCl (QHCl) solution, a significant increase in hypothalamic histamine release was observed. On the other hand, histamine release was decreased by sucrose and saccharin solutions. When rats were conditioned to acquire taste aversion to sucrose solution or saccharin solution, instead of the histamine decrease seen by the palatable solutions, the pattern of histamine release was similar to that seen by QHCl solution. From these observations, it is concluded that the histamine release by the infusion of these tastants may be explained by two mechanisms—by causing a transient increase after taste stimulation and by causing a decrease relative to the tastant's palatability.

Keywords: Histamine; Taste; Microdialysis; Anterior hypothalamus; Taste aversion; Palatability

1. Introduction

Although a substantial number of neuroanatomical and neurophysiological studies contribute to our understanding of the information processes of the central gustatory pathway, neurochemical information of transmitters remains poorly understood.

The central histaminergic system has been shown to play an important role in the modulation of food intake. The findings that acute injections of histamine into the lateral ventricle decreased food intake in rats [11] whereas an increase in food intake resulted from the depletion of histamine [14,22] indicate that central histamine decreases food intake. It has been shown that the increase in histamine release produced by leptin, a satiety factor, was abolished in bilaterally chorda tympani (CT)-transected rats [15,17] suggesting histaminergic activity is altered by taste information via the CT.

We previously investigated the effect of gustatory stimulation of the anterior part of the tongue on hypothalamic histamine using in vivo microdialysis. We reported that the administration of a four-basic taste mixture significantly increased histamine release, but not in the CT transected rats thus suggesting that taste information via the CT activates the central histaminergic system in anesthetized rats [26]. When each of the components of the four taste mixture were

* Corresponding author. Tel.: +81 6 6879 2566; fax: +81 6 6879 2566.
E-mail address: morimoto@sahs.med.osaka-u.ac.jp (T. Ishizuka).
[1] Present address: Department of Psychology, University of Florida, Gainesville, FL 32611-2250, USA.

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administered separately, an increase was observed by the administration of 0.1 M NaCl and 0.03 M HCl, whereas 0.5 M sucrose and 0.02 M quinine HCl (QHCl) showed no significant increase in hypothalamic histamine release. Because the relative magnitude of the CT response is higher for NaCl and HCl than sucrose and QHCl [2], these results suggest that hypothalamic histamine release is proportional to the electrophysiological response of the CT.

While these findings suggest taste information via the CT activates hypothalamic histamine release, the role of other taste nerves and the physiological roles of taste-induced histamine release remain unknown. Thus, to further investigate the relationship between histamine release and gustatory information, in the present study we investigated the effect of taste stimuli infused intraorally on histamine release of freely moving rats. The present study using free-moving rats allows stimulation of not only the anterior tongue innervated by the CT but also taste buds in the palate and posterior tongue innervated by the greater superficial petrosal (GSP) branch of the facial nerve and the glossopharyngeal (GL) nerve respectively. We also examined the effect of taste aversion learning on hypothalamic histamine release to clarify the involvement of taste palatability.

2. Materials and methods

2.1. Animals

Male Wistar strain rats (Japan SLC, Shizuoka, Japan) weighing 205–230 g were maintained on a 12–12 h light/dark schedule (lights on, 07:00–19:00 h) and maintained at 25 ± 1 °C with a humidity of 50 ± 10%. The rats were housed individually and given food pellets (Oriental Yeast Co., Osaka, Japan) and tap water ad libitum.

2.2. Surgical procedures

On the day of surgery, all subjects were anesthetized with sodium pentobarbital (50 mg/kg, i.p.). An intraoral catheter made of polyethylene tubing (0.9 mm diameter; Igarashi Ika Kogyo) with a flange at one end was inserted into the oral cavity and threaded subcutaneously to the top of the skull. A shorter piece of tubing of 1.6 mm in diameter and approximately 70 mm in length (Igarashi Ika Kyogyo) was threaded onto the intraoral catheter from the end coming out of the top of the skull so that it reinforced the intraoral catheter as it protruded from the skull. Rats were then placed on a stereotaxic apparatus (Kopf Instrument, Tujunga, CA, USA) and a guide cannula with its shaft dummy (MAB2/6: shaft length 14 mm, Microbiotech, Stockholm, Sweden) aimed at the anterior hypothalamus was stereotaxically implanted: AP = −1.5, ML = 0.5, DV = 9.2 relative to the bregma and the skull surface (Fig. 1) [23]. The intraoral catheter and guide cannula were fixed securely to the skull with stainless steel screws and dental acrylic. The rats were housed individually and given powdered chow (Oriental Yeast Co., Osaka, Japan) and tap water ad libitum during their recovery from surgery.

2.3. Training

After at least 3 days recovery, the rats were put on a 20 h water deprivation schedule (17:00–13:00 h) and were habituated to drink

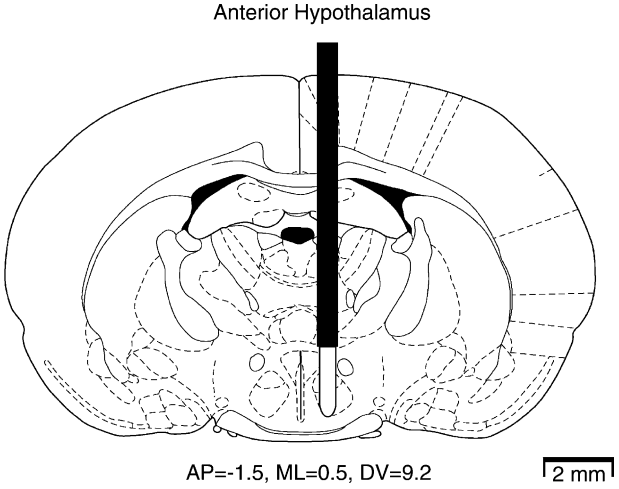

Fig. 1. Schematic representation of a coronal section and microdialysis probe placement.

5 ml of distilled water (DW) delivered by intraoral infusion over 20 min at a rate of 250 μl/min from 13:00 to 13:20 h. On the third and last day of training, 5 ml of the taste solution was delivered by intraoral infusion and this was the rat's first encounter with the taste solution. Infusing the taste stimulus on the third day of training is conducted to eliminate neophobia to the stimulus on the day of microdialysis. During these 20-min periods, rats were not given access to chow. For this training period, additional DW was given immediately after the intraoral infusion by a bottle until 17:00 h to avoid dehydration.

2.4. Conditioned taste aversion

To examine the effect of conditioned taste aversion (CTA), rats of the sucrose CTA group ($n = 5$) were given an i.p. injection of 0.15 M LiCl (2% of body weight; the unconditioned stimulus (US)) 20 min after intraoral sucrose solution (the conditioned stimulus (CS)) infusion on the third day of training. Similarly, rats of the saccharin CTA group ($n = 5$) were given an i.p. injection of 0.15 M LiCl after intraoral saccharin solution (CS) infusion on the third day of training.

2.5. Microdialysis

To minimize the possible effect of histidine and other amino acids contained in food on histamine release, food were removed from the cages the day before microdialysis.

A microdialysis probe (MAB6; membrane length 2 mm, Microbiotech, Stockholm, Sweden) was inserted in the anterior hypothalamus via the guide cannula and perfused with artificial cerebrospinal fluid (140 mM NaCl, 3 mM KCl, 2.5 mM $CaCl_2$ and 4.5 mM glucose, pH 7.4) at a rate of 1 μl/min. To achieve stabilization of histamine release, dialysates obtained during the first 1 h were discarded and collected every 20 min thereafter. After baseline samples were collected, rats received a 5 ml intraoral infusion for 20 min of 0.001 M quinine HCl (QHCl group, $n = 5$), 0.5 M sucrose (sucrose group, $n = 5$; sucrose CTA, $n = 5$), 0.01 M saccharin (saccharin group, $n = 5$; saccharin CTA $n = 5$), 0.1 M NaCl (NaCl group, $n = 5$), 0.01 M HCl (HCl group, $n = 6$) or distilled water (DW group, $n = 5$).