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Serotonin inhibits voltage-gated sodium current by cyclic adenosine monophosphate-dependent mechanism in bullfrog taste receptor cells

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Abstract

We have investigated the effect of 5-hydroxytryptamine (serotonin) (5-HT) on the membrane properties of bullfrog taste receptor cells (TRCs) using patch-clamp technique. External application of 5-HT reversibly suppressed the voltage-gated Na^+ current (I_{Na}) in about half of the TRCs sampled. The magnitude of suppression of peak I_{Na} was dependent on the holding potential of the cell. Forskolin and cyclic adenosine monophosphate (cAMP) mimicked the suppressive effect of 5-HT on I_{Na}, but an internal protein kinase A-inhibitor potentiated I_{Na}. These results suggest that 5-HT suppresses I_{Na} of bullfrog TRCs via protein kinase A-dependent phosphorylation, resulting in suppression of the excitability of bullfrog TRCs.

Keywords: Taste receptor cell; Gustatory; 5-Hydroxytryptamine (serotonin); Voltage-gated Na^+ current; Cyclic adenosine monophosphate; Phosphorylation; Frog

Taste receptor cells (TRCs) are excitable cells, which produce action potentials [14,15]. Hence, voltage-gated Na^+ current (I_{Na}) is thought to play an essential role in the gustatory transduction in TRC and the signal transmission from TRC to the gustatory nerve. If Na^+ channel activity could be modulated by a ligand, electrical excitability of TRCs and responsiveness of gustatory nerves elicited by taste stimuli can be regulated by its activity.

Serotonin-containing cells are present in the taste buds of vertebrates including mammals [5,14,17]. In the bullfrog taste disk, Merkel-like basal cells contain a neurotransmitter, 5-hydroxytryptamine (serotonin) (5-HT) [10,14]. Since these cells in the taste disk do not extend processes up to the oral cavity, they may not directly participate in taste reception but may indirectly play an important role in gustatory neural responses as interneurons or neuromodulator cells.

Although 5-HT modulates chemosensory responses of TRCs, effect of 5-HT on taste transduction is still controversial. Morimoto and Sato [16] have reported that 5-HT injected into the lingual artery suppresses the gustatory neural responses for KCl in frogs. However, Esakov et al. [7] have reported that subepithelial injection of 5-HT into the tongue enhances gustatory neural responses for all basic taste stimuli in frogs. 5-HT modulates activities of several ion channels including Ca^{2+}, Na^+ and K^+ channels [6,11,12]. In the present experiment, we investigated the effect of 5-HT on the properties of I_{Na} in isolated TRCs using patch-clamp recording technique. We found that 5-HT reversibly suppresses the I_{Na} by cAMP-dependent phosphorylation via protein kinase A (PKA) in TRCs.

Bullfrogs (*Rana catesbeiana*) weighing 300–400 g were used. The fungiform papillae were dissected out from isolated tongues and collected into a nominally Ca^{2+}-free saline solution. The papillae were treated with papain (8.4 U/ml, Sigma) activated by cysteine (2 mg, Sigma) in 2 ml divalent cation-free saline solution containing 2 mM ethylene diamine tetra-acetic acid (EDTA) for 10 min. The papillae were washed by normal saline to remove the enzyme and gently triturated to dissociate the TRCs [8,15,18]. Dissociated cells were filtered across a 100 μm-square nylon mesh and stored in ice-cold saline solution. Electrical recordings were made from TRCs settled on the bottom of a recording chamber (0.7 ml) mounted on the stage of an inverted microscope (Nikon, Diaphot 300). Patch pipettes were fabricated with borosilicate glass capillaries (Clark, GC150–10)

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