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PERTUSSIS TOXIN-SENSITIVE G PROTEIN MODULATES THE ABILITY OF HISTAMINE TO STIMULATE cAMP PRODUCTION IN THE CHICK PINEAL GLAND

Jolanta B. Zawilska[1,2,#], Jolanta Rosiak[2], Jerzy Z. Nowak[2,3]

[1]Department of Pharmacodynamics and [3]Department of Pharmacology, Medical University of Łódź, Muszyńskiego 1, PL 90-151 Łódź, [2]Centre for Medical Biology, Polish Academy of Sciences, Lodowa 106, PL 93-232 Łódź, Poland

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Histamine (HA) is a potent stimulator of cAMP synthesis in various structures of chick brain, including the pineal gland. The action of HA is mediated by specific, membrane bound H_2-like receptors, whose pharmacological profile is different from that described for H_2-receptors in mammalian tissues. In this work, we analyzed the effects of cholera toxin (CTX) and pertussis toxin (PTX), well-known modulators of G_s and G_i/G_o protein, respectively, on the stimulatory action of HA on cAMP synthesis in the chick pineal gland organ cultures. HA and its two biologically active methylated derivatives, 2-methylHA and 4-methylHA, markedly increased cAMP content in the chick pineal glands. Pretreatment of the chick pineal glands with CTX potently stimulated basal cAMP production. In CTX-pretreated glands, elevations of cAMP synthesis evoked by HA, 2-methylHA and 4-methylHA were additive to those produced by CTX, which is an observation suggesting that H_2-like HA receptors in the chicken pineal gland are not coupled to G_s proteins. Pretreatment of the chick pineal glands with PTX significantly enhanced the stimulatory effect of HA and, to a greater extent, 2-methylHA on cAMP production. The enhancing action of PTX on the HA-evoked cAMP formation was not modified by mepyramine, a selective H_1-type HA receptor antagonist. It is suggested that in the chick pineal gland, a population of HA receptors is coupled to G_i (or G_o) protein. Stimulation of these receptors would tonically suppress the activity of the cAMP generating system functionally linked to H_2-like HA receptors.

Key words: *histamine receptors, chick, pineal gland, cAMP, G proteins, cholera toxin, pertussis toxin*

[#] *correspondence;* e-mail: jzawilska@pharm.am.lodz.pl