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

Jolanta B. Zawilska1,2,†, Jolanta Rosiak2, Jerzy Z. Nowak2,3

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


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 H₃-like receptors, whose pharmacological profile is different from that described for H₂-receptors in mammalian tissues. In this work, we analyzed the effects of cholera toxin (CTX) and pertussis toxin (PTX), well-known modulators of G₁₂ and G₁₅ 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 H₃-like HA receptors in the chicken pineal gland are not coupled to G₁₂ 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 H₁-type HA receptor antagonist. It is suggested that in the chick pineal gland, a population of HA receptors is coupled to G₁₅ (or G₁₁) protein. Stimulation of these receptors would tonically suppress the activity of the cAMP generating system functionally linked to H₂-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