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Coupling Efficiencies of m1, m3 and m5 Muscarinic Receptors to the Stimulation of Neuronal Nitric Oxide Synthase

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Through molecular cloning, five muscarinic receptors have been identified. The muscarinic receptors can be generally grouped according to their coupling to either stimulation of phospholipase C (m1, m3, and m5) or the inhibition of adenylate cyclase (m2 and m4). Each m1, m3, and m5 receptors has the additional potential to couple to the activation of phospholipase A_2, C, and D, tyrosine kinase, and the mobilization of Ca^{2+}. However, the differences in coupling efficiencies to different second messenger systems between these receptors have not been studied well. Ectopic expression of each of these receptors in mammalian cells has provided the opportunity to evaluate the signal transduction of each in some detail. In this work we compared the coupling efficiencies of the m1, m3 and m5 muscarinic receptors expressed in chinese hamster ovary (CHO) cells to the Ca^{2+} mobilization and the stimulation of neuronal nitric oxide synthase (nNOS). Because G protein/PLC/PI turnover/$[Ca^{2+}]i$/NOS pathway was supposed as a main pathway for the production of nitric oxide via muscarinic receptors, we studied on m1, m3 and m5 receptors. Stimulation of guanylate cyclase activity in detector neuroblastoma cells was used as an index of generation nitric oxide (NO) in CHO cells. The agonist carbachol increased the cGMP formation and the intracellular $[Ca^{2+}]$ in concentration dependent manner in three types of receptors and the increased cGMP formation was significantly attenuated by scavenger of NO or inhibitor of NOS. m5 receptors was most efficiently coupled to stimulation of nNOS. And, the coupling efficiencies to the stimulation of neuronal nitric oxide synthase in three types of receptors were parallel with them to the Ca^{2+} mobilization.