Studies on muscarinic acetylcholine receptors focus both on ligand-binding and on defining the physical properties of muscarinic receptors.
Project Description:

Major Findings: $^{3}H$-Quinuclidinyl-benzilate (QNB) was used to study muscarinic acetylcholine receptors in NG108-15 membrane preparations. The apparent dissociation constant of $^{3}H$QNB is $1 \times 10^{-10}$ M; the average NG108-15 cell possesses 30,000 specific sites for $^{3}H$-QNB. Activation of the receptors with acetylcholine or carbachol results in cell depolarization, a small increase in cellular cGMP, and inhibition of adenylate cyclase. Cell depolarization and rise in cGMP levels desensitize in 30 sec; whereas, the inhibition of adenylate cyclase does not desensitize. Scatchard analysis revealed only one homogeneous class of $^{3}H$-QNB binding sites; however biphasic rates of $^{3}H$-QNB association with and dissociation from receptors were found. Evidence was obtained for the formation of a dissociable $[^{3}H]$-QNB-Receptor complex which then is converted to a form which dissociates only slowly. Hill coefficients of approximately 1.0 were found for receptor antagonists and approximately 0.5 for receptor activators. A sequential series of reactions were proposed to account for these observations and for the various states of the muscarinic acetylcholine receptor that were detected.

Publications: