

The function of intracellular muscarinic acetylcholine receptor: influence of physiological stress

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Brain acetylcholine is an important neurotransmitter to regulate synaptic transmission in neural circuits and to enhance learning, memory and cognition. Acetylcholine released from nerve terminals acts on muscarinic and nicotinic acetylcholine receptors on plasma membrane followed by the rapid hydrolytic degradation. We found that muscarinic acetylcholine receptors M1 (M1-mAChRs) are highly expressed on intracellular membranes, such as endoplasmic reticulum and Golgi apparatus, in neurons of central nervous system and activate signaling cascades distinct from those of cell surface receptors. The intracellular M1-mAChRs is activated by endogenous acetylcholine following its uptake *via* a putative transport system and causes cholinergic facilitation of synaptic long-term potentiation in the hippocampus. In addition, the cholinergic synaptic regulation is found to disappear after chronic restraint stress. We herein introduce function of intracellular M1-mAChR in the brain and discuss about possible relation to stress-related neuropsychiatric disorder.