Title:	Investigation of the cellular dynamics of antagonist-mediated endocytosis of group I metabotropic glutamate receptors
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Abstract:	G-protein coupled receptors bind to a variety of ligand molecules. An agonist is a ligand that when binds to the receptor leads to its activation and consequently a biological cascade in the cell. An antagonist however, is known to pharmacologically block the action of the agonist by binding to the receptor and preventing activation of the receptor by blocking receptor-agonist interaction and downstream signaling. Subsequent to the activation of the second messenger pathways, many G-protein coupled receptors (GPCRs) are known to get desensitized and get internalized. Till date, antagonists, which are viewed as pharmacological blockers only, were not known to promote sequestration of receptors upon binding. However, some studies have reported antagonist-induced desensitization of a few GPCRs and uncoupling of the receptor from the G-protein involved. Group I metabotropic glutamate receptors (mGluRs) play crucial roles, especially in inducing different forms of synaptic plasticity which are responsible for learning and memory formation. Group I mGluRs activate the phospholipase C pathway by coupling to the G αq/11 pathway. In this study I determined whether the lesser known concept antagonists-mediated endocytosis is applicable to group I mGluRs in primary hippocampal neurons. It has been reported earlier that group I mGluRs show maximum internalization 30 mins post agonist stimulation. The objective of this study was to check if antagonists induce the internalization of mGluR1 and mGluR5, the two subtypes of the group I mGluRs. Further, I was interested to investigate the kinetics and the fate of the receptor subsequent to the internalization. Our results add to the understanding of the little known concept of antagonist-mediated internalization which is perhaps crucial because these antagonists are widely used in therapeutics. The detailed cellular mechanisms need to be investigated in future
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