ABSTRACT

G-protein-coupled receptors (GPCRs) are seven transmembrane receptors that transduce information provided by the extracellular stimuli into intracellular signals via their coupling with G-proteins. Activation of GPCR also triggers a variety of cellular and molecular mechanisms, viz., receptor desensitization and internalization. Due to the diversity in the GPCR regulation, each GPCR is unique and an extensively studied GPCR may not provide all the details about other GPCRs. Glutamate is a major excitatory neurotransmitter in the central nervous system. It activates three types of receptors, viz., NMDARs, AMPARs and metabotropic glutamate receptors (mGluRs). Among these three types of receptors, mGluRs belong to the GPCR family. Among the eight subtypes of mGluRs, mGluR1 and mGluR5 belong to the group I family. These receptors play important roles in the brain and are believed to be involved in multiple forms of experience dependent synaptic plasticity including learning and memory. In addition, group I mGluRs also have been implicated in various neuropsychiatric disorders like Fragile X syndrome, autism etc. Similar to many other GPCRs, group I mGluRs have been reported to get desensitized subsequent to the ligand exposure and undergo rapid internalization. However, very little is known about the mechanisms that control these trafficking events, and the functional consequences of these trafficking events. Sorting Nexin 1 (SNX1) has been shown to regulate the endosomal sorting of few cell surface receptors either to lysosomes where they are downregulated or back to the cell surface. The objective of this study is to investigate the role of Sorting Nexin 1 (SNX-1) in the ligand-mediated trafficking of group I mGluRs and its physiological significance in the central nervous system.