Title:	A critical role for sorting nexin 1 in the trafficking of metabotropic glutamate receptors
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Abstract:	Group I metabotropic glutamate receptors (mGluRs) function as modulators of neuronal physiology and they have also been implicated in various neuropsychiatric disorders. Trafficking of mGluRs plays important roles in controlling the precise localization of these receptors at specific region of the cell, as well as it regulates the activity of these receptors. Despite this obvious significance, we know very little about the cellular machineries that control the trafficking of these receptors in the CNS. 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. Using “molecular replacement” approach in hippocampal neurons derived from mice of both sexes, we show here that SNX1 plays critical role in the trafficking of mGluR1, a member of the group I mGluR family. Overexpression of dominant-negative SNX1 or knockdown of endogenous SNX1 resulted in the rapid recycling of the receptor. Importantly, recycling via the rapid recycling route, did not allow the resensitization of the receptors. Our data suggest that both, N-terminal and C-terminal region of SNX1 play critical role in the normal trafficking of the receptor. In addition, we also show here that SNX1 regulates the trafficking of mGluR1 through the interaction with Hrs (hepatocyte growth factor-regulated tyrosine kinase substrate), a protein that has been implicated in both signaling and vesicular trafficking. Thus, these studies reveal a mechanistic role of SNX1 in the trafficking of group I mGluRs and its physiological implications.
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