Auxiliary subunits regulate dendritic turnover rates of AMPA receptors in hippocampal neurons

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AMPA-type glutamate receptors (AMPARs) mediate synaptic transmission at the vast majority of glutamatergic synapses in the central nervous system, and their dynamic recruitment to postsynaptic sites putatively underlies synaptic plasticity as well as homeostatic synaptic scaling. AMPARs associate with different auxiliary subunits that facilitate their forward trafficking from ER to plasma membrane and also modulate channel function. While two prominent auxiliary subunits, TARPγ8 and CKAMP44a, were shown to govern AMPAR function in hippocampal neurons, the role of these auxiliary subunits in local dendritic receptor turnover has remained unclear. Here, we show that the basal turnover of AMPAR via recycling endosomes is strongly regulated by the abundance of TARPγ8 or CKAMP44a: Overexpression of either auxiliary subunit prolongs the lifetime of extrasynaptic AMPA receptors on the surface by reducing constitutive internalization rate. Under basal conditions, AMPAR surface expression remains largely unchanged, when TARPγ8 or CKAMP44a are overexpressed, and accordingly we not only found a reduced pool of AMPAR in recycling endosomes but also a diminished fusion rate of AMPAR-containing transport organelles with the plasma membrane. These novel data indicate that association with auxiliary subunits protects AMPAR from rapid turnover, thus stabilizing the extrasynaptic receptor pool.