Nanoscale colocalization of AMPA receptor nanodomains with neuroligin 1 regulates synaptic transmission efficiency

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Key words: synaptic transmission, super-resolution microscopy, d-STORM

Abstract: The nanoscale organization of neurotransmitter receptors relative to pre-synaptic release sites is a fundamental determinant of the amplitude and the reliability of synaptic transmission. How modifications of the alignment of pre to postsynaptic machinery affect synaptic current properties has only been approached with simulations, and therefore remains hypothetical. Using single molecule based super-resolution microscopy, we found that expression of a C-terminal truncated form of neuroligin-1, a trans-synaptic adhesion protein playing major roles in synapse development and function, spatially decorrelates neuroligin 1 and AMPA receptor synaptic clusters by tens of nanometers, without affecting the intrinsic organization of AMPARs in nanodomains. We show by electrophysiology and computer simulations that this physical separation is sufficient to induce a large decrease in synaptic transmission. We propose that separation of neuroligin 1 from AMPA receptor clusters disrupts the pre- to post-synaptic organization, revealing the necessity for synapses to release glutamate in front of AMPAR nanodomains to maintain a high fidelity of synaptic response.