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The C-terminal amphipathic helix of Complexin helps drive synaptic vesicle exocytosis by sculpting membranes

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Neurotransmitter release is mediated by proteins that drive synaptic vesicle fusion with the presynaptic plasma membrane. While soluble N-ethylmaleimide sensitive factor attachment protein receptors (SNAREs) form the core of the fusion apparatus, additional proteins play key roles in the fusion pathway. I will describe my recent work that found the C-terminal amphipathic helix of the mammalian accessory protein, complexin (Cpx), exerts profound effects on membranes, including the formation of pores and the efficient budding and fission of vesicles. Using nanodisc-black lipid membrane electrophysiology, we demonstrate that the membrane remodeling activity of Cpx modulates the structure and stability of recombinant exocytic fusion pores. Cpx had particularly strong effects on pores formed by small numbers of SNAREs. Under these conditions, Cpx increased the current through individual pores 3.5-fold, and increased the open time fraction from roughly 0.1 to 1.0. This work proposes a model where the membrane sculpting activity of Cpx contributes to the phospholipid rearrangements that underlie fusion by stabilizing highly curved membrane fusion intermediates.

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