Is Zinc the Link to How We Think?
Understanding the Role of Zinc in Synaptic Function at Developing Synapses

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Billings Building—Rosedale Room

SPEAKER:

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Abstract

Zinc represents a new frontier in second messenger signaling in neurons. It is prevalent at glutamatergic synapses, its effective intracellular concentration range (pM to nM) is highly regulated, and multiple mechanisms are available for generating rapid intracellular zinc signals. Potentially rivaling calcium in importance, zinc is emerging as a dynamic player in neuronal signaling and promises to reshape our current understanding of synaptic function and dysfunction. Using a combination of imaging, electrophysiology, biochemistry and biophysical analyses, we investigated the Shank family since zinc is known to regulate the structure and function of Shank2 and Shank3 and their scaffolding of a whole host of key postsynaptic players. In young neurons, zinc elevation was found to enhance synaptic efficacy by preferentially recruiting GluA2 into synapses with the concomitant dispersion of GluA1 (schematic, blue box). This cooperative dynamic regulation of AMPAR composition by zinc was dependent on Shank2 and Shank3 at developing synapses, a critical period for local control of AMPAR composition. Beyond synaptic transmission, zinc has also been implicated in synaptogenesis and synaptic plasticity. We recently have discovered a new postsynaptic zinc-dependent protein zyxin that is recruited to dendritic spines during F-actin polymerization in neurons. Zyxin, a focal adhesion protein that promotes cytoskeletal reorganization, has been well characterized in fibroblasts and cancer cells but has never been described in the central nervous system. Concentrated in the soma and dendrite, zyxin is localized in dendritic protrusions with clear colocalization with F-actin in spines and is dynamic at spines and translocates with actin. Activity and elevated zinc also trigger zyxin recruitment to spines (schematic, red box). We are testing the hypothesis that zyxin serves as a postsynaptic protein that links multiple zinc signaling cascades to the actin cytoskeleton to regulate postsynaptic spine development and plasticity. Our long-term research goal is to understand the role of zinc, an underappreciated modulator of neuronal signaling, in the fundamental biology and pathology of neurons.

Publications:
