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## Inhibitory Modulation of Glutamatergic Neuron Activity by Zinc in the Hippocampus

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## Abstract:

Zinc exists in high densities in the giant boutons of hippocampal mossy fibers. Zinc decreases extracellular glutamate concentration in the hippocampus, suggesting inhibitory modulation of glutamatergic neurotransmitter system by zinc. Zinc-specific fluorescent (ZnAF-2) signals are increased in both extracellular and intracellular compartments in the mossy fiber terminals during the delivery of tetanic stimuli to the dentate granule cell layer. It is likely that zinc released from mossy fibers is immediately retaken up by mossy fibers and taken up into postsynaptic CA3 neurons. In mossy fiber terminals preferentially double-stained with zinc and calcium indicators, the increase in calcium orange signal during delivery of tetanic stimuli to the dentate granule cell layer is enhanced by addition of CaEDTA, a membrane-impermeable zinc chelator, while suppressed by addition of zinc. The decrease in FM4-64 signal (vesicular exocytosis) during tetanic stimulation, which induces mossy fiber long-term potentiation, is also enhanced in mossy fiber terminals by addition of CaEDTA and is suppressed by addition of zinc. Zinc released from mossy fibers may serve as a negative-feedback factor of presynaptic activity.

**Key words:** zinc, glutamate, mossy fiber, hippocampus, calcium, exocytosis, synaptic plasticity

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