

Zinc and Nitric Oxide Imaging in the Brain

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ABSTRACT The brain represents an exciting new frontier for investigation in bioinorganic chemistry. Metalloneurochemistry refers to the interface between bioinorganic chemistry and neuroscience. Mobile zinc is housed in pre-synaptic vesicles in the hippocampus, a substructure in the brain vital to learning and memory, and its uncontrolled release has been associated with a variety of neurological diseases and toxic events. It also binds to proteins, including zinc finger proteins and metallothionein. Understanding the roles that zinc plays in brain function and toxicity is an important objective in metalloneurochemistry. The mobilization of zinc is controlled in part by neurochemical signals, including NO. Nitric oxide has been implicated as a retrograde transmitter in long-term potentiation and memory formation. Loss of NO homeostasis, like that of zinc, has been associated with neurotoxic brain tissue-damage. To investigate these phenomena, our laboratory has designed and employed fluorescent sensors for zinc and nitric oxide. Recent progress will be described in the synthesis and characterization of fluorescein-based sensors for zinc, of rhodium-, copper-, and conjugated polymer-based sensors for NO, and of derivatives of these probes for selectively attaching them to cellular targets. Applications to image zinc and nitric oxide in cultured cells as well as live hippocampal slices from the rat will also be reported. This work is supported by the NIH and NSF (SJL) and by the Howard Hughes Medical Institute (MS).