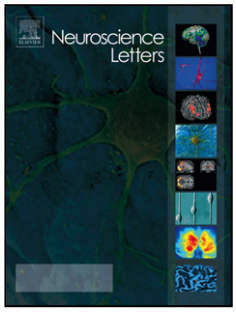

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Evidence for mast cell-mediated zinc homeostasis: Increased labile zinc in the hippocampus of mast-cell deficient mice

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Highlights

- Mast cell deficient mice have higher levels of labile brain zinc than wild type animals
- Total brain zinc levels remain unchanged
- Granule cell layer and hilar regions of the dentate gyrus are not significantly different
- Data support mast cell-mediated zinc homeostasis in hippocampus

ABSTRACT

The dentate gyrus of the hippocampus is a site of adult neurogenesis, and is also known to contain one of the highest concentrations of labile brain zinc (Zn), thought to aid in learning and memory by supporting neurogenesis. At the same time, it is known that unbound Zn, when present at excessive levels, decreases the formation of new neurons. Since mast cells contain Zn transporters capable of moving this essential element across their plasma membrane, as well as Zn-rich granules that are dispelled upon secretion, we reasoned that mast cells contribute to Zn homeostasis in this area of the brain, as they are found in greatest numbers in and around the dentate gyrus. This line of evidence was tested by comparing Timm-stained hippocampal sections of mast cell-deficient C57BL/6-*Kit*$^{W\text{-}sh/W\text{-}sh}$ (Sash$^{-/-}$) mice to those of mast cell-containing wild type (Sash$^{+/+}$) animals. Mast cell deficient mice were found to have significantly increased Timm-positive staining as compared to controls, reflecting an increase in labile or bioactive Zn in this region. As we observed no change in total brain Zn (protein-bound plus unbound Zn), these increases indicate that mast cells may serve to bind what would otherwise be excessive or deleterious levels of labile Zn, or that they are able to recruit metallothionein proteins. Because elevated levels of labile Zn are observed in the brains of patients with neurodegenerative diseases such as Alzheimer's, the potential contribution of mast cells to these diseases remains a compelling one. Overall, these data support a role for