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Studies of Manganese Speciation in Liver, Heart and Brain Mitochondria

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ABSTRACT: The toxicological effects of Mn are primarily caused by damage to the striatum and to the globus pallidus. It has been hypothesized that oxidation of dopamine by Mn^{3+} causes the damage to striatum; however, the amount of Mn^{3+} in striatal neurons has never been determined. Most intracellular Mn is found in mitochondria. We have used the shift in the manganese absorption edge in x-ray absorption near edge structure (XANES) spectroscopy to determine the oxidation state of Mn in brain, heart, and liver mitochondria. XANES spectra of intramitochondrial Mn in each of these three types of mitochondria were compared with those of Mn standards or model compounds. The spectra of intramitochondrial Mn in all three types of mitochondria were most similar to those of Mn(II)ATP and Mn(II)HPi complexes. Fits of the spectra of intramitochondrial Mn to spectra of these standards gave R^2 's greater than 0.99. Additions of small amounts of the spectra of other Mn(II) complexes gave either no change in R^2 or very small decreases in R^2 , while additions of small amounts of the spectra of Mn(III) complexes such as Mn(III)porphyrin and Mn(III) Ac caused significant decreases in R^2 . Neither longer incubation times for intramitochondrial Mn, incubation in the presence of 40 nmoles/ mg protein of intramitochondrial Ca^{2+} , nor increased phosphorylation of ADP caused spectroscopic changes indicative of increased Mn^{3+} within the mitochondria. There was no significant difference between the spectra of Mn inside brain, liver, or heart mitochondria, suggesting that the same Mn^{2+} complexes are formed in each of these cases. The data suggest that the primary complexes formed are Mn(II)ATP and Mn(II)HPi and that the amount of Mn(III) complexes formed is quite low. Preliminary Mn XANES work has also been initiated using cultured astrocytes and neuron-like cells (PC12 cells and NT2 cells).