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High-resolution x-ray absorption spectroscopy studies of metal compounds in neurodegenerative brain tissue

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Abstract. Fluorescence mapping and microfocus X-ray absorption spectroscopy are used to detect, locate and identify iron biominerals and other inorganic metal accumulations in neurodegenerative brain tissue at sub-cellular resolution (< 5 microns). Recent progress in developing the technique is reviewed. Synchrotron X-rays are used to map tissue sections for metals of interest, and XANES and XAFS are used to characterise anomalous concentrations of the metals *in-situ* so that they can be correlated with tissue structures and disease pathology. Iron anomalies associated with biogenic magnetite, ferritin and haemoglobin are located and identified in an avian tissue model with a pixel resolution ~ 5 microns. Subsequent studies include brain tissue sections from transgenic Huntington's mice, and the first high-resolution mapping and identification of iron biominerals in human Alzheimer's and control autopsy brain tissue. Technical developments include use of microfocus diffraction to obtain structural information about biominerals *in-situ*, and depositing sample location grids by lithography for the location of anomalies by conventional microscopy. The combined techniques provide a breakthrough in the study of both intra- and extra-cellular iron compounds and related metals in tissue. The information to be gained from this approach has implications for future diagnosis and treatment of neurodegeneration, and for our understanding of the mechanisms involved.

1. Introduction

The links between neurodegeneration and metal accumulation in the brain are increasingly accepted, but the underlying mechanisms involved are poorly understood. Brain iron accumulation is a feature

