DETERMINING THE SOURCE OF ELEVATED IRON CONCENTRATIONS IN THE HUMAN PONS IN NEURODEGENERATIVE DISORDERS

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Introduction: Disregulation of transition metal ions is implicated in many neurodegenerative disorders, and altered status may both affect disease progression and hold biomarker potential. The analytical challenges in this field often lead to isolated evidence for altered concentration, distribution, chemical or mineral state, limiting the conclusions that can be drawn. Combining methods that are highly sensitive to a range of these properties can give new insight.

Aim: A complementary set of analytical techniques was used to quantify iron concentration and ferritin cores in the MSA, PD, and AD pons, and correlate findings with iron distribution and form.

Methods: Fresh-frozen human pons was imaged by MRI microscopy, and characterized with synchrotron microfocus X-ray fluorescence spectroscopy (XRF). Isothermal magnetic remanence (IRM) was measured in adjacent blocks of pons, and total iron was quantified by graphite furnace analysis.

Results: IRM/g was elevated at 5 K in disease cf control, consistent with an increased ferritin core concentration. For MSA, analysis of total iron confirmed elevated iron cf control, and findings indicated that a higher proportion of the iron was contained in ferritin. XRF mapping showed highly-localised iron clusters in context with the corresponding distributions for copper, zinc, and manganese. X-ray absorption spectra from isolated iron clusters were consistent with brain ferritin.

Conclusions: The results indicate iron sequestration by ferritin in MSA, and give insight into the distribution of trace metals in the pons. The combined techniques provide a powerful approach to analyse trace metals in tissue, applicable to a range of neurodegenerative disorders.