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The Contribution of Brain Metal Homeostasis to Memory Loss and Dementia

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Dementia has increasing prevalence in western society and poses significant health and economical concerns. It is expected that 131.5 million people will be affected by 2050 (1) and the associated health care cost will be USD \$2 trillion in 2030 (2). In light of this, it is important to further characterise the chemical pathways leading to dementia onset and memory loss, which may help identify potential targets for therapeutic intervention. There is substantive evidence of increased free radical mediated oxidative stress during ageing, which may drive a switch from healthy brain function to dementia. Many studies have examined increased metal levels in the brain during ageing, as a potential driver of heightened oxidative stress, yet, localised metal deficiency may also contribute to the pathology. Fe, Cu and Zn are essential for healthy brain function, and metal deficiency during neurodevelopment is catastrophic. Therefore, we are currently investigating the hypothesis that localised metal deficiency during ageing may contribute to memory impairment observed in dementia. To test this hypothesis we have begun characterisation of brain-metal levels in a mouse model of accelerated ageing (senescence accelerated mouse (SAM) model) using X-Ray Fluorescence Microscopy (see attached figure 1). Our results have revealed alterations to copper, zinc and iron concentration within the brain during ageing, in this model (3). Specifically, the accelerated ageing model is characterised by substantial Zn deficiency within the hippocampus –a key brain region for spatial learning and memory. We have complemented our XFM elemental analyses with Fourier Transform infrared Microscopy studies, which appear to highlight a correlation between biochemical alterations to lipids and metal homeostasis (3). We hope continued investigation of our hypothesis may provide further insights into disease and memory loss mechanisms, which in turn, could reveal strategies for prevention.

References

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