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Spectroscopic Studies of Brain Zinc Homeostasis and Its Role During Cognitive Decline and Ageing

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The greatest risk factor for dementia is ageing. With no cure or effective therapies to slow progression, and with an ageing population, dementia has reached crisis levels in Australia. The content and distribution of metals such as Fe, Cu, Zn is known to change in the ageing brain (metal dis-homeostasis)(1, 2), and thus, increased understanding of the mechanistic role of metal dis-homeostasis may illuminate new therapeutic strategies. Specifically, Zn homeostasis and dis-homeostasis appears to be a potent modulator of memory function (3-5), yet, the exact chemical form(s) of Zn that are vital to memory function are unknown (6,7). Development of new spectroscopic methods to image different chemical forms of Zn may help increase understanding of Zn-modulated memory function and dysfunction. There are currently no available imaging protocols to differentiate between different chemical forms of Zn, however, substantive evidence supports that X-ray absorption techniques could provide such capability (8-10). Recently, our group has utilised X-ray absorption spectroscopy (XAS) to build a spectroscopic library of Zn compounds that reflects the chemical forms of Zn likely to be present in the brain. Preliminary analysis has revealed that XAS is able to differentiate between multiple Zn compounds across anatomically separate brain regions (Figure 1). Future experiments hope to reveal which Zn compounds change, in which brain regions, during ageing or neuorodegenerative disease. Such insights into whether specific types of zinc are affected with ageing may reveal mechanisms contributing to cognitive decline, in turn presenting potential pathways for targeted therapeutic interventions.

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