A longitudinal investigation of metal accumulation in brain regions of Göttingen minipigs, and a first glimpse of Ca isotopes in the mammalian brain

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The metallome is fundamentally important to the biological sphere, and a wealth of evidence suggests that metals are inherent to the mechanisms of neurodegenerative diseases and/or their pathological manifestations. A prominent example of this is the neuronal/brain accumulation of metals such as Fe, Cu, and Ca associated with Alzheimer's Disease (AD). Stable metal isotopes have shown utility in differentiating healthy vs. diseased states, sometimes prior to traditional diagnoses, highlighting their potential as early diagnostics. Here we have mapped out the distribution of numerous biologically relevant elements (Mg, P, K, Ca, Fe, Cu, and Zn) in brain regions of Göttingen minipigs ranging in age from three months to nearly six years, including wild type, single- and double-transgenic models of AD (PS1, APP/PS1). Preliminary results track tell-tale rises in brain metals with age, namely Fe and Cu. Moreover, we have characterized Ca isotopes in the mammalian brain for the first time, and find that the brain represents the most isotopically depleted Ca reservoir in the body currently known, with $\delta^{44}Ca$ consistently ~1.5‰ lighter than the liver. These results suggest that our efficient Ca purification and isotopic analysis techniques are robust and can provide critical information on Ca homeostasis in future studies.