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The K isotope composition of Göttingen minipig brain regions and implication for Alzheimer's Disease

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Biometals play an inherent role in healthy and diseased brain functioning, notably with respect to neurodegenerative diseases like Alzheimer's (AD). While the AD brain accumulates some metals (e.g. Ca, Fe, Cu, Zn), it may induce deficits of other such as K and Rb. The natural stable isotope compositions of metals have shown utility in differentiating between healthy and diseased states, and while isotope studies exist for those metals that accumulate with AD, no isotopic data exist for metals that express deficits in AD (namely K). Furthermore, limited isotopic data exists altogether for porcine models, even though these are our best physiological proxies for the human condition.

To this end, we have characterized the K isotope composition —δ^{41}K—of six Göttingen minipig brain regions – amygdala, basal ganglia, brain stem, cerebellum, cerebral cortex and hippocampus. Potassium isotope measurements were undertaken using the Proteus prototype collision cell MC-ICP-MS/MS (collaborative platform developed by Bristol Isotope Group and Thermo Fisher Scientificâ„¢). To explore the possible utility of K isotopes in the study of AD, this has been done in two female AD models roughly at middle age – one PS1 model (aged 70 months; approx. 40 years in human equivalency) and one APP/PS1 model (aged 43 months; approx. 25 years in human equivalency).

Results detail considerable variability of K isotope compositions among Göttingen minipig brain regions (range of nearly 0.5 per mil, or ‰), and all brain region K isotope compositions are markedly different from that reported for blood. In the more general sense, these results indicate that changes in brain K may be detectable downstream in blood, earmarking K isotopes as potential diagnostic indicators of neurodegenerative disease(s). Moreover, the K isotope composition of the APP/PS1 AD model in this study was systematically enriched in heavy K isotopes (by ~0.2 ‰), suggestively due to: (i) binding to aspartate/glutamate in Na/K-ATPase (altered in AD); and/or (ii) amyloid beta accumulation, which may further alter or enhance heavy isotope enrichment.