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Impact of Aging on Copper Isotopic Composition in the Brain

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The process of aging is often accompanied by various diseases such as Alzheimer's disease (AD) which has been linked with a change in metal homeostasis. This shift in metal isotopic composition has been identified as a potential biomarker for future diagnosis of AD .

Cu isotopes have been used to study changes in Cu homeostasis associated with various diseases. In AD mice models, the accumulation of ^{63}Cu in the brain has been observed to be related to the progression of the disease [1]. However, our understanding of how the normal aging process can impact the isotopic composition of copper in the brain remains limited.

This study aims to establish a baseline of the evolution of Cu isotopic composition in normally aging mice. We determined the overall copper concentration and isotopic composition of 30 mice (15 males and 15 females) aged 6, 9 and 12-months. Our analyzes build upon previous data obtained from 3-month-old mice, which we incorporated into our study [2]

Our study reveals no significant difference in the Cu isotopic composition of male and female, therefore we combine the data for all mice. We observed that ^{65}Cu is enriched in the 12-month old mice compared to the youngest, which show no distinguishable difference. Additionally, the overall copper concentration in the brain tends to increase with age. Given that the brain of AD mice were shown to be enriched in the lighter isotopes compared to wild types, therefore supporting the notion that AD affects the isotopic composition of the brain.

Copper accumulation in the aging brain may be caused by astrocyte senescence and chronic neuroinflammation. Aging astrocytes become less efficient in regulating copper levels, while chronic inflammation releases copper-importing microglia. Increased oxidative stress in the aging brain may also perturb copper homeostasis due to the redox-active nature of copper.

[1] Moynier et al. 2020 A&D DADM

[2] Moynier et al. 2022 Metallomics