

Correlative imaging of mineral deposits in brain tissue of Alzheimer's Disease patients: application to the valence state of iron deposits by STEM-EELS

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It is known that abnormal mineral deposits containing zinc, aluminum or iron are found in the brain tissue of former patients with severe Alzheimer's Disease (AD). In this work, we have applied correlative imaging methods which are common either in biological or in physical sciences, but rarely together, to characterize such deposits in the same samples (e.g. [1,2]). For iron deposits, it has been suggested that ferrous rather than ferric irons are more responsible for adverse biochemical activity in AD development (e.g. [3,4]). We have used correlative magnetic resonance imaging, histological analysis, optical and scanning electron microscopy methods to locate iron deposits in AD brain tissue, and subsequently site-specific focused ion beam specimen preparation for scanning transmission electron microscopy-electron energy loss spectroscopy (STEM-EELS) to determine the iron valence state [5]. A significant proportion of the ferrous state is formed in three severe AD patients compared to equivalent tissue from healthy patients, showing the usefulness of the combined imaging techniques [6].

[1] M. Zeineh et al., *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, **13** (7), pp. 1129-1130 (2017).

[2] S. J. Madsen et al., *J. Alzheimer's Disease Reports*, **4**, pp. 525-536 (2020)

[3] M.M. Zeineh et al., *Neurobiol. Aging* **36** (9) pp. 2483-2500 (2015).

[4] J.F. Collingwood et al., *J. Alzheimer's Disease*. **14** (2) pp. 235-245 (2008).

[5] Y. Zeng et al., *Ultramicroscopy*, **231**, pp. 113254-113261 (2021)

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