
# Metrology for metallomics

## Discovering the roles of metals in brain disorders

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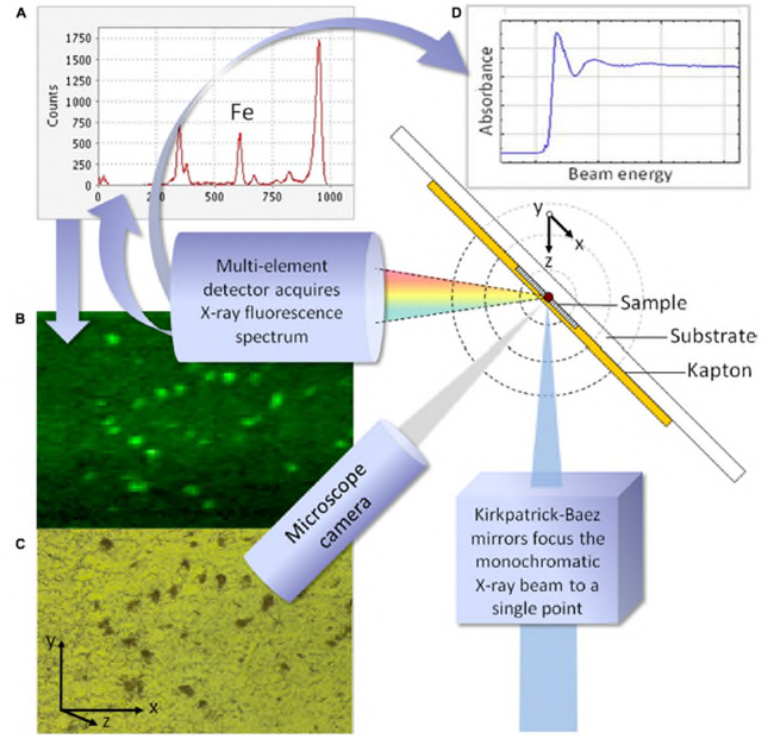
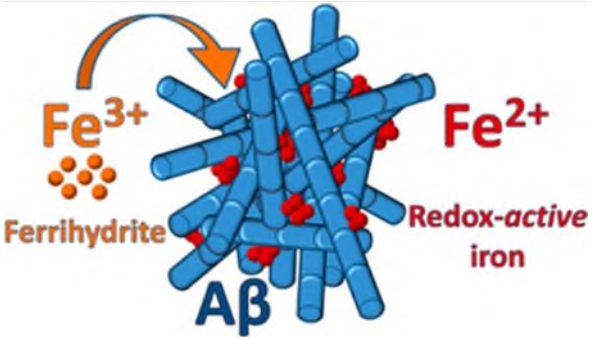
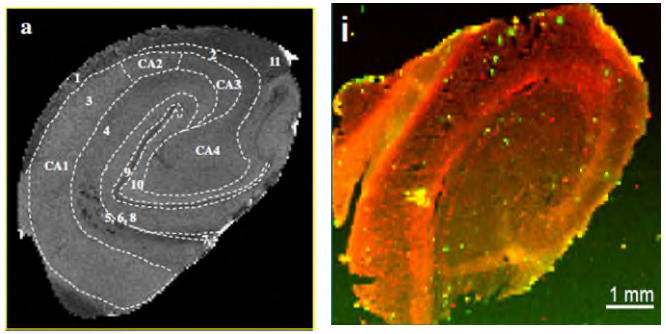
# How we use synchrotron x-rays to study metal elements in the brain – and why!

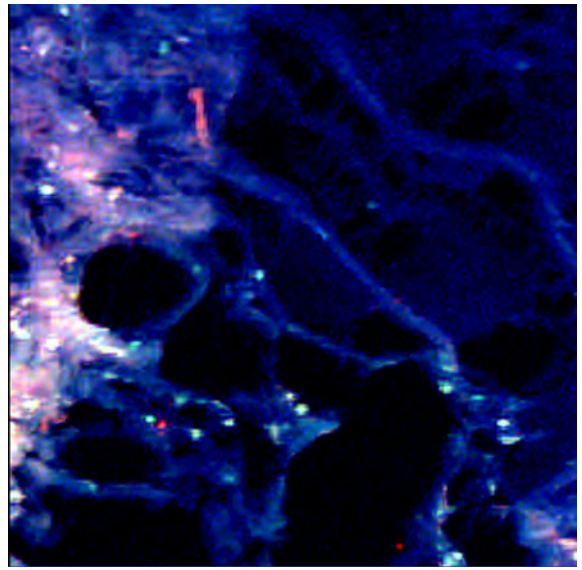



Iron nanoparticle chemistry in pathology




Understanding how MRI signal is affected by iron in neurodegenerative diseases



Super-resolution approaches to speed up XRF imaging of tissue samples

# Metal elements are essential to normal brain function

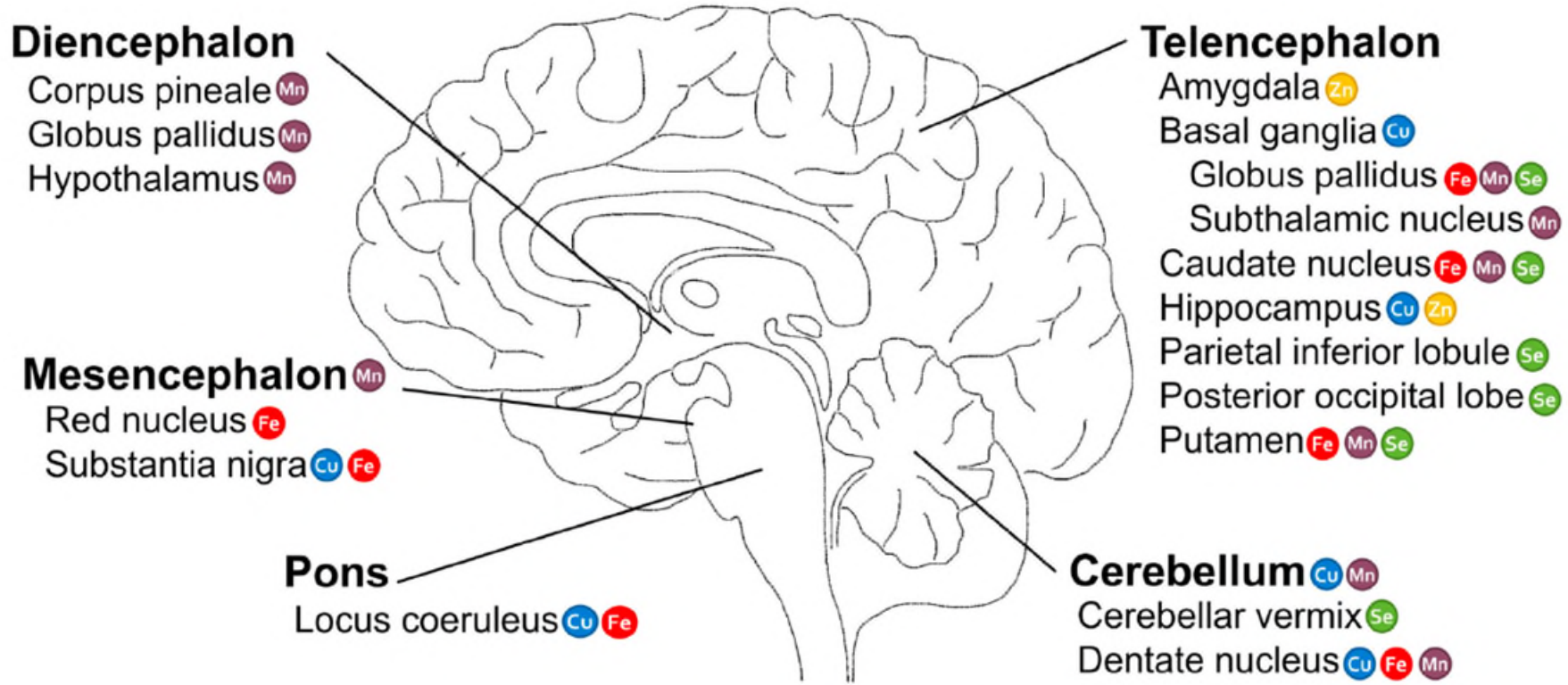
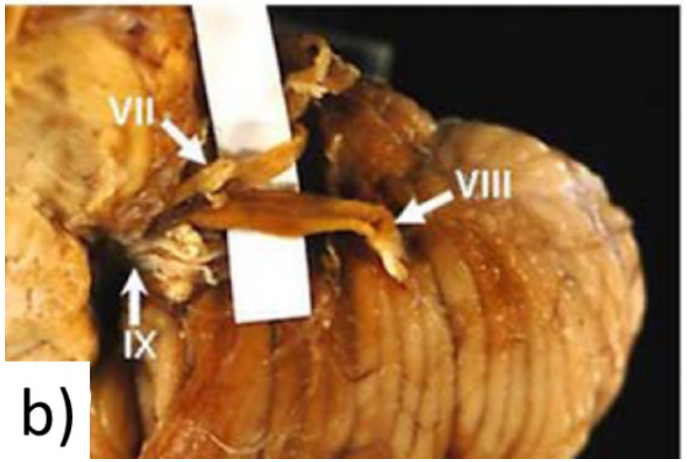


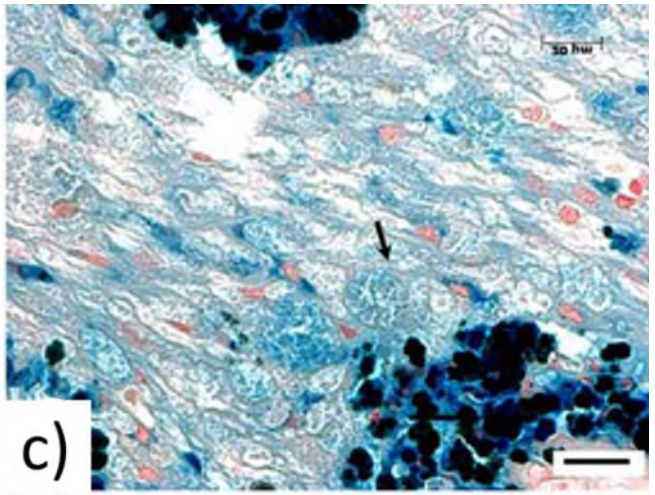

**Fig. 2. Schematic overview of brain regions and distribution of Fe, Cu, Mn, Zn, and Se highlighting areas of TE enrichments under physiological conditions.** Illustrated is a schematic longitudinal section of the brain with its five main brain regions. Additionally shown are the respective subsections for each main brain region with their particular TE enrichment. A detailed summary of the different TE brain concentrations is reviewed in Grochowski et al. [31,105].

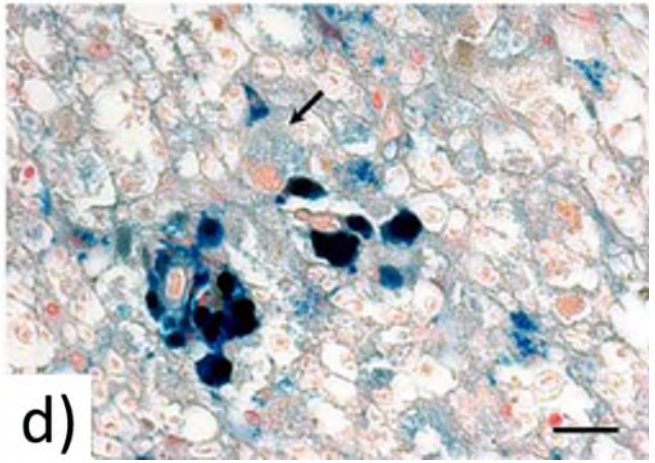
Fe
Zn
Cu
Mn
Se

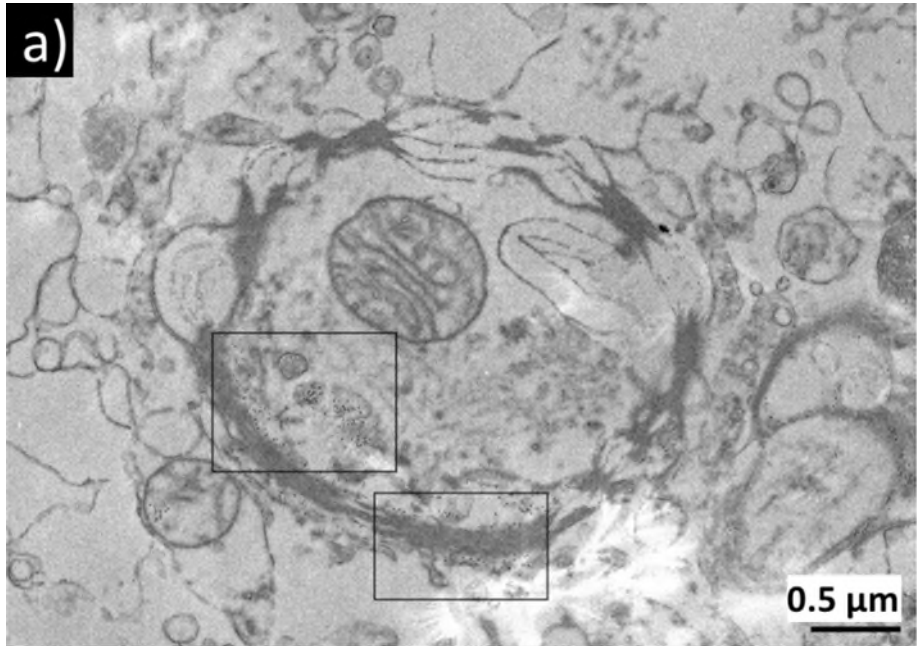
Wandt et al, Redox Biology 2021, 41, 101877

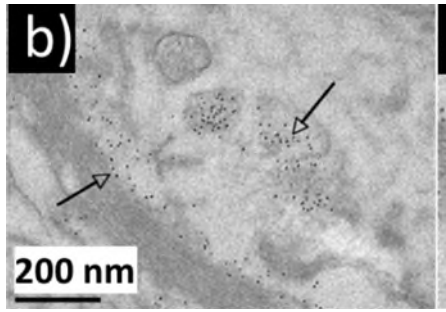
# Transport & storage of metals is disrupted in some disorders

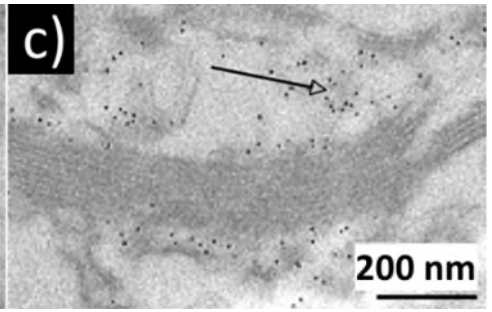




"*Iron Oxides in the Human Brain*", Collingwood & Telling, in Faivre's 'Iron Oxides – from Nature to Applications', Wiley-VCH, 2016

# How to measure what is happening?

## Alzheimer's amyloid plaque

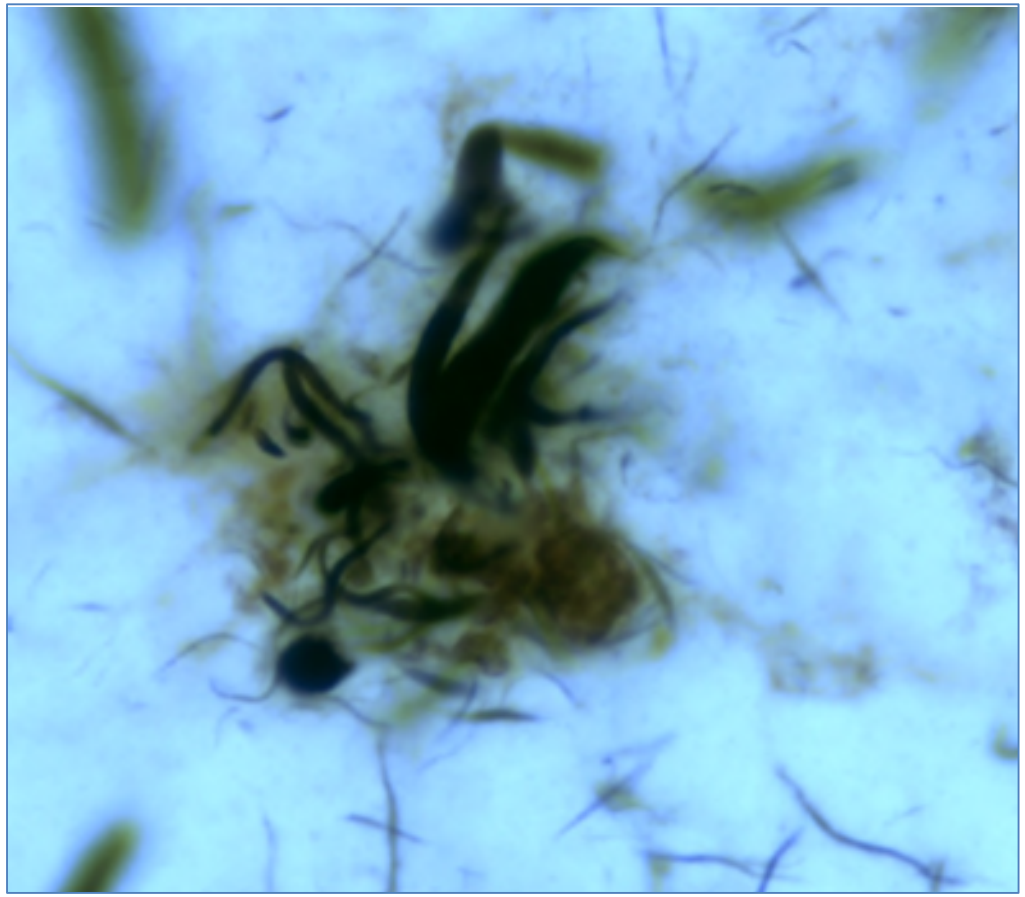


Figure 3 from Collingwood et al, Journal of Alzheimer's Disease 2005, v7, pp267-272

## Iron accumulation in Parkinson's

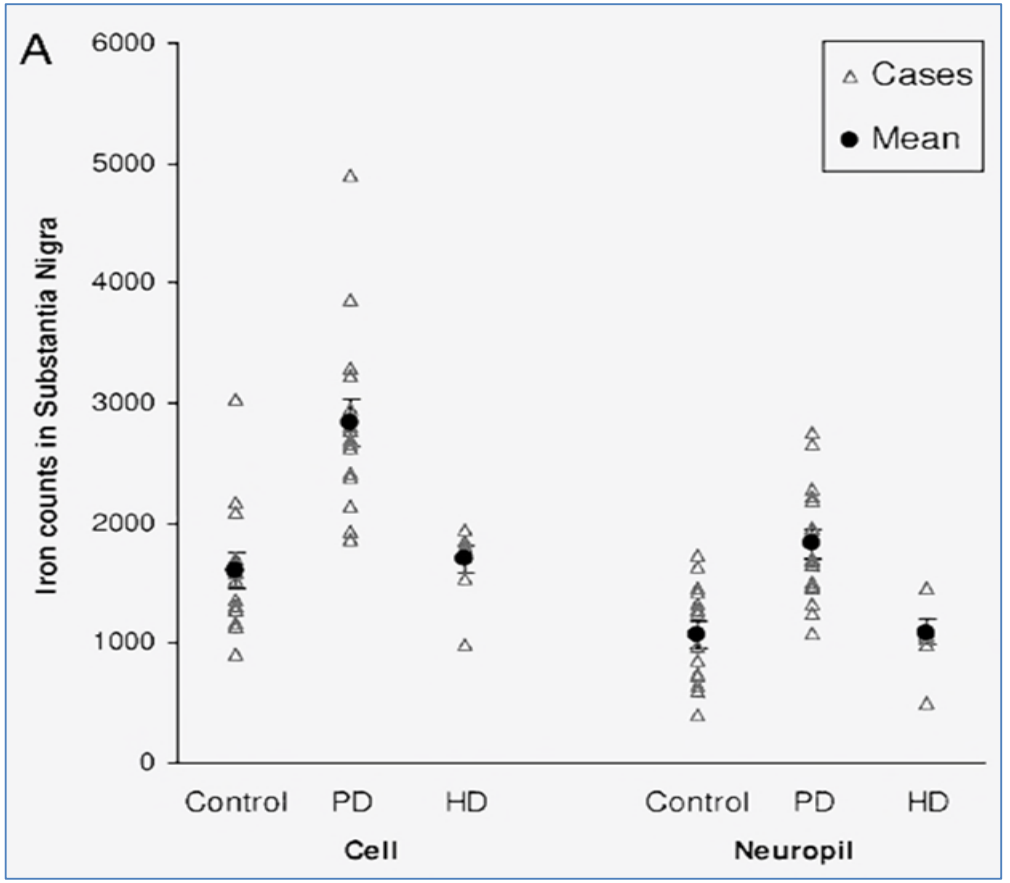
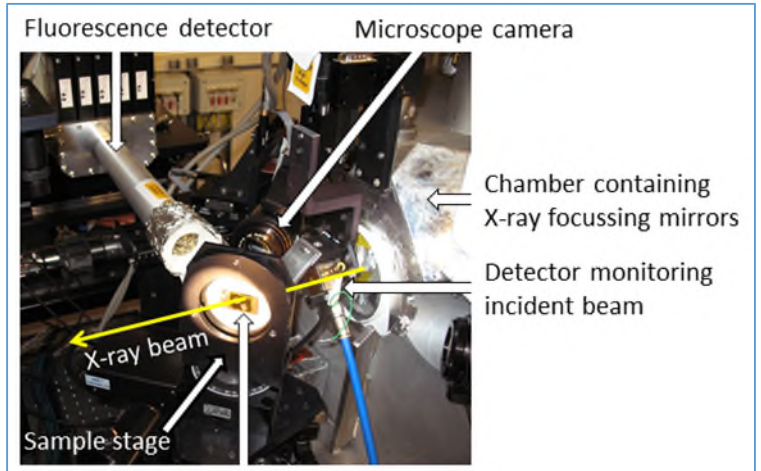
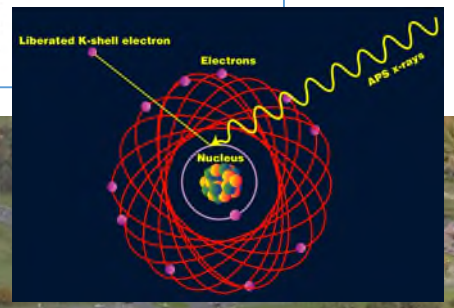


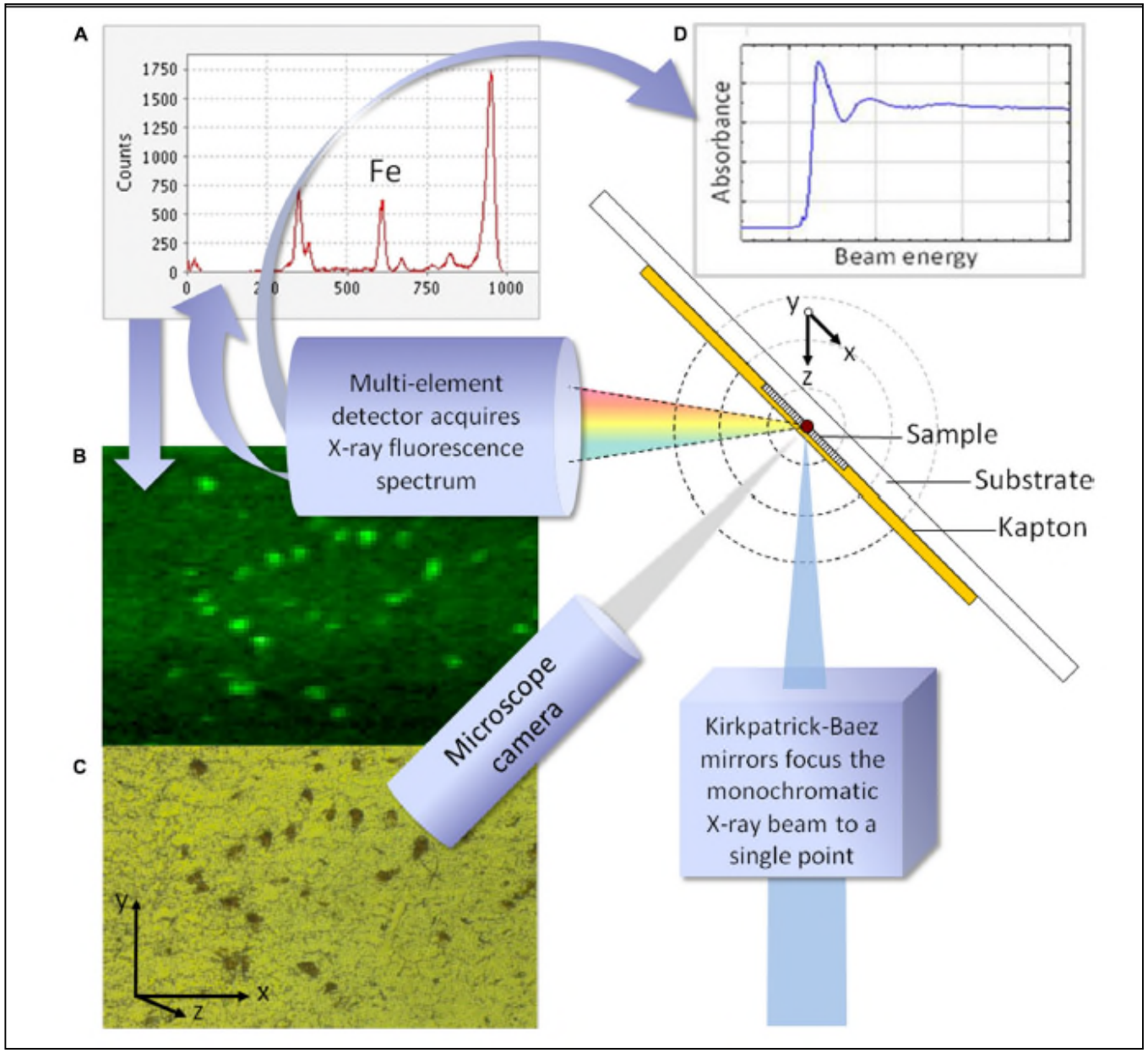

Figure 2A from Oakley et al, Neurology, 2007, v68, pp1820-1825

# Non-destructive imaging & analysis – synchrotron X-ray spectromicroscopy



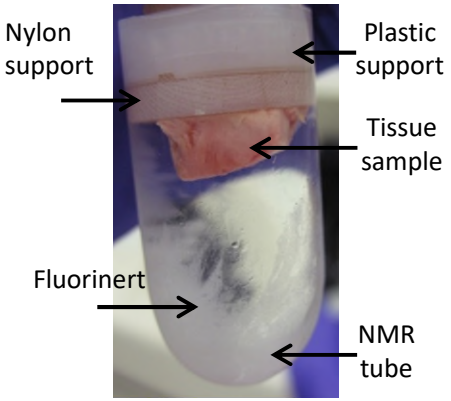


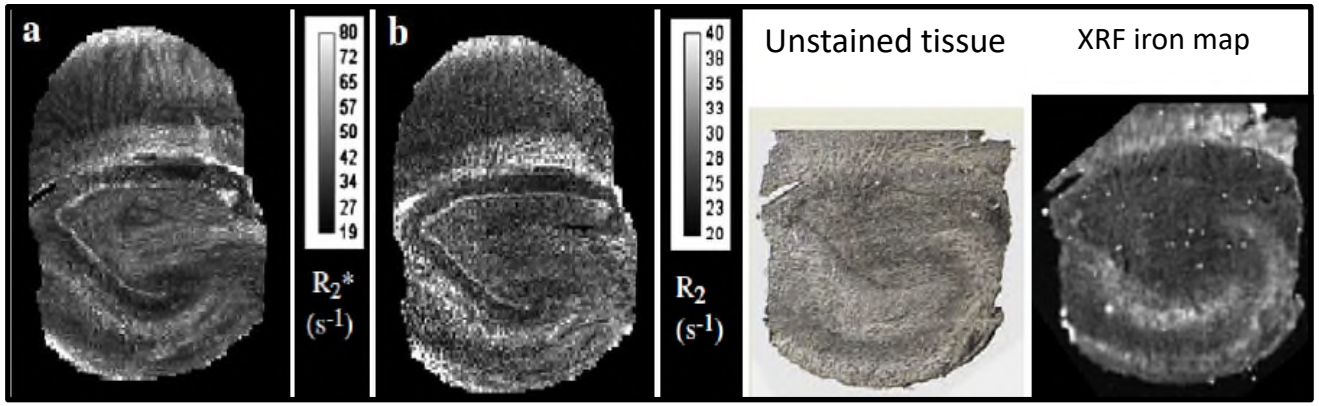



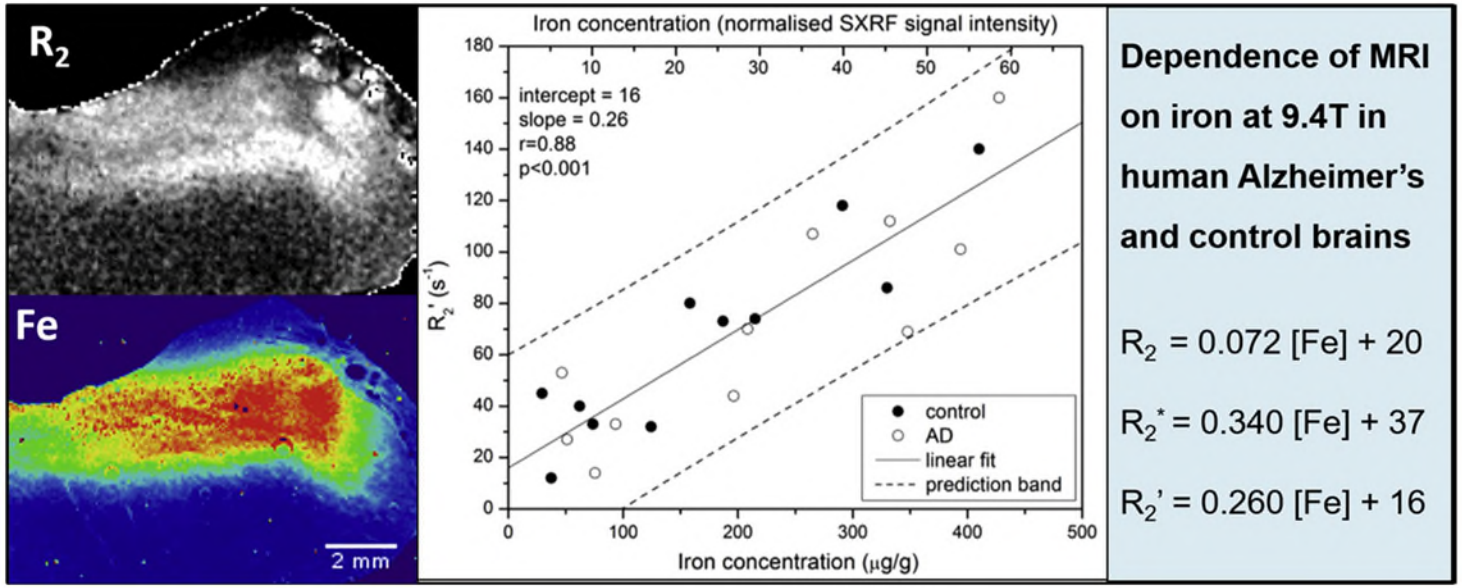

J.F. Collingwood & M.R. Davidson, Front. Pharmacol., doi: 10.3389/fphar.2014.00191, 2014

# What is the relationship between brain iron and MRI contrast?

Tissue @ 3°C during measurement




**Dependence of MRI on iron at 9.4T in human Alzheimer's and control brains**

$R_2 = 0.072\ [Fe] + 20$

$R_2^* = 0.340\ [Fe] + 37$

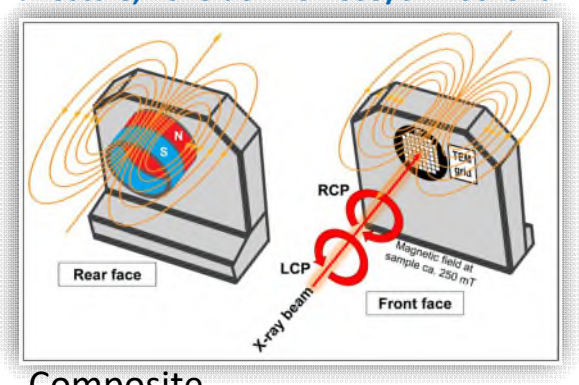
$R_2' = 0.260\ [Fe] + 16$

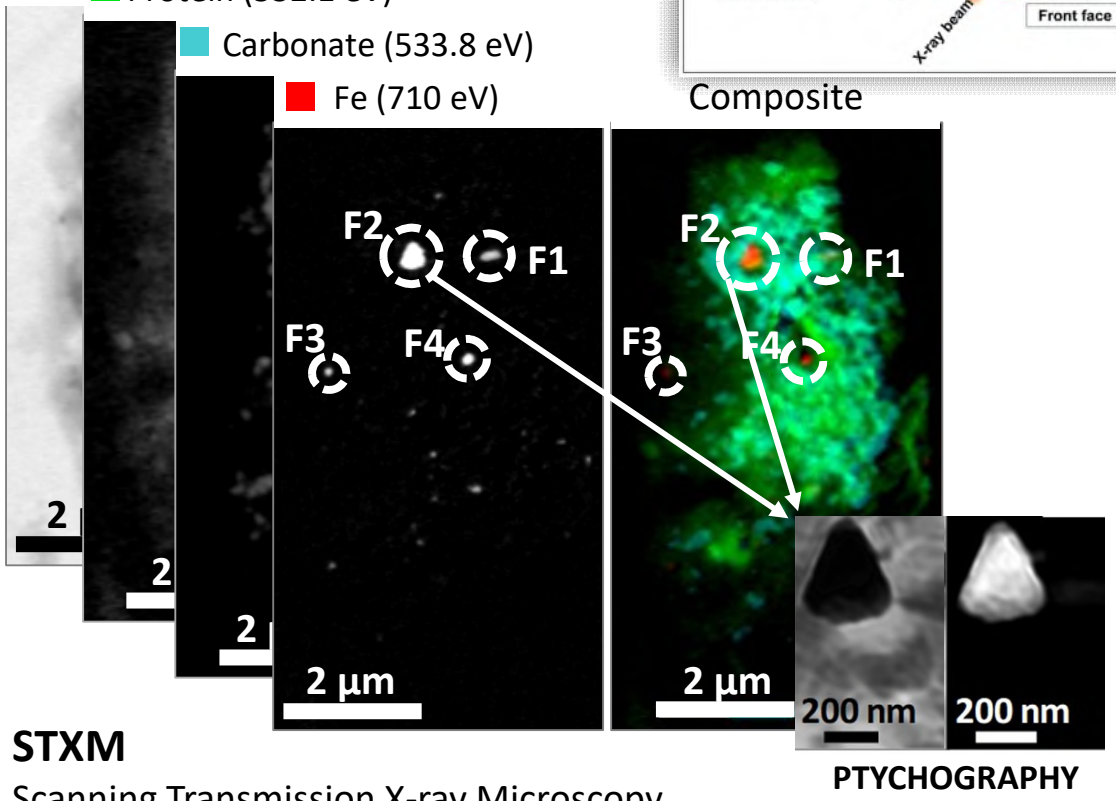
V. Antharam, J. F. Collingwood, et al. (2012) Neuroimage 59 1249-1260

M.E. Finnegan et al, (2019) Journal of Neuroscience Methods 319, 28-39

# Synchrotron X-ray spectromicroscopy of Alzheimer's amyloid plaque cores

Everett J, Collingwood JF, Tjendana-Tjhin V et. al., Nanoscale, 2018 doi: 10.1039/c7nr06794a



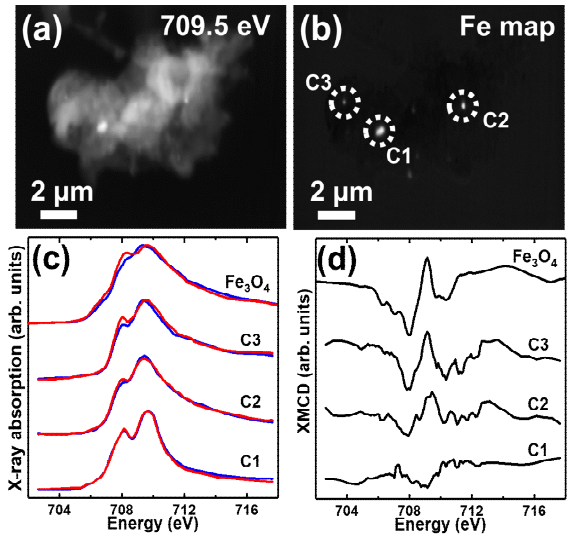



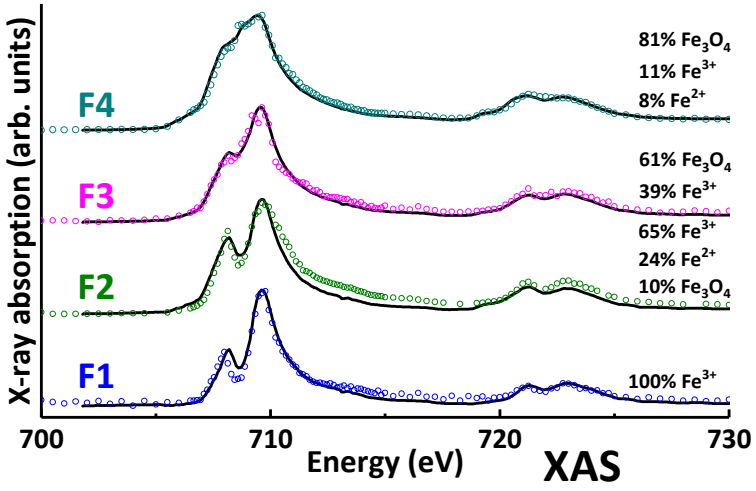

**STXM**

Scanning Transmission X-ray Microscopy

**PTYCHOGRAPHY**

**X-ray Magnetic Circular Dichroism (XMCD)**



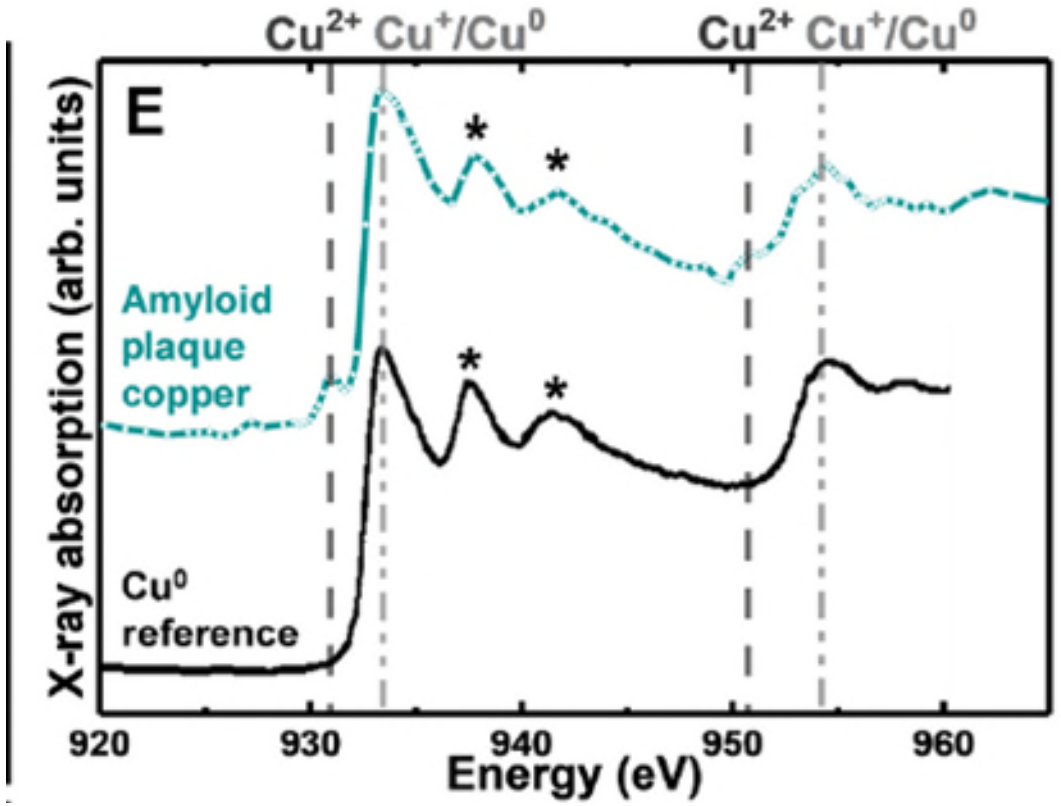



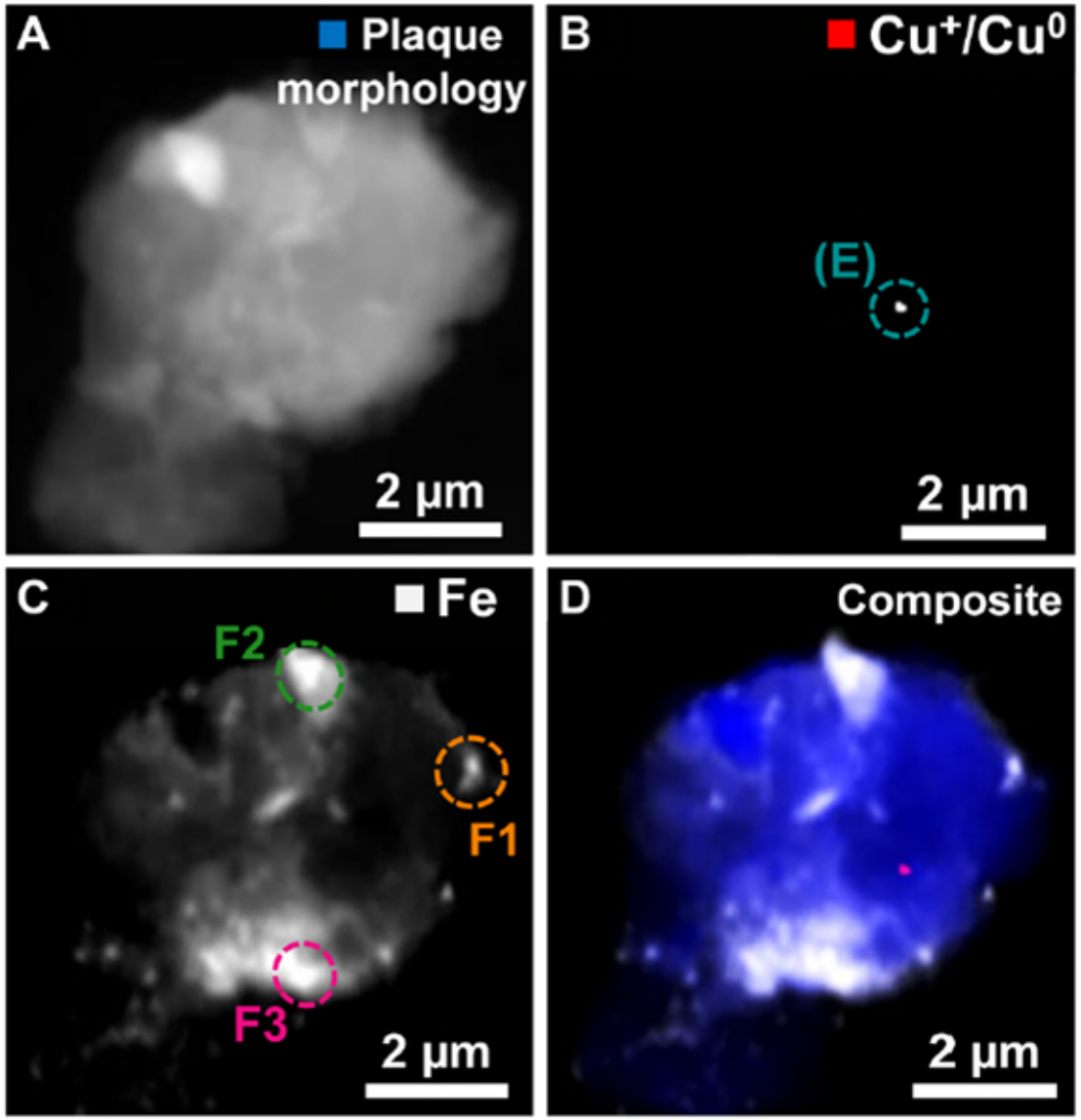

X-ray absorption spectroscopy

APPLIED SCIENCES AND ENGINEERING

# Biogenic metallic elements in the human brain?

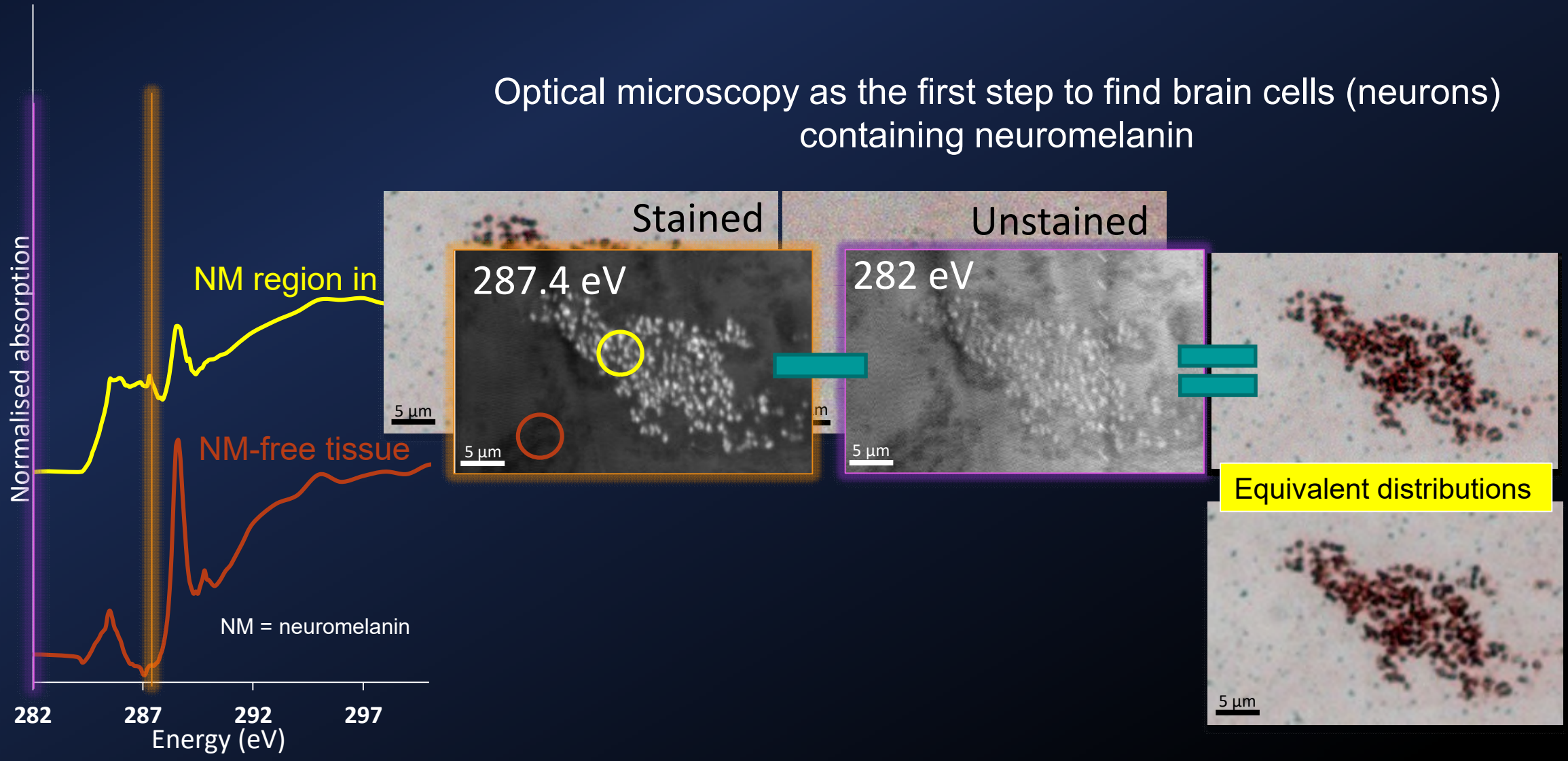
James Everett[1,2], Frederik Lermyte[2,3], Jake Brooks[2], Vindy Tjendana-Tjhin[2], Germán Plascencia-Villa[4], Ian Hands-Portman[5], Jane M. Donnelly[2], Kharmen Billimoria[2,6,7], George Perry[4], Xiongwei Zhu[8], Peter J. Sadler[6], Peter B. O'Connor[6], Joanna F. Collingwood[2], Neil D. Telling[1]*



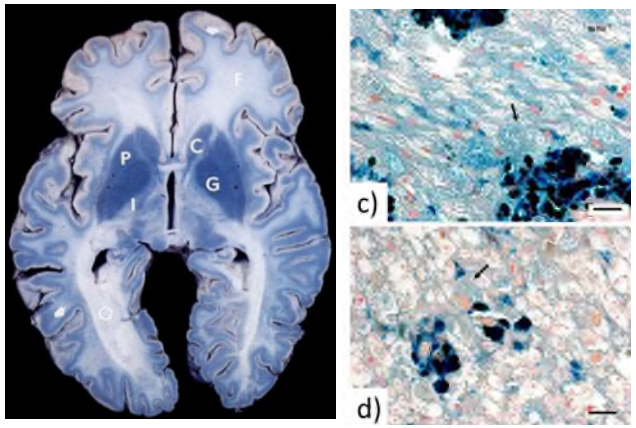
# Finding melanin pigment in human brain with X-ray microscopy

Optical microscopy as the first step to find brain cells (neurons) containing neuromelanin



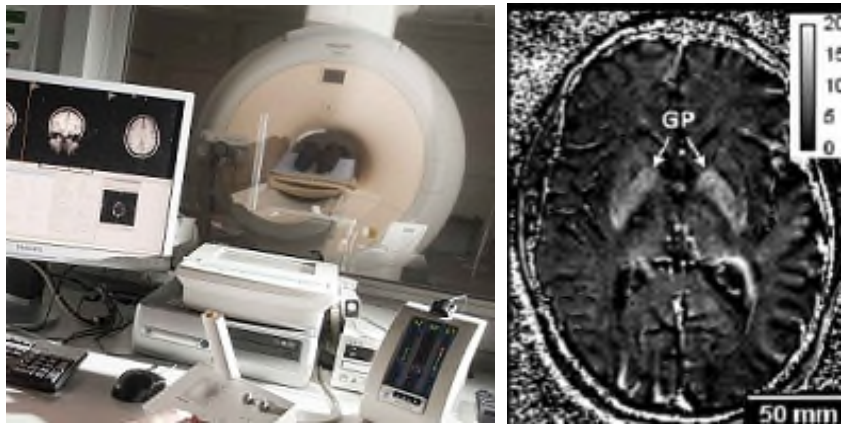

Brooks J et. al., Angewandte Chemie, 2020

# Conclusion



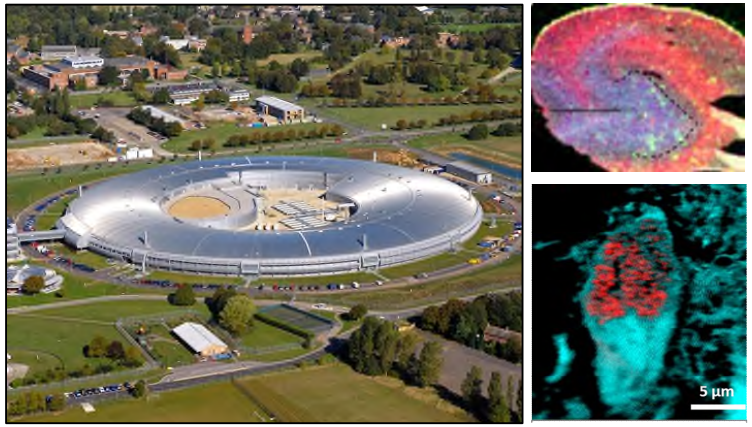

Metal elements are essential to normal brain metabolism, but are not all easy to picture in detail with staining methods in the lab.

Need more sensitive and accurate ways of looking at brain tissue samples.




Some metal elements, particularly iron, give contrast in certain clinical scanning methods, particularly Magnetic Resonance Imaging.

Patterns of change in the brain, & impact of treatment, could be imaged in people




Synchrotron X-ray microscopy is extremely sensitive and accurate to allow metal elements to be identified

Documenting change and discovering what is happening to metal distributions and metal chemistry

# THANK YOU!

Trace Metals in Medicine group, School of Engineering, University of Warwick

James Everett & Neil Telling, School of Pharmacy & Bioengineering, Keele University

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Dr Mary Finnegan*

Dr Vindy Tjendana Tjhin

Yunxing Ma

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Dr Julia Parker

**University of Florida**

Dr Mark Davidson

Prof Jon Dobson

Dr Albina Mikhailova

Dr Vijay Antharam

Prof Chris Batich

Dr John Forder

UKRI Engineering and Physical Sciences Research Council

diamond

ALS ADVANCED LIGHT SOURCE

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Alzheimer's Society United Against Dementia