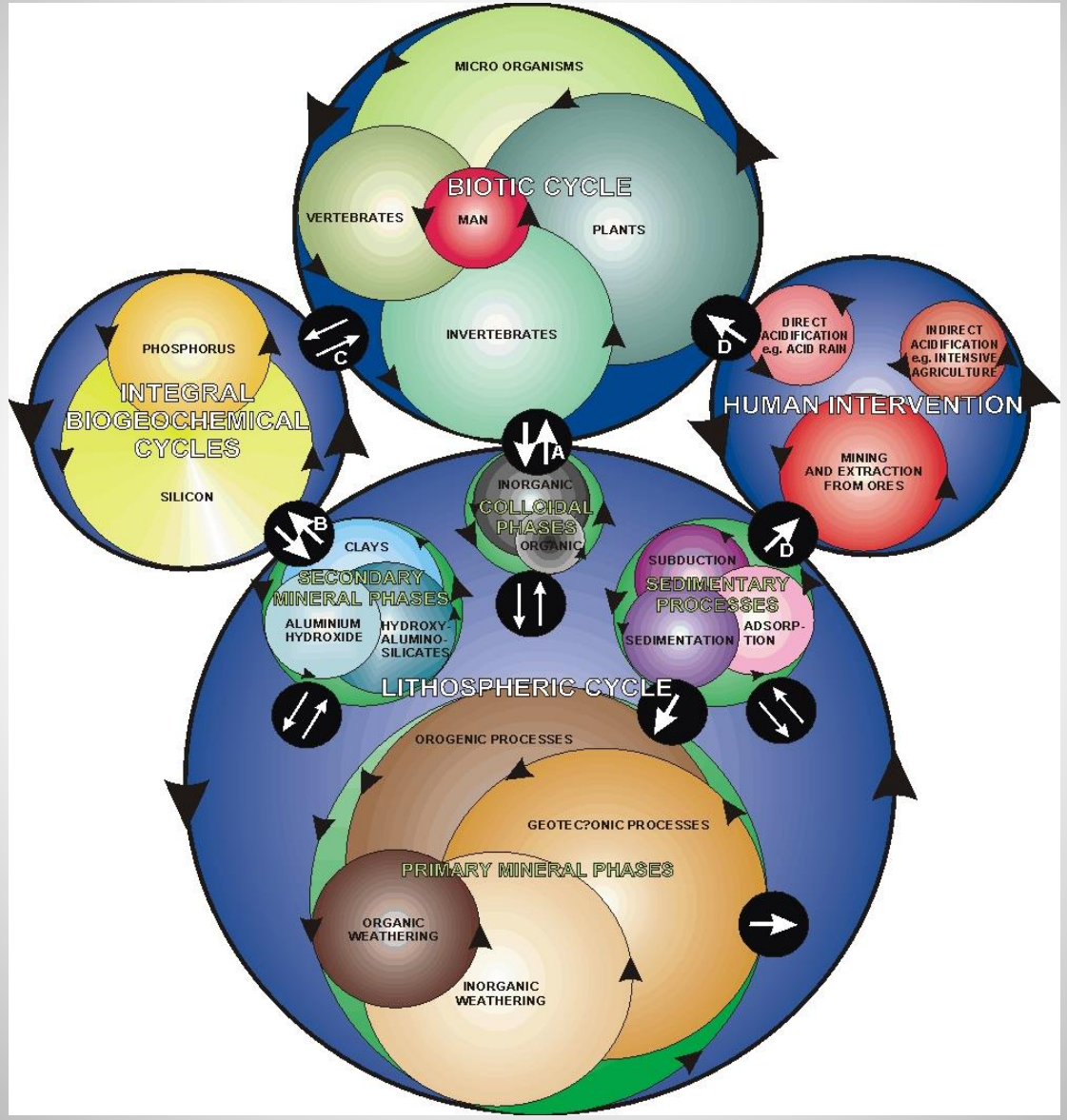
Human Exposure to Aluminium Implications for Neurodegenerative Diseases Including Alzheimer's Disease

Christopher Exley PhD
Professor in Bioinorganic Chemistry
Aluminium and Silicon Research Group
The Birchall Centre, Lennard-Jones Laboratories,
Keele University, Staffordshire, ST5 5BG, UK
Tel: 44 1782 734080; Email: c.exley@keele.ac.uk
http://www.keele.ac.uk/aluminium

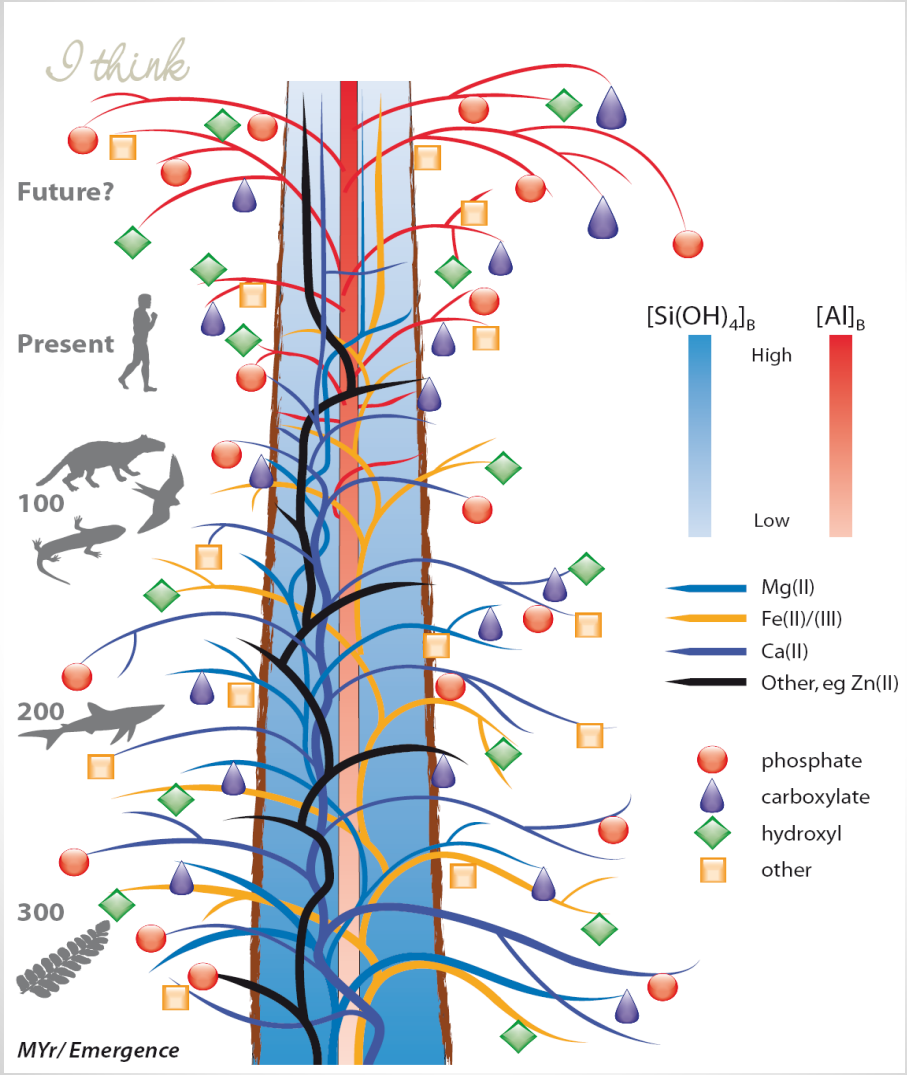
Honorary Professor, University of the Highlands and Islands

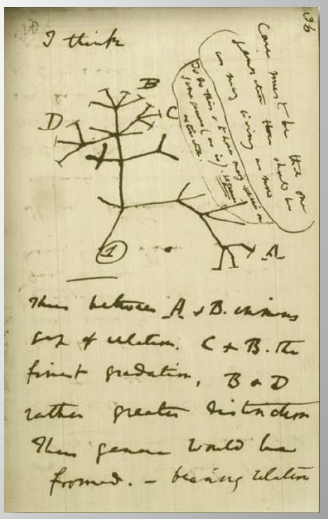
The Aluminium Age



Exley C (2003) A biogeochemical cycle for aluminium? J. Inorg. Biochem. 97, 1-7.

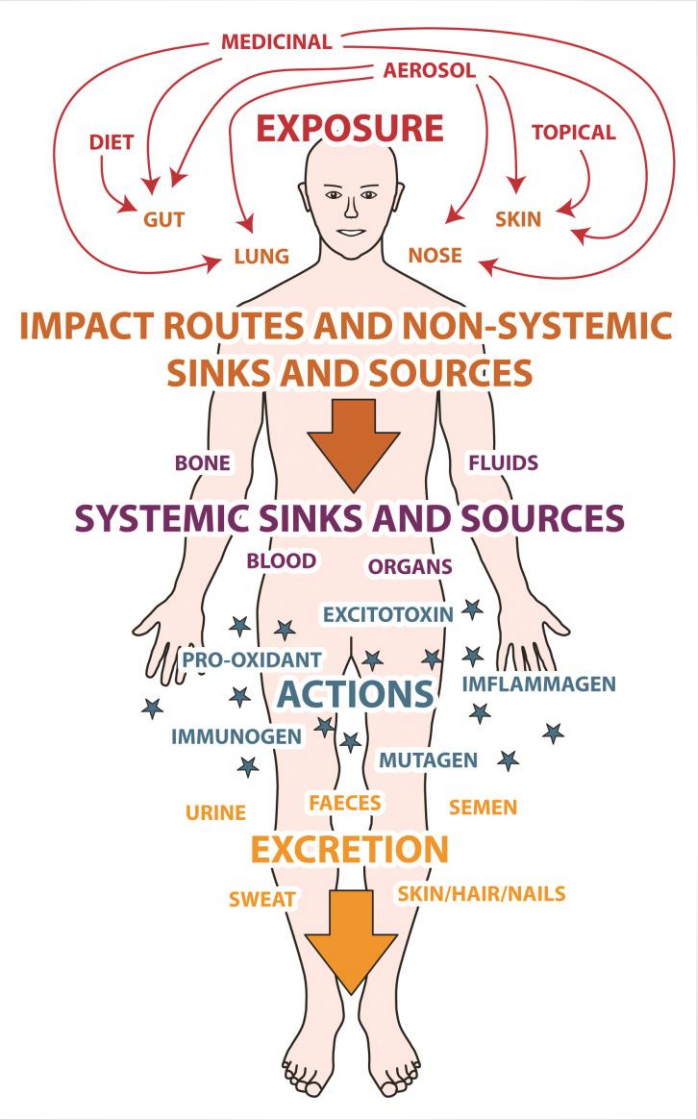
Aluminium is Non-Essential





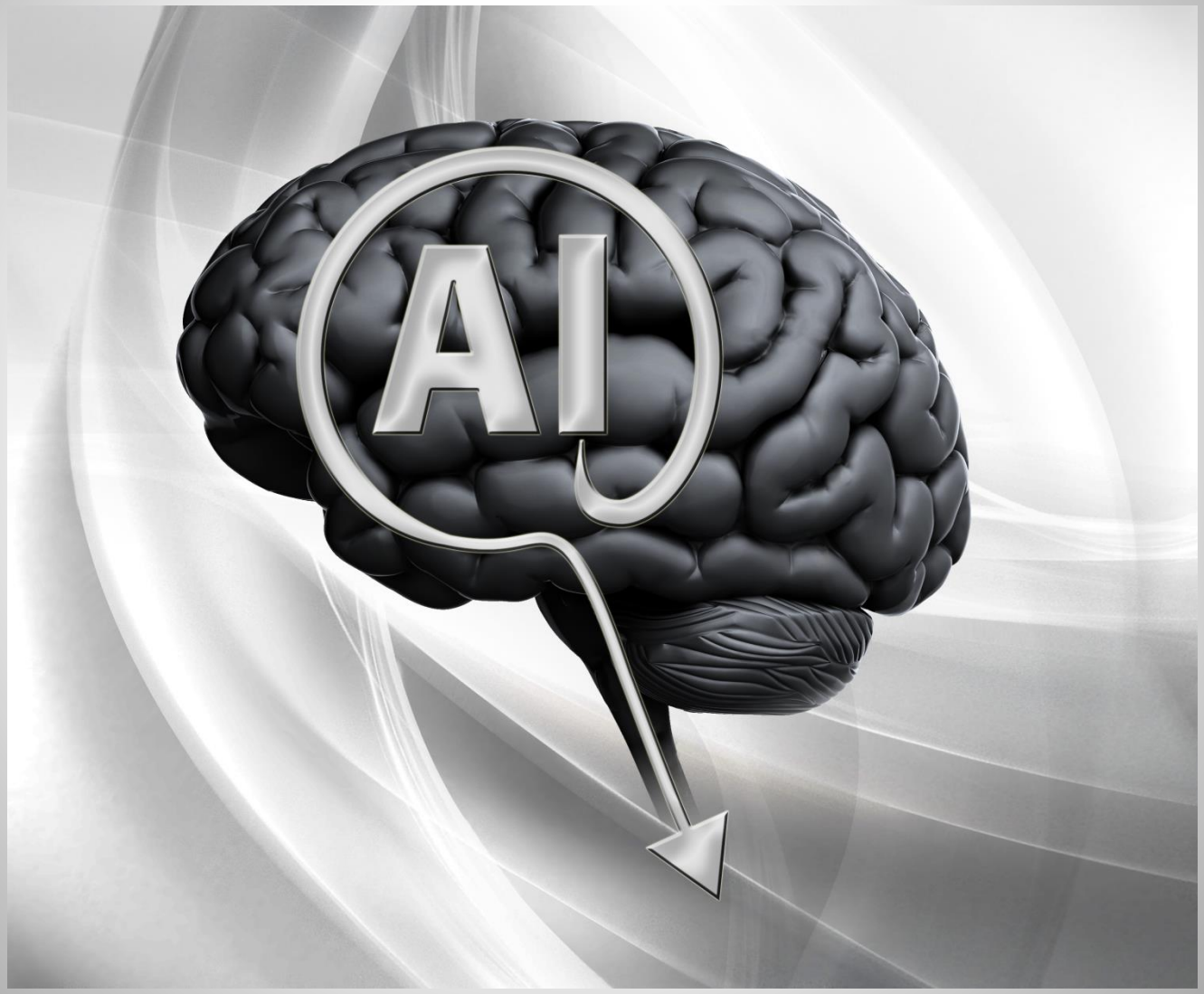
Exley C (2009) Darwin, natural selection and the biological essentiality of aluminium and silicon. Trends in Biochemical Sciences 34, 589-593.

Human Exposure to Aluminium

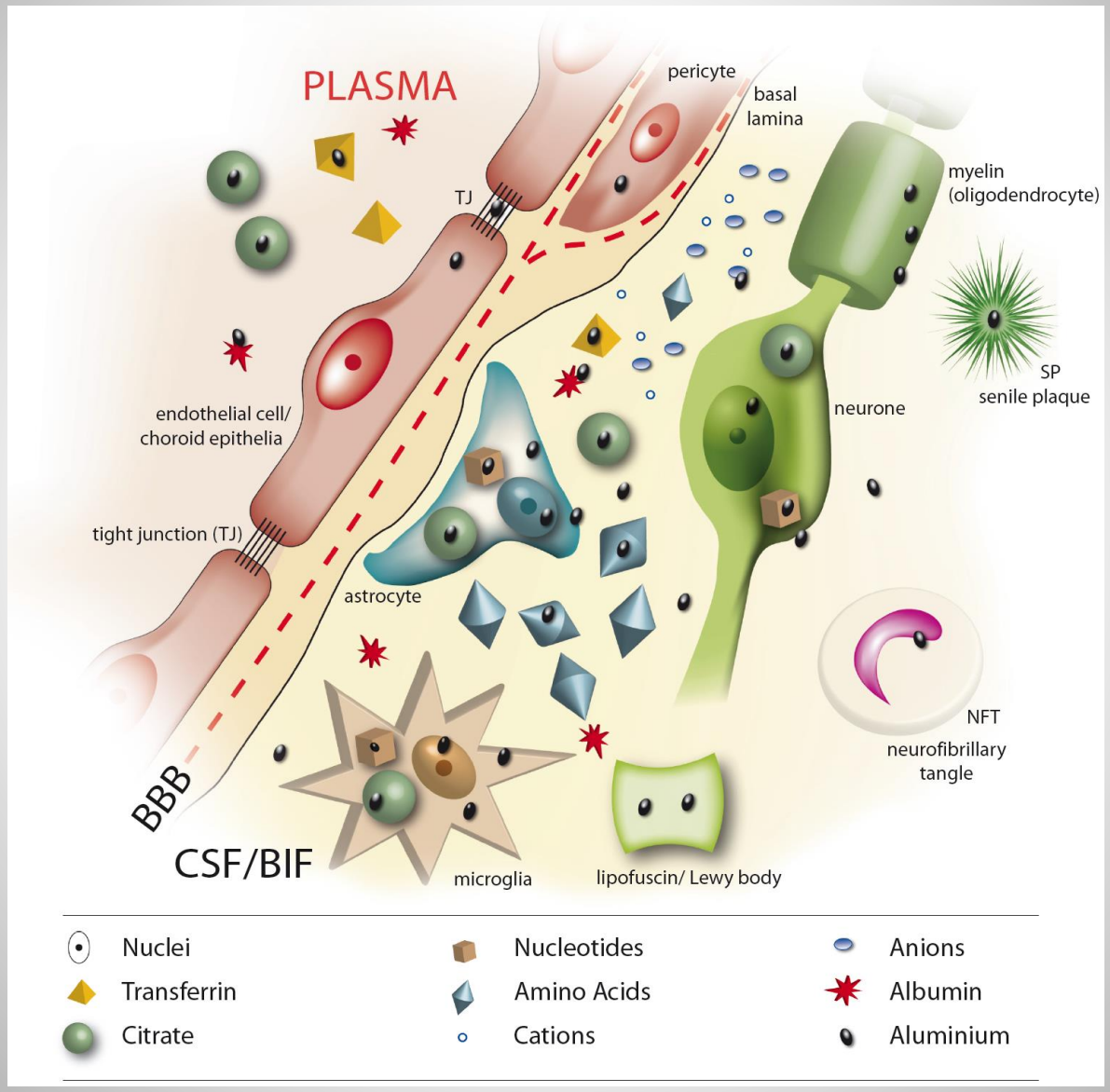


Exley C (2013) Human exposure to aluminium. Environmental Science:Processes and Impacts 15, 1807-1816.

Aluminium and The Brain



Aluminium in the Brain



Exley C and House E (2011) Aluminium in the human brain. Monatshefte für Chemie - Chemical Monthly 142, 357-363.

Aluminium Content of Human Brain

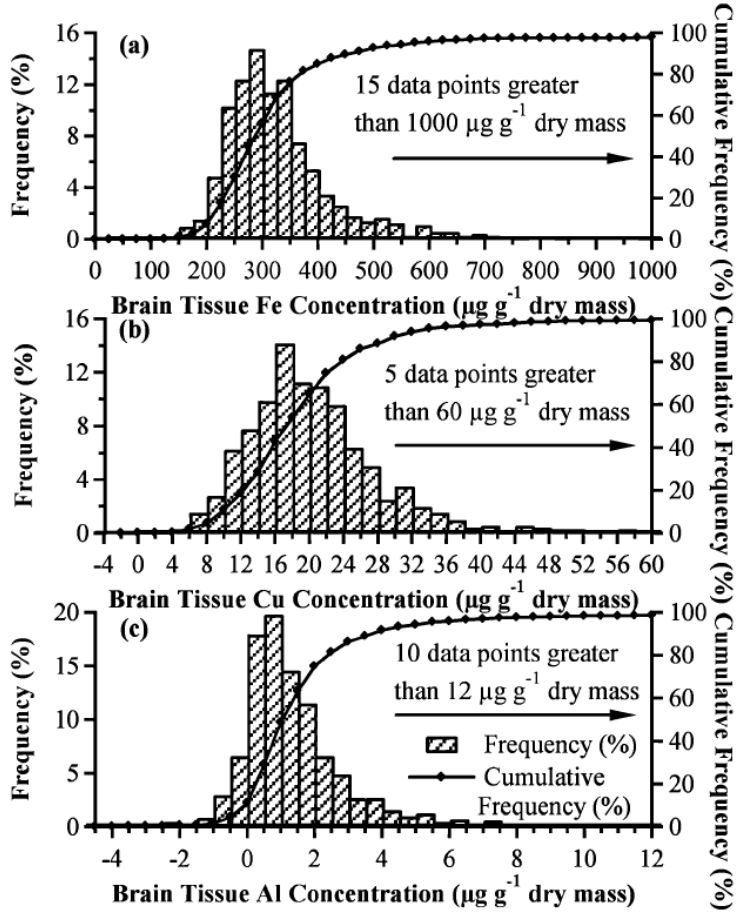


Fig. 3 Percentage frequency (bars) and cumulative frequency (line and marker) distributions of (a) Fe, (b) Cu and (c) Al concentrations in (n = 719, 720 and 713 respectively) brain tissues after subtraction of contamination.

The median Al content of tissues from all **60 brains** (n=713) is 1 μg/g dry wt.

In 52 out of 60 individuals at least one tissue sample exceeded 2 μg Al/g dry wt.

In 41 out of 60 individuals at least one tissue sample exceeded 3.5 μg Al/g dry wt.

Approximately 70% of individuals aged 70 – 103 years had at least one tissue Al content which should be considered as pathological.

House E, Esiri M, Forster G, Ince PG and Exley C (2012) Aluminium, iron and copper in human brain tissues donated to the medical research council's cognitive function and ageing study. Metallomics 4, 56-65.

Accidental Exposure to Aluminium

Camelford, Cornwall, United Kingdom, 1988

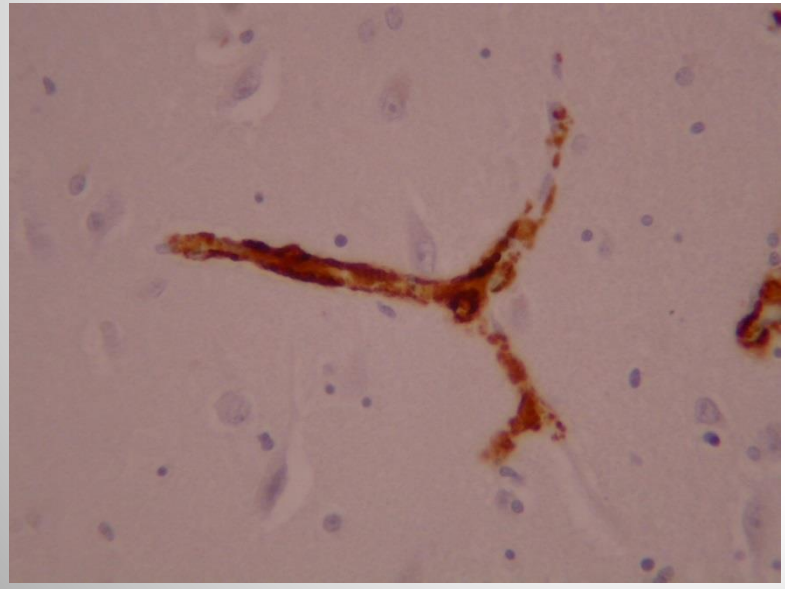
SHORT REPORT

Severe cerebral congophilic angiopathy coincident with increased brain aluminium in a resident of Camelford, Cornwall, UK

C Exley, M M Esiri

See Editorial Commentary, p 811

J Neurol Neurosurg Psychiatry 2006;**77**:877–879. doi: 10.1136/jnnp.2005.086553



Frontal Cortex, n=5.

1. 23.00* μg/g dry wt.
2. 3.24
3. 11.01
4. 4.33
5. 5.71

*Noted during measurement as a heavily vascularised piece of tissue.

Occupational Exposure to Aluminium

Exley and Vickers *Journal of Medical Case Reports* 2014, **8**:41
http://www.jmedicalcasereports.com/content/8/1/41

JOURNAL OF MEDICAL CASE REPORTS

CASE REPORT Open Access

Elevated brain aluminium and early onset Alzheimer's disease in an individual occupationally exposed to aluminium: a case report

Mean Al content of frontal lobe tissue (n=46) is 2.98 (2.73) μgAl/g dry wt.

Range is 0.00 (less than the method blank) to 12.97 μgAl/g dry wt.

More than 30% of tissue samples had an Al content considered as pathological, greater than 3.50 μgAl/g dry wt.

Everyday Exposure to Aluminium

Male, 60 years of age, cause of death, stroke. Units μgAl/g tissue dry wt.

Brain Lobes	No of samples	Mean	SD
Hippocampus	21	2.20	2.71
R. Temporal	22	2.20	2.65
L. Temporal	15	2.22	2.73
R. Parietal	29	2.58	2.61
L. Parietal	26	1.29	2.95

Male, 74 years of age, post mortem revealed mild, subclinical, tau pathology associated with the hippocampus. Units μgAl/g tissue dry wt.

Brain Lobes	No of samples	Mean	SD
Hippocampus	6	1.75	1.01
Frontal	11	0.84	0.97
Occipital	9	0.70	0.80
Parietal	10	0.54	0.58
Temporal	13	0.75	1.42

Everyday Exposure to Aluminium

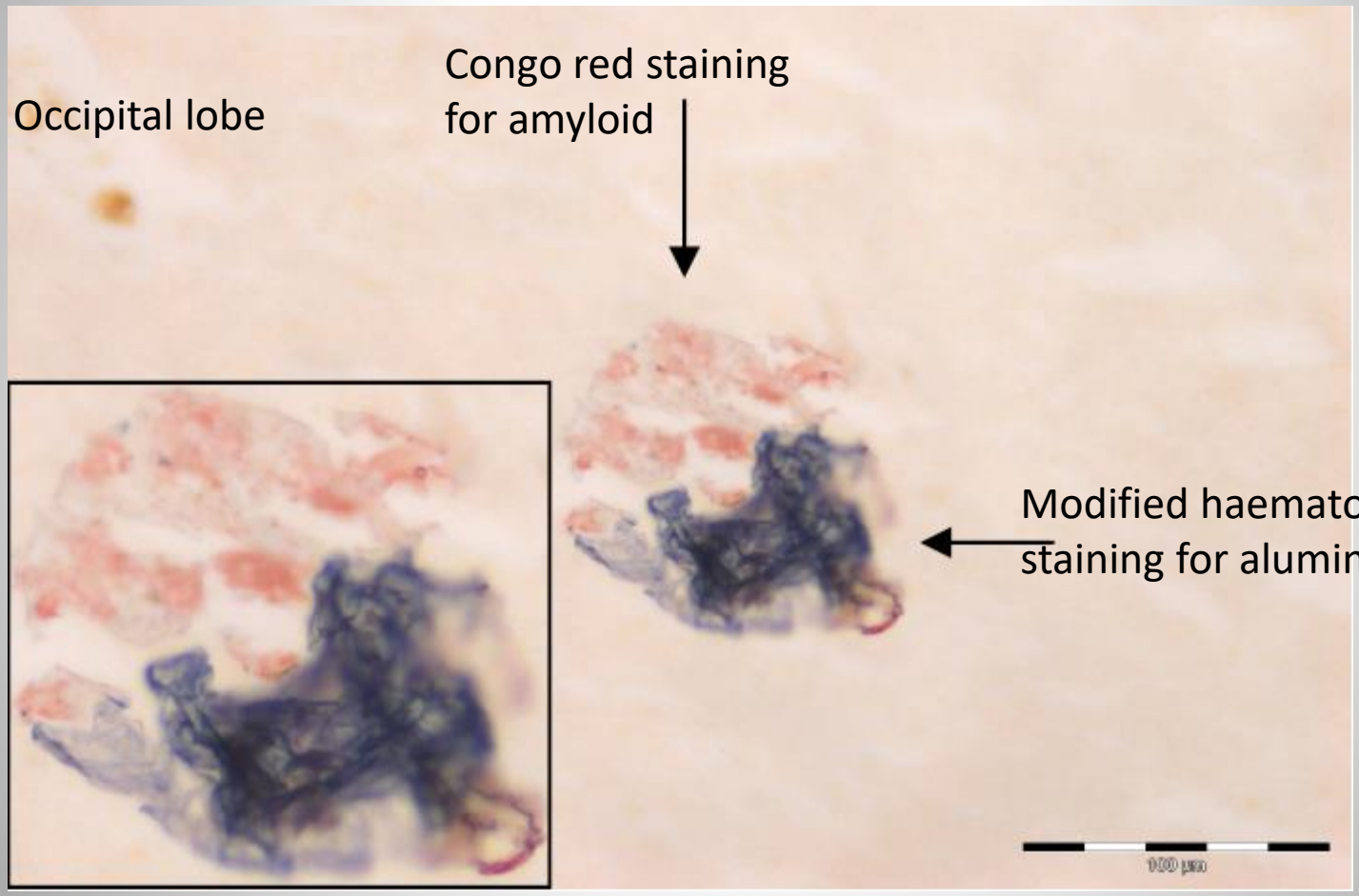
Male, 60 years of age, late onset epilepsy* (died of asphyxiation following an epileptic fit).
Units μgAl/g tissue dry wt.

Brain Lobes	No of samples	Mean	SD
Hippocampus	5	4.35	2.80
Frontal	5	0.81	0.59
Occipital	5	2.22	2.23
Parietal	5	0.50	0.35
Temporal	5	0.78	0.48

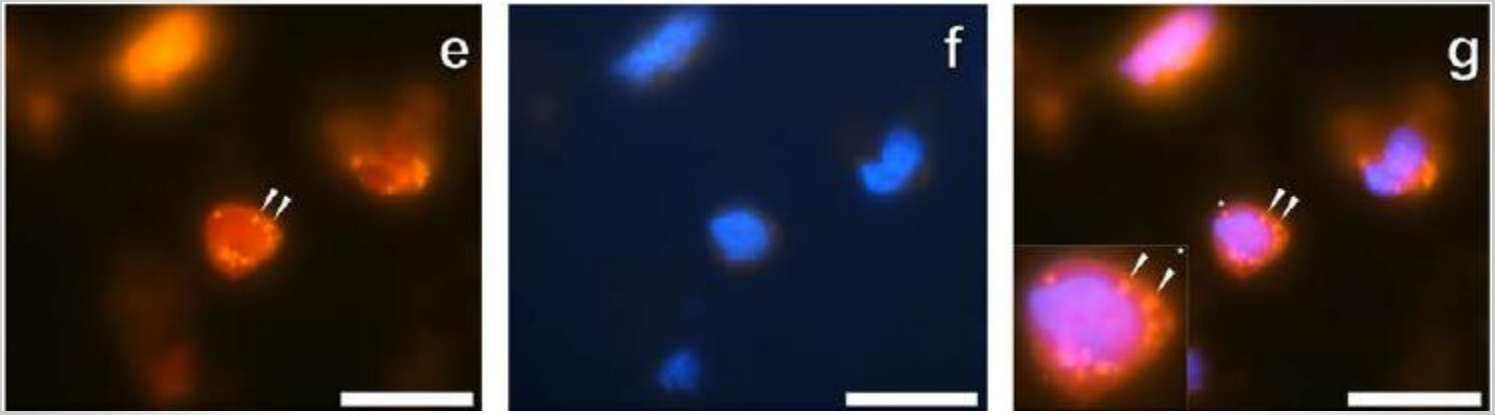
*First known measurement of brain aluminium in human epilepsy?

Identifying Aluminium in Human Brain Tissue

Exley C and House E (2011) Aluminium in the human brain. Monatshefte für Chemie - Chemical Monthly 142, 357-363.

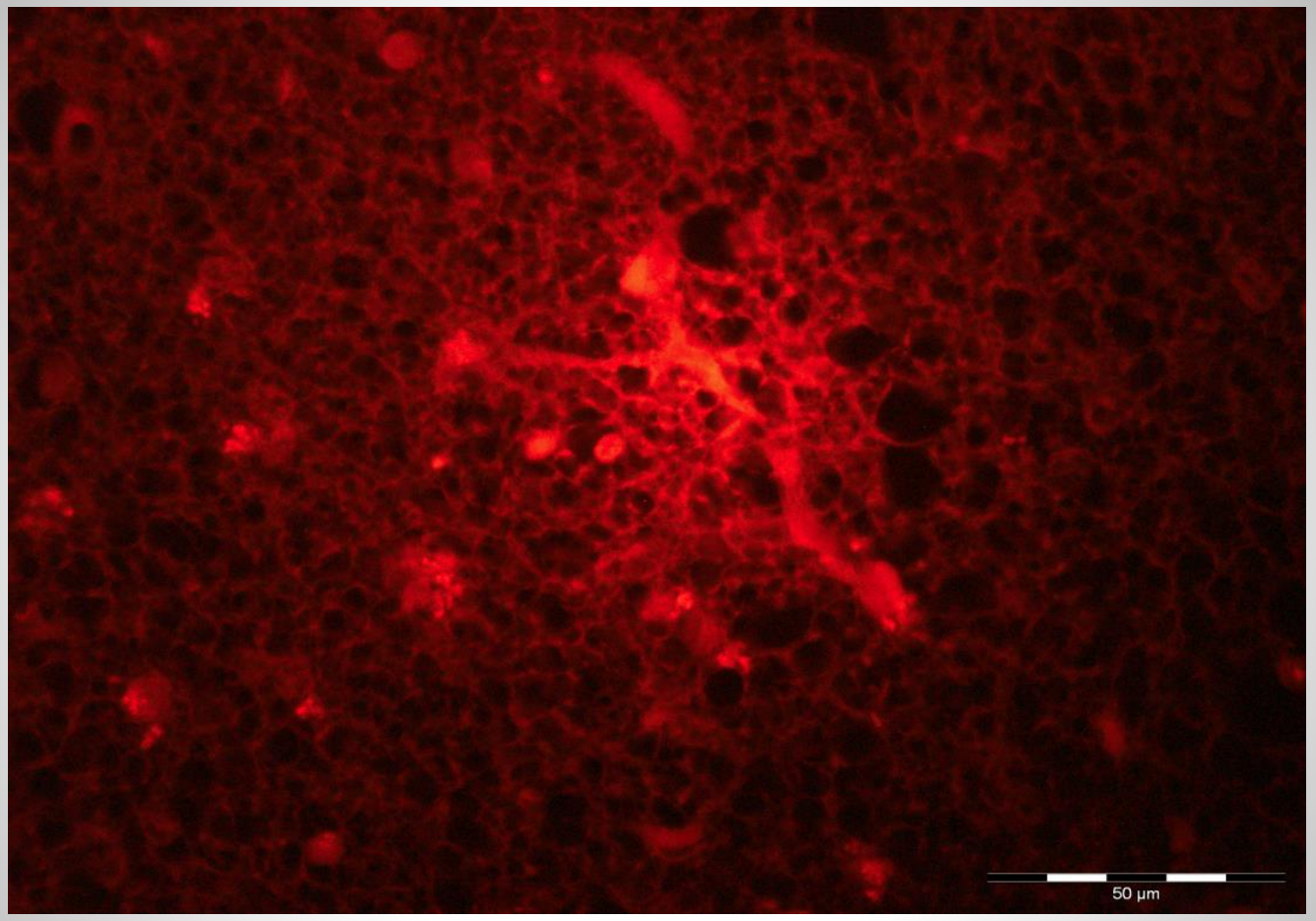


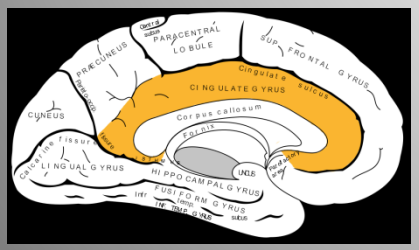
Fluorescence Microscopy for Aluminium



Mold M, Eriksson H, Siesjö P, Darabi A, Shardlow E and Exley C (2014) Unequivocal identification of intracellular aluminium adjuvant in a monocytic THP-1 cell line. Scientific Reports 4, 6287.

Fluorescence Microscopy and Aluminium in Human Brain Tissue





Cingulate or Limbic Cortex

Mechanisms of Toxicity

$Al^{3+}_{(aq)}$ + Biological Ligand $\leftrightarrow$

Biochemical Disruption $\rightarrow$

Molecular/Cellular/Tissue Damage


Pro-oxidant
Immunogen
Excito-toxin
Aluminium is Neurotoxic!
Inflammagen
Mutagen

frontiers in
NEUROLOGY

REVIEW ARTICLE
published: 27 October 2014
doi: 10.3389/fneur.2014.00212

Why industry propaganda and political interference cannot disguise the inevitable role played by human exposure to aluminum in neurodegenerative diseases, including Alzheimer's disease

Christopher Exley*

The Birchall Centre, Lennard-Jones Laboratories, Keele University, Stoke-on-Trent, UK

Edited by:
Christopher Ariel Shaw, University of British Columbia, Canada

Reviewed by:
Nelson Silva Filho, Universidade Estadual Paulista, Brazil
Lucija Tomljenovic, University of British Columbia, Canada

Correspondence:
Christopher Exley, The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire ST5 5BG, UK
e-mail: c.exley@keele.ac.uk

In the aluminum age, it is clearly unpalatable for aluminum, the globe's most successful metal, to be implicated in human disease. It is unpalatable because for approximately 100 years human beings have reaped the rewards of the most abundant metal of the Earth's crust without seriously considering the potential consequences for human health. The aluminum industry is a pillar of the developed and developing world and irrespective of the tyranny of human exposure to aluminum it cannot be challenged without significant consequences for businesses, economies, and governments. However, no matter how deep the dependency or unthinkable the withdrawal, science continues to document, if not too slowly, a burgeoning body burden of aluminum in human beings. Herein, I will make the case that it is inevitable both today and in the future that an individual's exposure to aluminum is impacting upon their health and is already contributing to, if not causing, chronic diseases such as Alzheimer's disease. This is the logical, if uncomfortable, consequence of living in the aluminum age.

Keywords: aluminium, Alzheimer's disease, human exposure, neurodegenerative disease, body burden

Complacency?
Aluminium in Drugs for Alzheimer's Disease

The Al content of Reminyl (Galantamine hydrobromide) is approximately 600 μg/g. When a single tablet is added to 50 mL of a simulated stomach solution (0.25% *w/v* sodium lauryl sulphate, 0.05% w/v sodium azide, 35mM sodium chloride, 5mL 15.8M HNO_3 and ultapure water, pH 1.5 – 1.7) and incubated for 1h at 37°C the tablet dissolves giving an orange solution*. The total [Al] of this solution is **1300.0 (76.7) μg/L (n=9).**

*Contains orange-yellow S-aluminium lake, E110

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