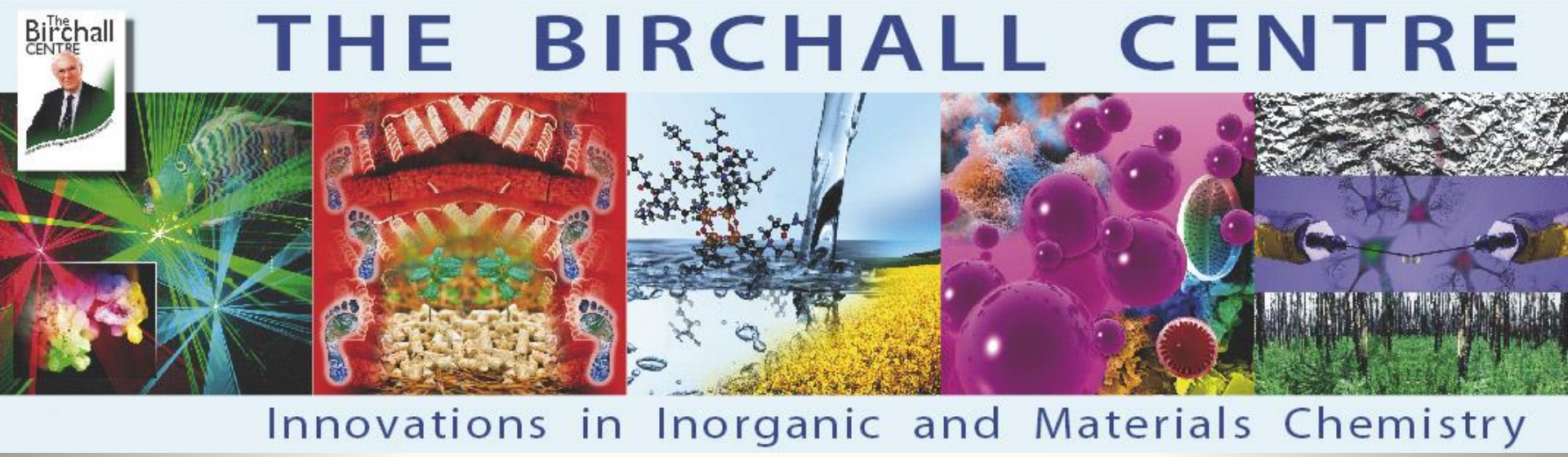

Aluminium and Alzheimer's Disease

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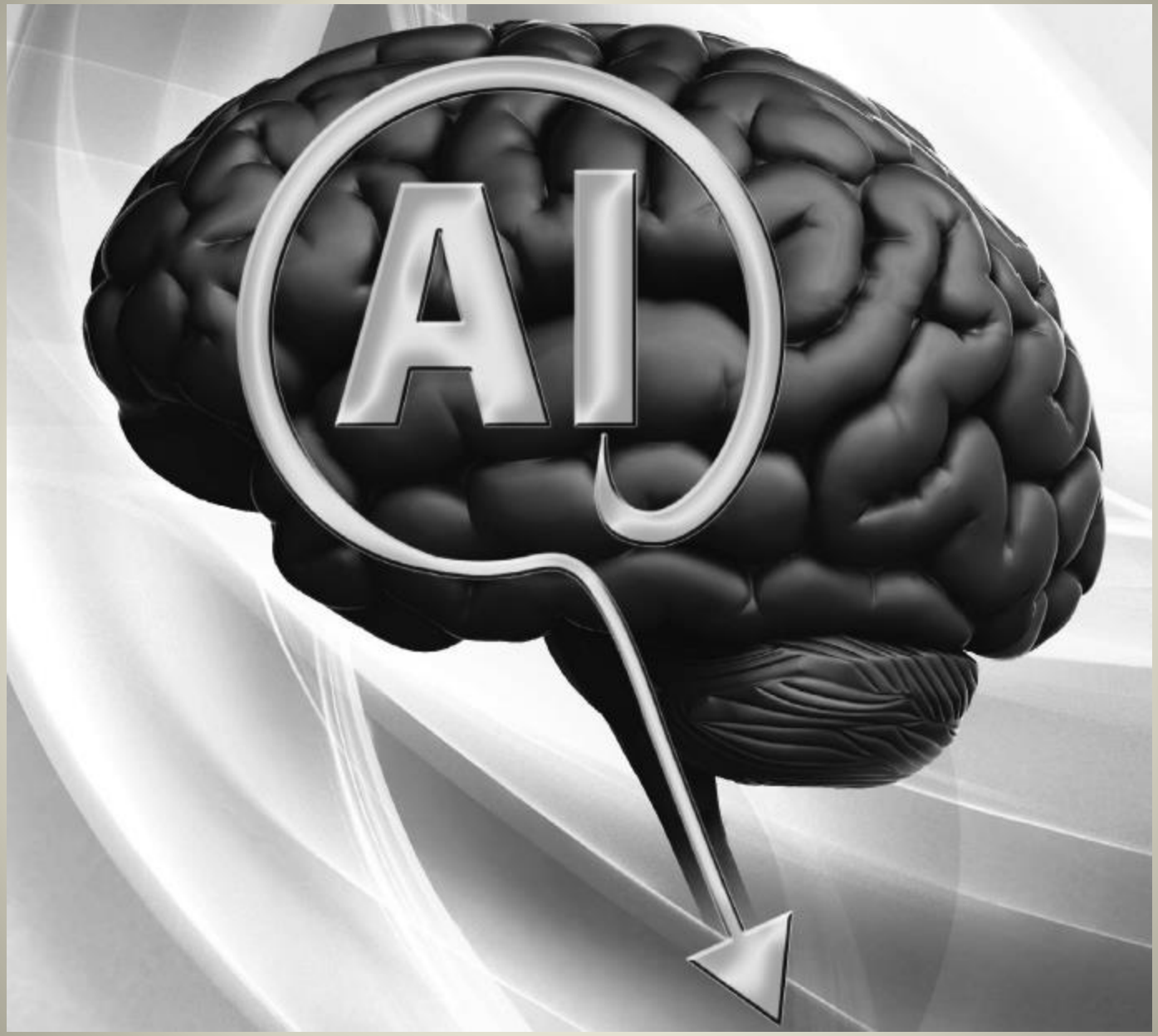
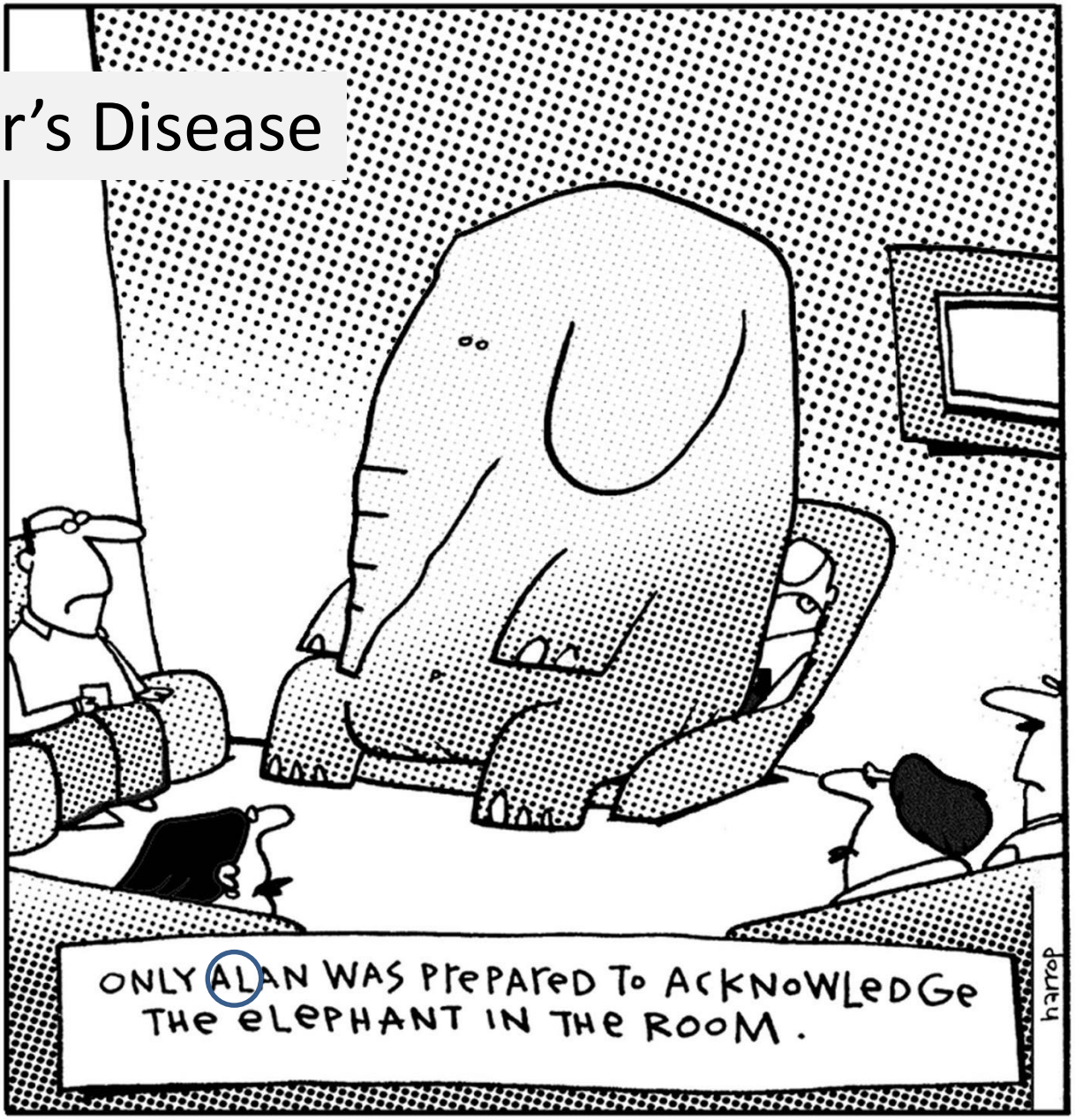
http://www.keele.ac.uk/aluminium/

CMSRI


AI

Alzheimer's Disease



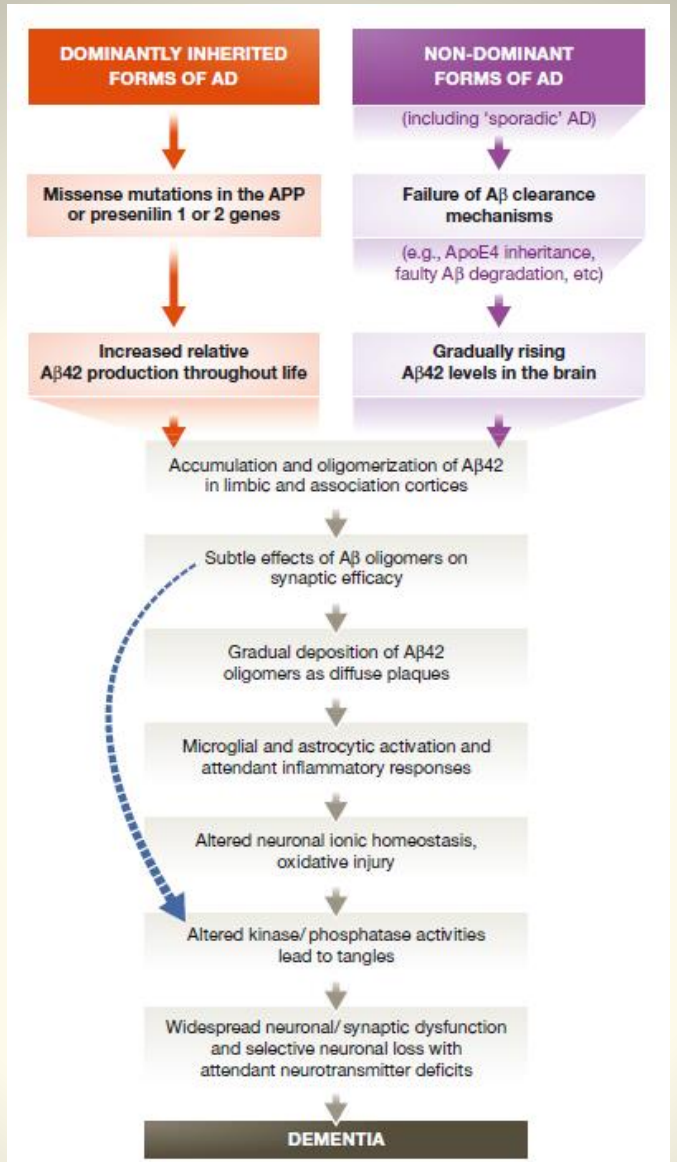


Figure 1. The sequence of major pathogenic events leading to AD proposed by the amyloid cascade hypothesis.
The curved blue arrow indicates that Aβ oligomers may directly injure the synapses and neurites of brain neurons, in addition to activating microglia and astrocytes.

Selkoe & Hardy (2016) EMBO Mol Med 8, 595.

frontiers in NEUROLOGY

REVIEW ARTICLE
published: 27 October 2014
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Why industry propaganda and political interference cannot disguise the inevitable role played by human exposure to aluminum in neurodegenerative diseases, including Alzheimer's disease

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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

Metallomics

Dynamic Article Links

Cite this: *Metallomics*, 2012, **4**, 56–65

www.rsc.org/metallomics

PAPER

Aluminium, iron and copper in human brain tissues donated to the medical research council's cognitive function and ageing study

Emily House,[a] Margaret Esiri,[b] Gill Forster,[c] Paul G Ince[c] and Christopher Exley*[a]

Sixty Human Brains

>700 tissue digests (250 mg wet weight)

174 Method Blanks; Al = 54 ng Al/vessel (Mean + 1.654SD)

House et al. (2012) Metallomics 4, 56.

Aluminium Content of Human Brain

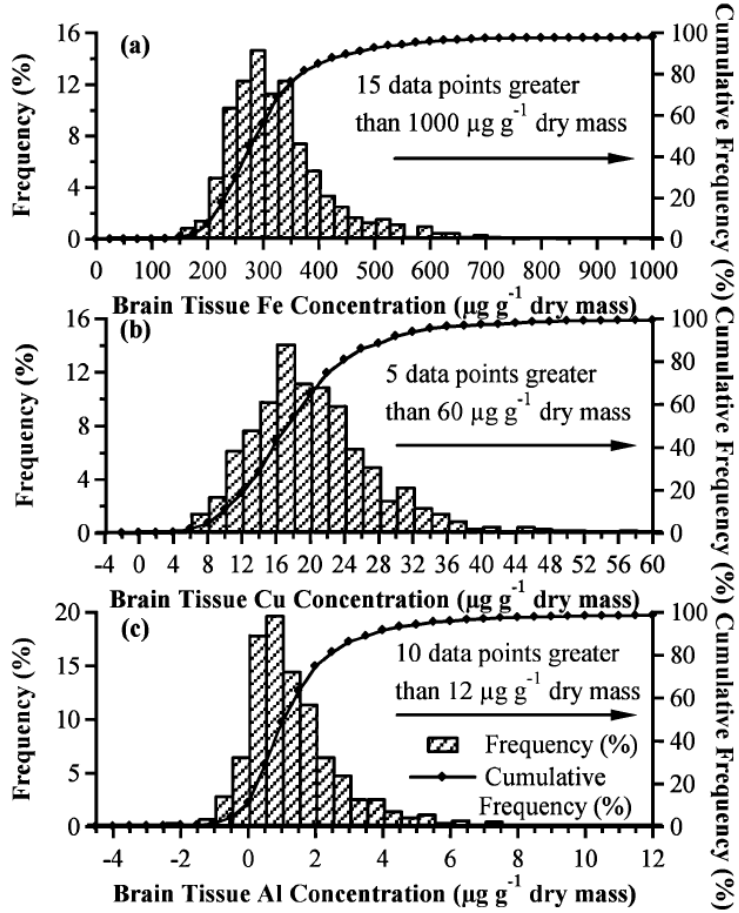


Fig. 3 Percentage frequency (bars) and cumulative frequency (line and marker) distributions of (a) Fe, (b) Cu and (c) Al concentrations in (n = 719, 720 and 713 respectively) brain tissues after subtraction of contamination.

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 et al. (2012) Metallomics 4, 56.

Accidental Exposure to Aluminium

Camelford, Cornwall, United Kingdom, 1988

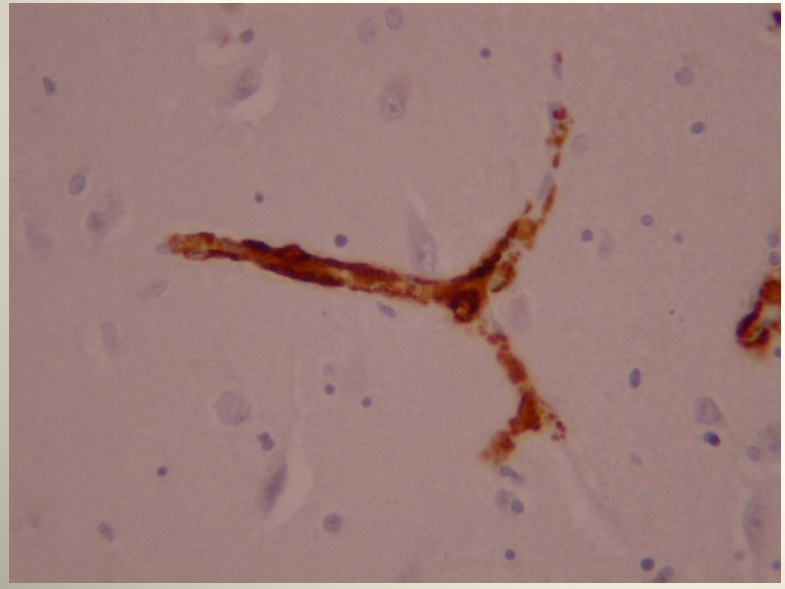
SHORT REPORT

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.

Exley & Esiri (2006) J Neurol Neurosurg Psychiat 77, 877.

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.

Exley & Vickers (2014) J Med Case Rep 8, 41.

Another case of early onset ‘sporadic’ Alzheimer’s disease from Camelford

Table 1

The aluminum content of each tissue replicate from each brain region (μg/g dry wt.) with pathologically-concerning values highlighted in **bold** and pathologically-significant values highlighted in ***bold italics***. Mean and SD are also given for each region for between 9 and 21 replicates

Replicate	Temporal	Hippocampus	Occipital	Frontal	Parietal
1	0.81	0.41	***4.45***	1.31	1.21
2	0.12	0.01	**2.68**	0.40	**2.05**
3	***3.51***	**2.73**	0.09	0.77	1.84
4	0.66	0.76	0.19	1.01	0.84
5	0.01	0.41	1.19	0.27	0.04
6	0.74	0.01	0.57	1.89	0.36
7	1.18	0.11	0.24	0.48	**2.78**
8	0.24	0.01	**2.82**	0.01	***5.58***
9	1.71	0.01	0.39	0.02	0.41
10		0.01	1.03	0.32	0.98
11			0.27	0.27	0.01
12			0.72	0.26	0.01
13			**2.79**	0.28	1.23
14			***4.00***	0.14	0.93
15			0.58	0.39	0.29
16			1.56	0.20	0.34
17			**2.16**	0.69	**2.62**
18			*3.73*	0.43	0.31
19			**2.16**	0.20	***3.91***
20			1.23	***3.38***	1.33
21			***3.86***	1.03	0.79
Mean	1.00	0.45	1.75	0.66	1.33 (1.42)
(SD)	(1.08)	(0.84)	(1.43)	(0.78)	(1.42)

Mirza et al. (2016) J Alzh Dis

http://content.iospress.com/articles/journal-of-alzheimers-disease/jad160648

What about; Familial Alzheimer's Disease?

Summary indicating the lobe with the highest content of Al (Mean (SD) n=3)

(Pathologically Concerning/Pathologically Significant / 12 tissues)

Donor ID	Lobe	[Al] μg/g dry wt.
A1 0/0 /12	Frontal	0.44(0.31)
A2 0/4 /12	Occipital	9.99(1.61)
A3 6/3 /12	Occipital	4.29(3.21)
A4 3/2 /12	Parietal	3.30(4.43)
A5 1/2 /12	Frontal	7.05(6.10)
A6 1/3 /12	Occipital	9.57(14.08)
A7 2/0 /12	Temporal	1.81(0.78)
A8 3/6 /12	Frontal	14.41(18.44)
A9 4/2 /12	Frontal	3.81(4.11)
A10 5/1 /12	Occipital	2.97(1.01)
A11 2/2/12	Occipital	9.31(12.71)
A12 2/3 /12	Temporal	2.91(2.89)

http://www.sciencedirect.com/science/article/pii/S0946672X16303777

From the ‘Discussion’

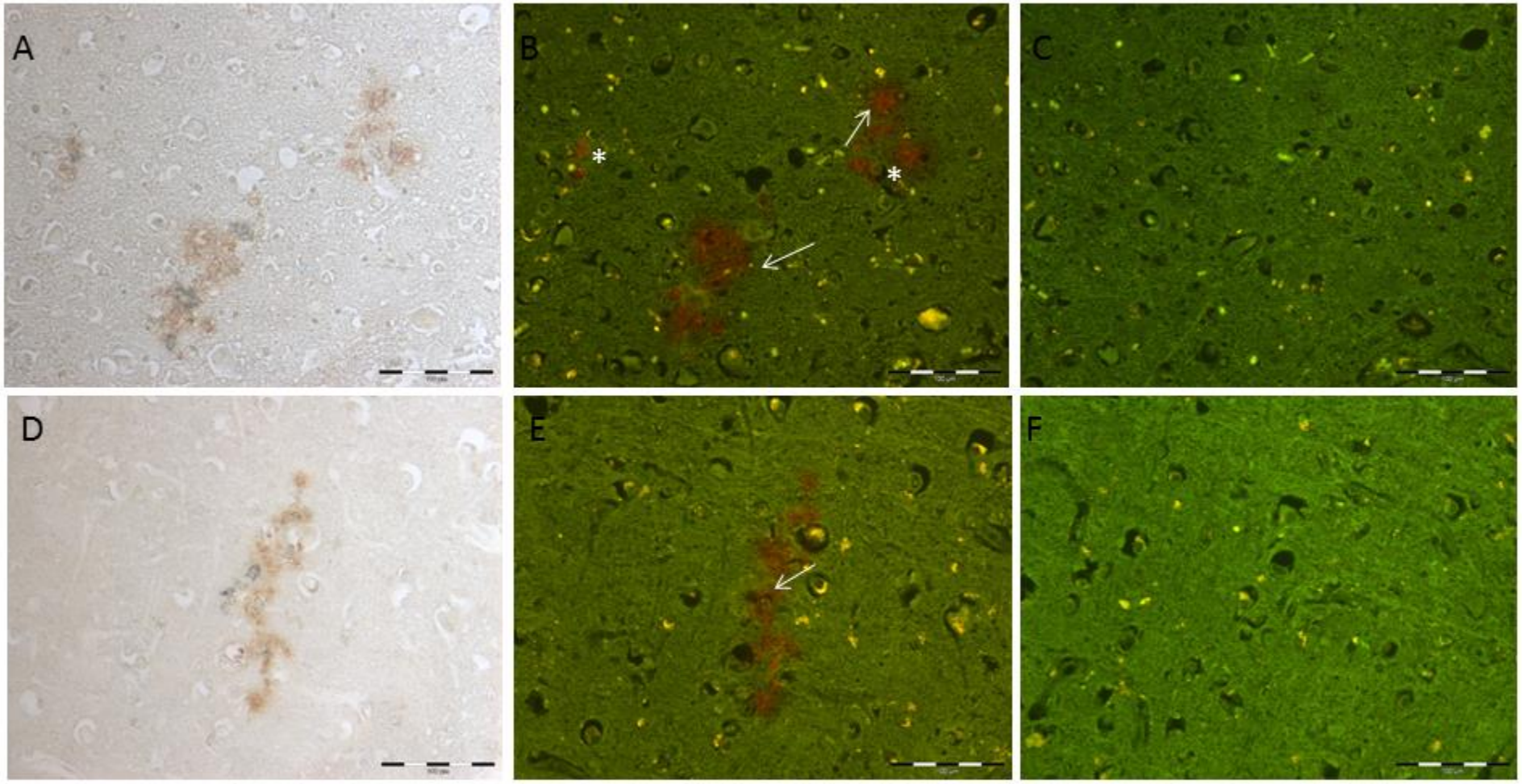
“The aluminium content of brain tissue donated by individuals with a diagnosis of familial AD was, overall, extremely high. We measured some of the highest values recorded for human brain tissues, for example to highlight just a few, 11.54 μg/g in the occipital lobe of donor A2, 13.41 μg/g in the frontal lobe of A5, 25.80 μg/g in the occipital lobe of A6, 35.65 μg/g in the frontal lobe of A8 and 23.93 μg/g in the occipital lobe of A11 (Table 1)”

Another case of early onset sporadic Alzheimer's disease in a Camelford resident!

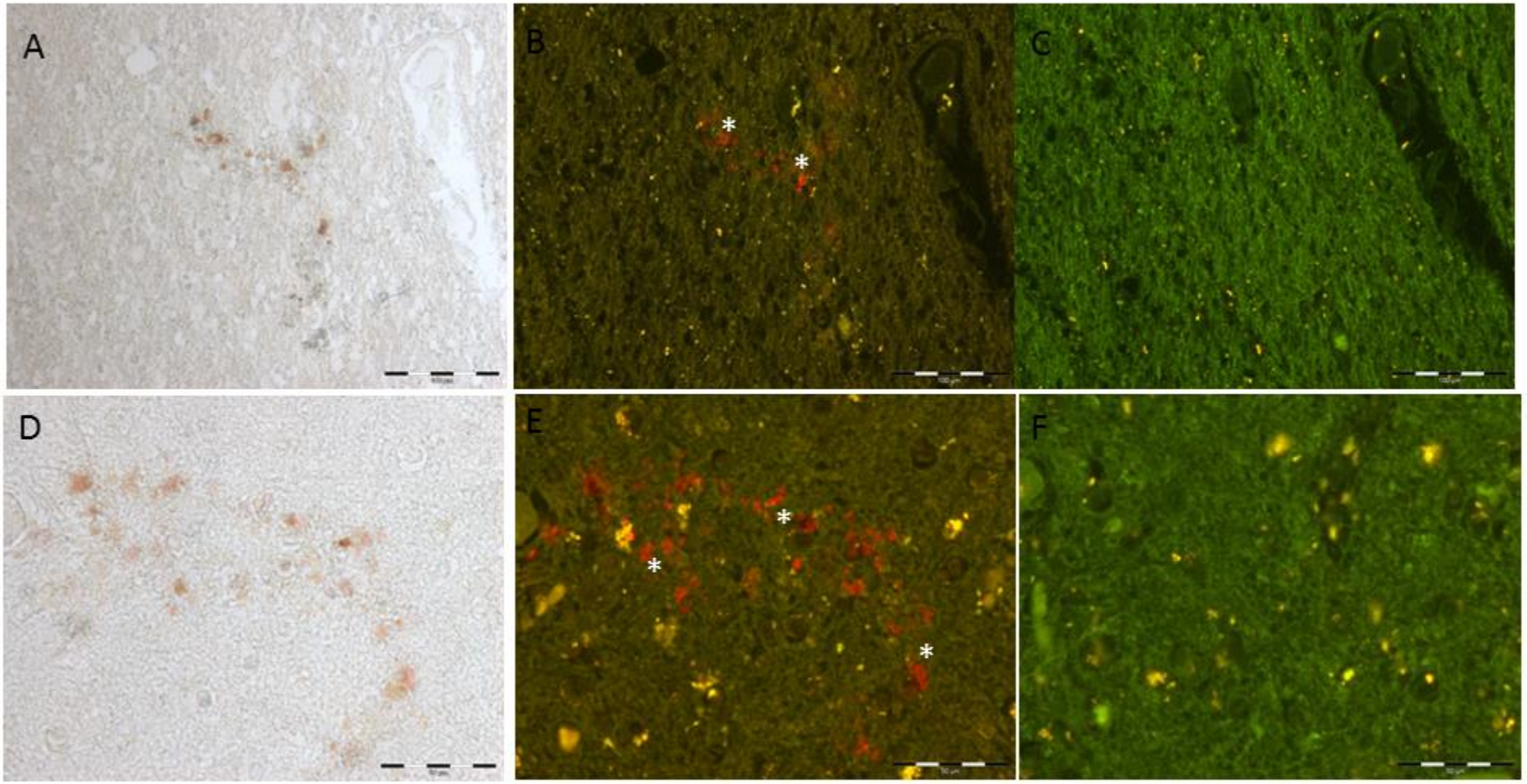
Journal of Alzheimer's Disease xx (20xx) x–xx
DOI 10.3233/JAD-160648
IOS Press

The Identification of Aluminum in Human Brain Tissue Using Lumogallion and Fluorescence Microscopy

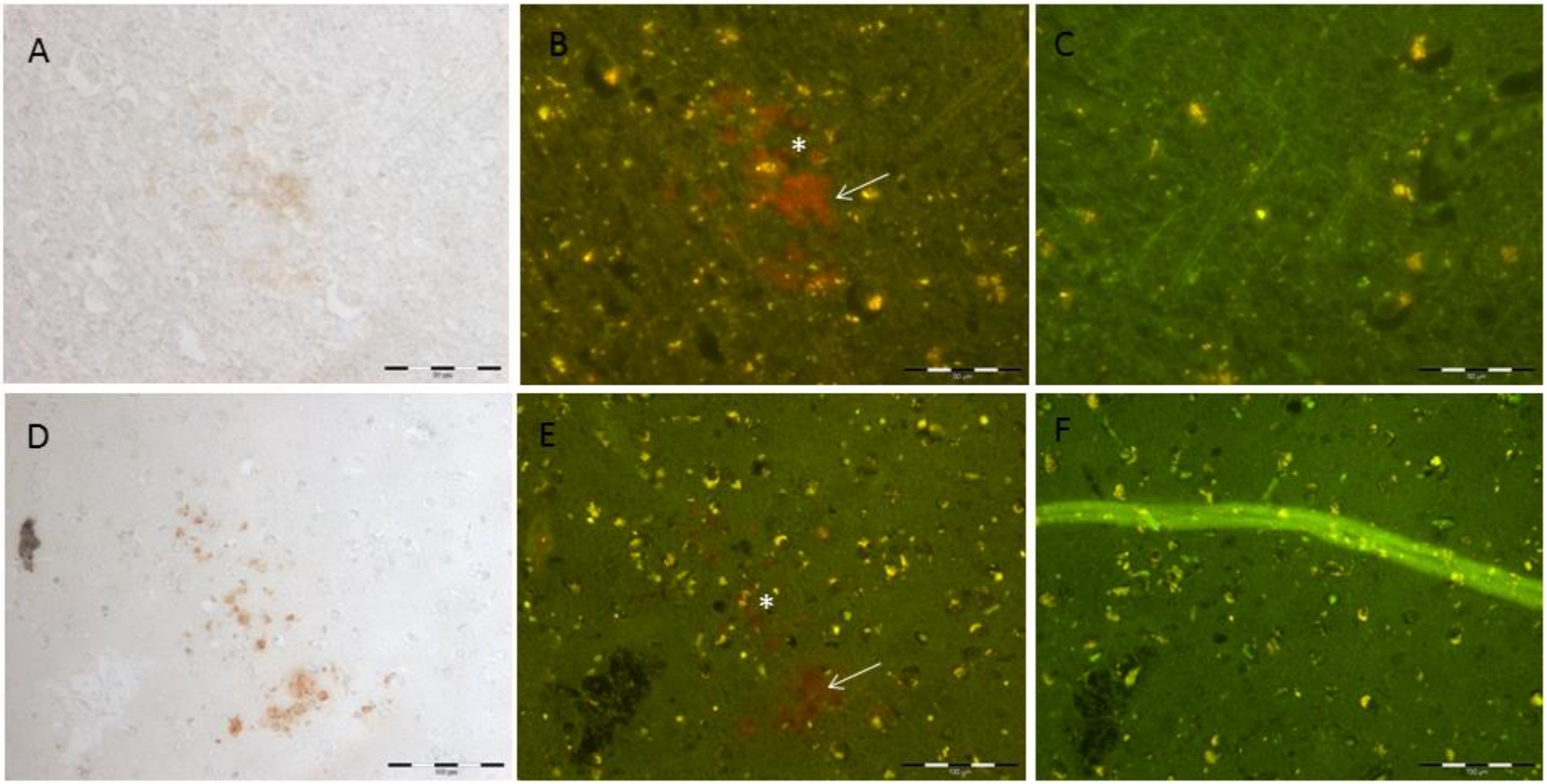
Ambreen Mirza[a], Andrew King[b,c], Claire Troakes[c] and Christopher Exley[a,*]
[a]*The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, UK*
[b]*Department of Clinical Neuropathology, King's College Hospital, London, UK*
[c]*MRC London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology and Neuroscience, King's College, London, UK*



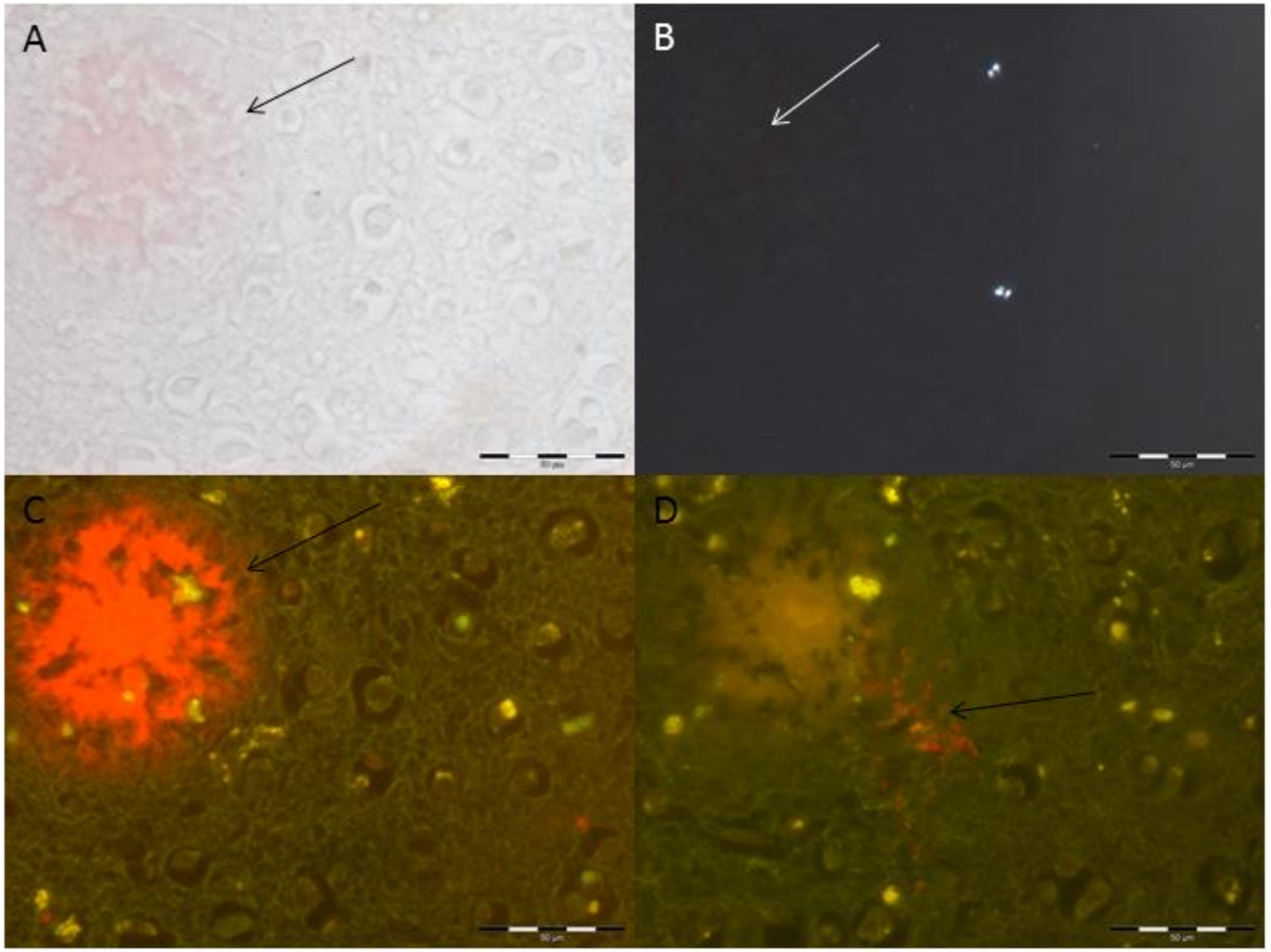
Frontal Cortex



Parietal Cortex



Frontal (A-C) and Temporal D-F) Cortex



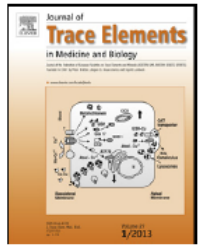
Occipital Cortex

Journal of Trace Elements in Medicine and Biology 40 (2017) 30–36

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.com/locate/jtemb



Toxicology

Aluminium in brain tissue in familial Alzheimer's disease

Ambreen Mirza[a], Andrew King[b,c], Claire Troakes[c], Christopher Exley[a,*]

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[b] Department Of Clinical Neuropathology, King's College Hospital, London, SE5 9RS, United Kingdom
[c] MRC London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology and Neuroscience, King's College, London, SE5 8AF, United Kingdom

"Aluminium is neurotoxic and the concentrations of aluminium found in these familial AD brains are unlikely to be benign and indeed are highly likely to have contributed to both the onset and the aggressive nature of any ongoing AD. These data lend support to the recent conclusion that brain aluminium will contribute towards all forms of AD under certain conditions."

http://www.sciencedirect.com/science/article/pii/S0946672X16303777

Position Paper for JAD Reports
Aluminium must now be considered to be the primary aetiological factor in Alzheimer's disease

Christopher Exley
The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, United Kingdom

Ageing is the major risk factor for Alzheimer's disease though the advent of Alzheimer's disease within a normal human lifespan is brought about through human exposure to aluminium. Without aluminium in brain tissue there would be no Alzheimer's disease. There are a number of predispositions to the development of Alzheimer's disease, involving both environmental and genetic factors, and each of these acts to increase the aluminium content of brain tissue at specific periods in an individual's life. This interplay between environmental and genetic factors explains both early and late onset disease, the catalyst for the disease is always the brain aluminium content and how robustly an individual's brain responds or copes with this aluminium burden.