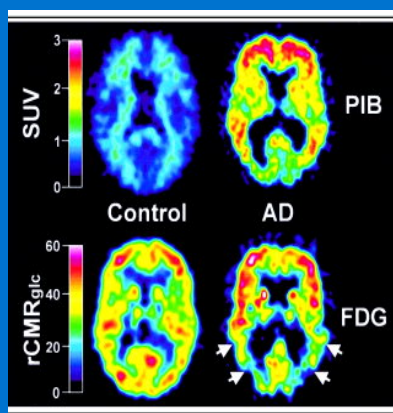
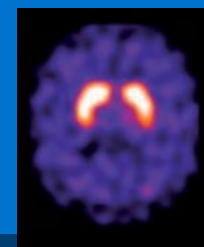
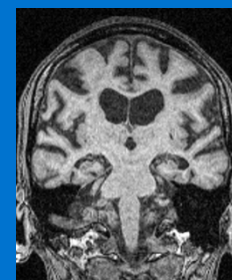


# Brain Imaging for Dementia



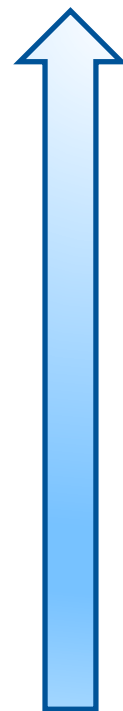
John O'Brien  
Professor of Old Age Psychiatry  
NIHR National Specialty Lead for Dementia  
Department of Psychiatry  
University of Cambridge



# Brain imaging in dementia

- Rule out other brain disorders
- Assist with subtype diagnosis
- Select subjects for clinical trials/ treatments
- Outcome biomarker for clinical trials
- Investigate underlying causes and mechanisms of disease

**Clinical practice**



**Research use**

# Types of brain imaging

- **Structure**

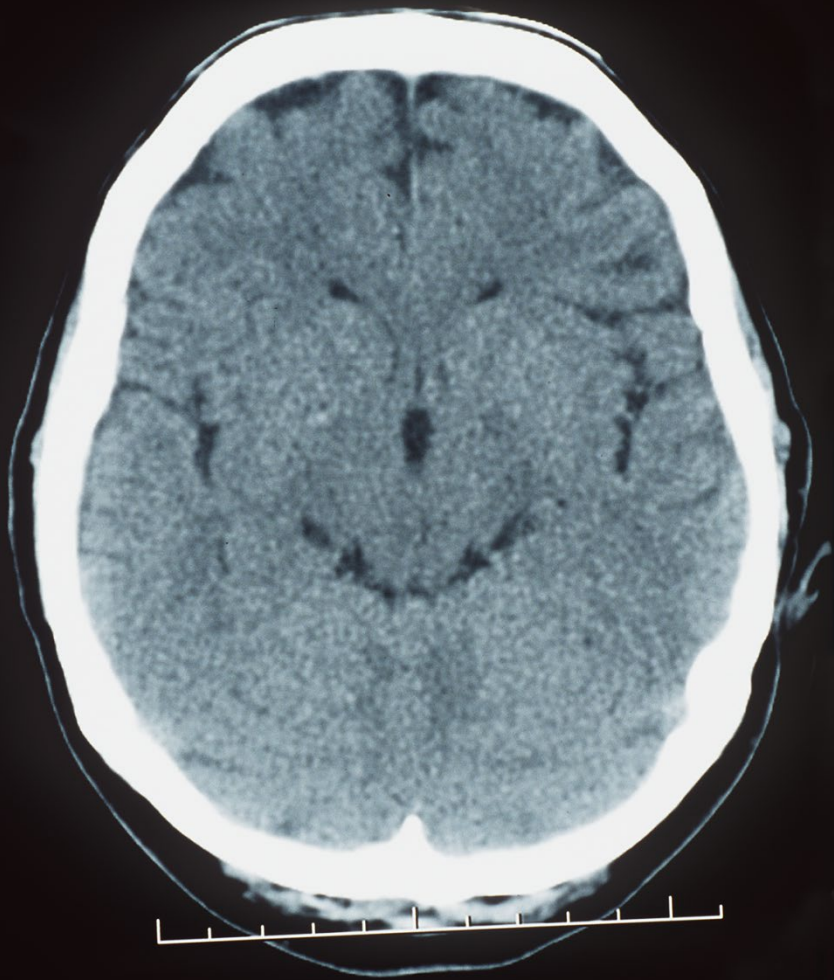
- Computed tomography (CT)
- Magnetic resonance imaging (MRI)

- **Function**

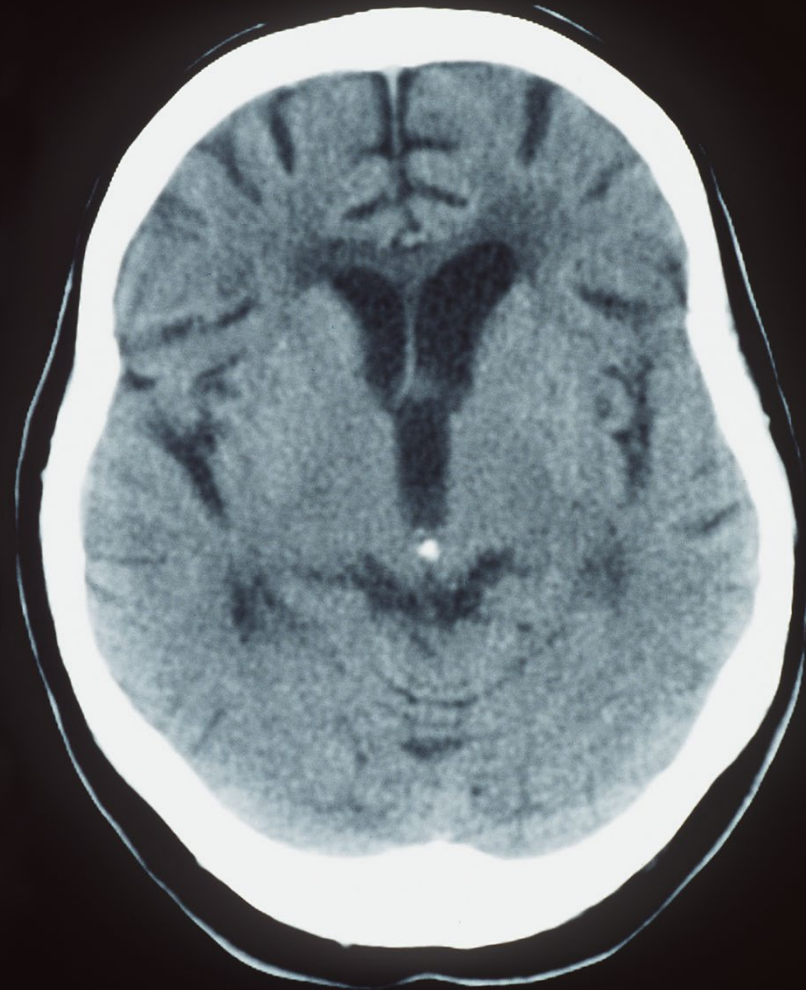
- Blood flow/ metabolism (SPECT/ Glucose PET)
- Chemical imaging (Dopaminergic SPECT)
- Specific proteins (amyloid PET and **tau PET**)
- **Other (inflammation, synapses, receptors)**



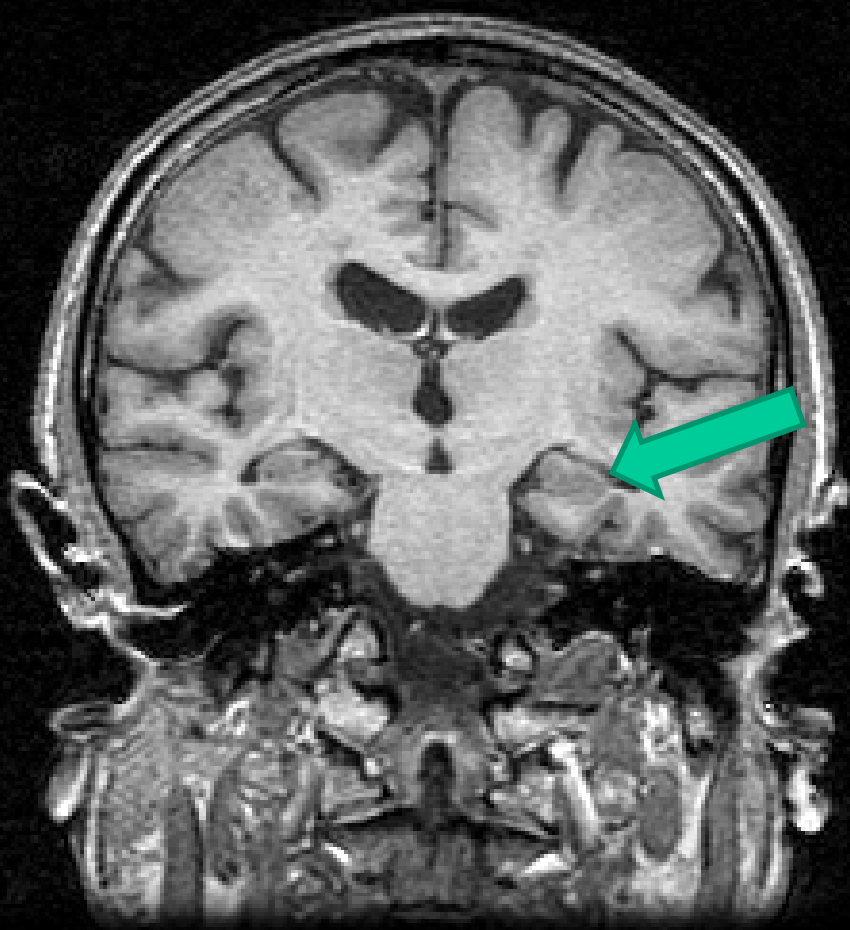
A space occupying lesion (frontal meningioma) in someone presenting to the Memory Clinic with suspected dementia



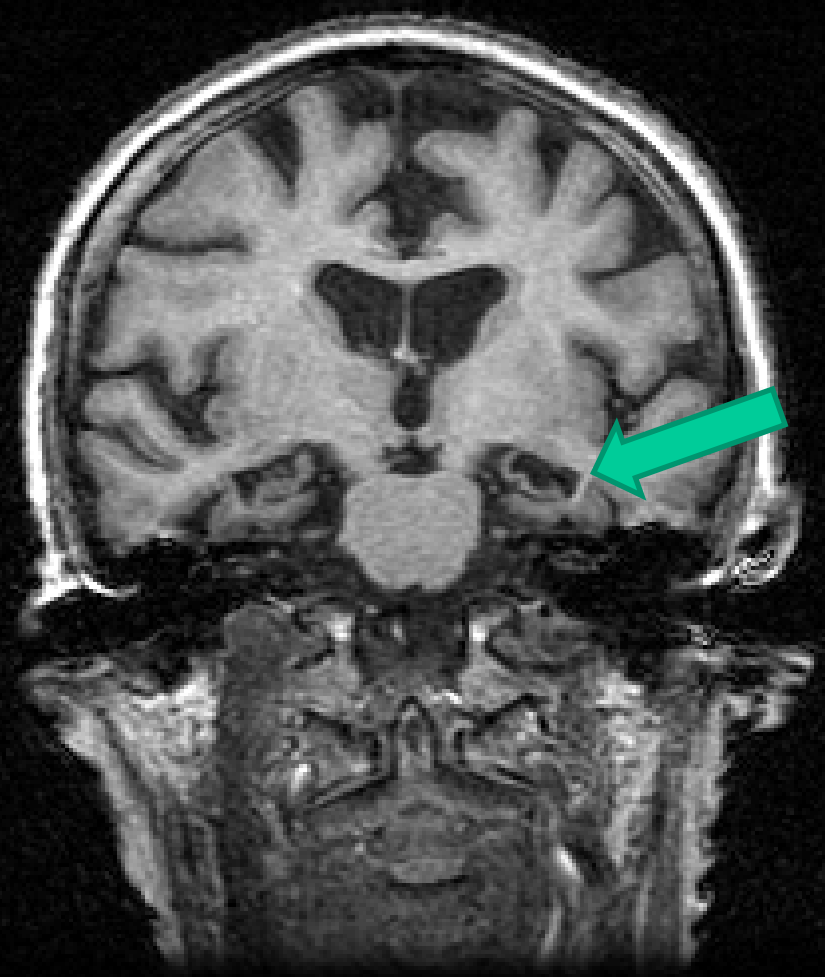
Healthy Control



Alzheimer's disease



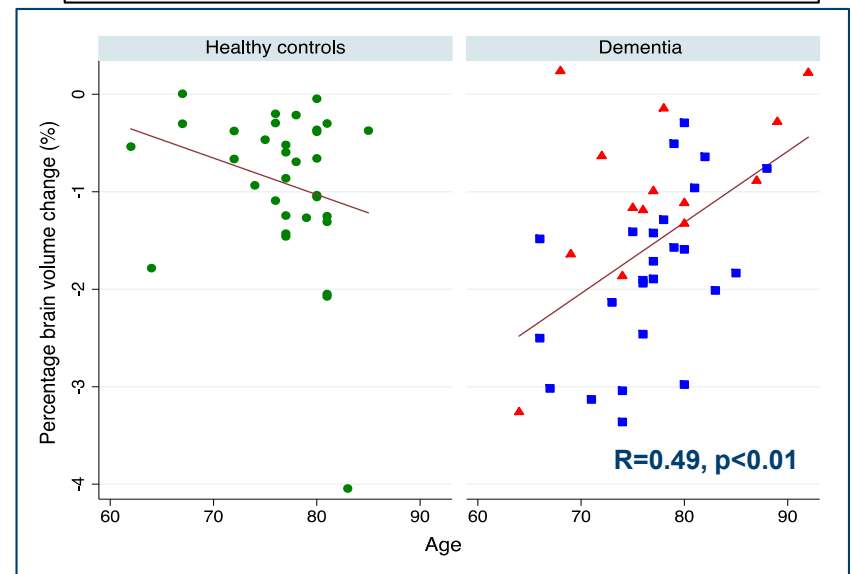
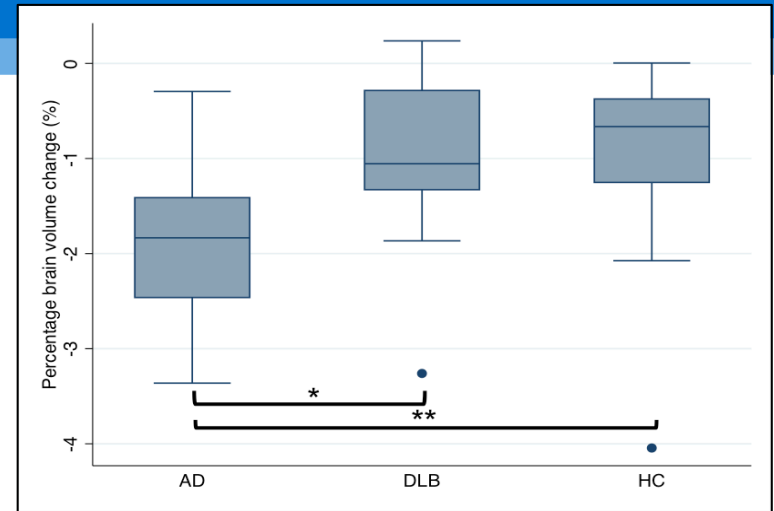
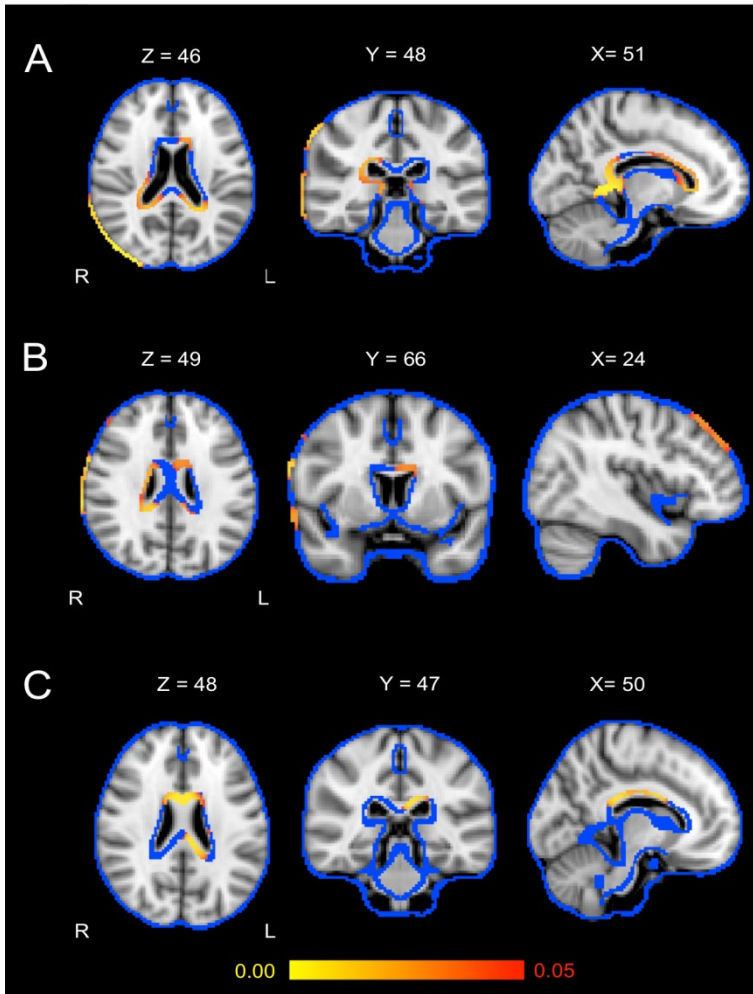
Control



AD

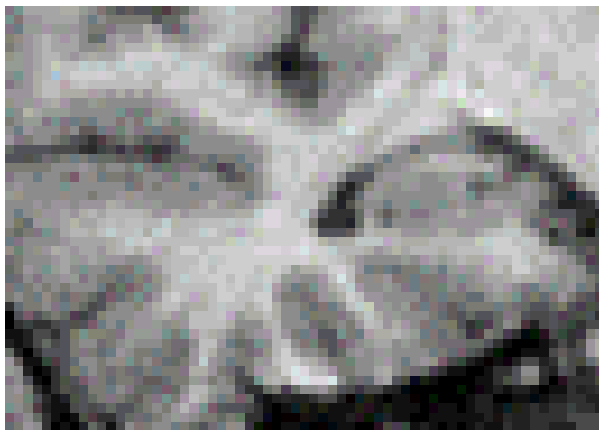
Atrophy of the medial temporal lobe (hippocampus) seen in approx. 80% people with Alzheimer's disease and 10-15% controls

# Serial MR Imaging in AD and DLB

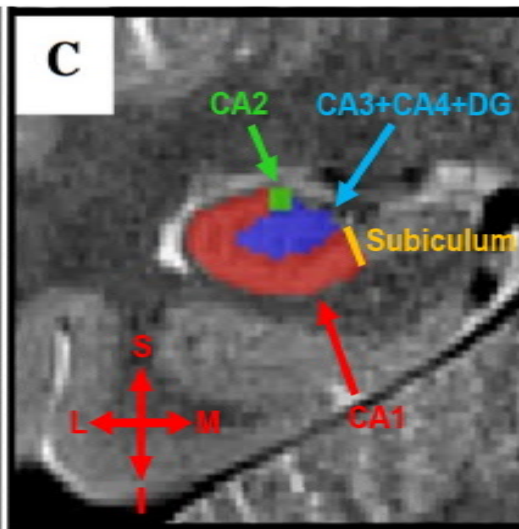
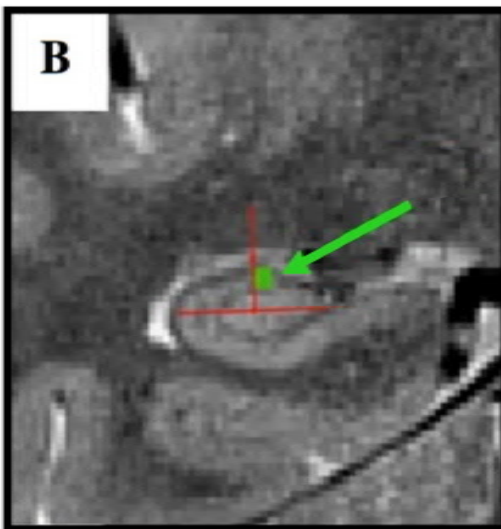
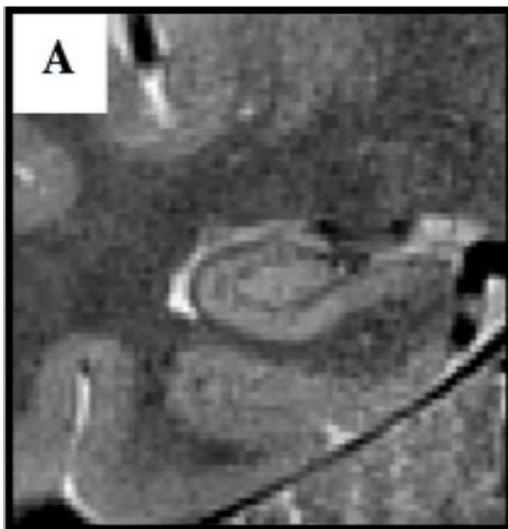




# Advantages of higher field strength MR imaging



Medial temporal lobe and hippocampus at 1.5 T

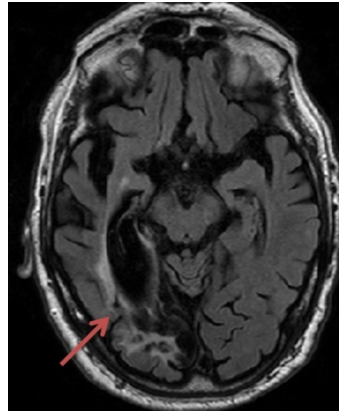


3T

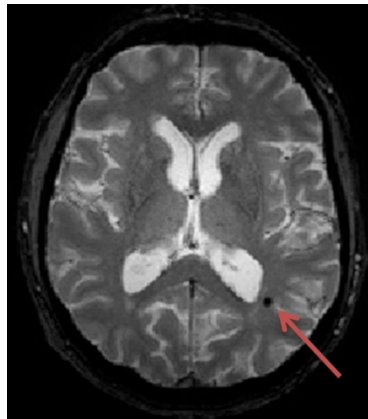


# Imaging changes associated with VaD

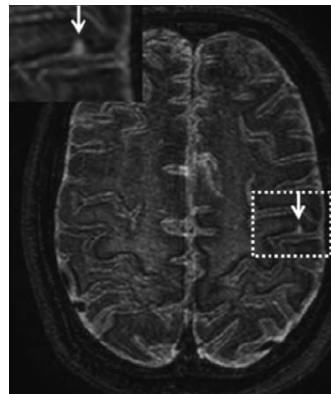
Cortical infarcts  
(FLAIR)



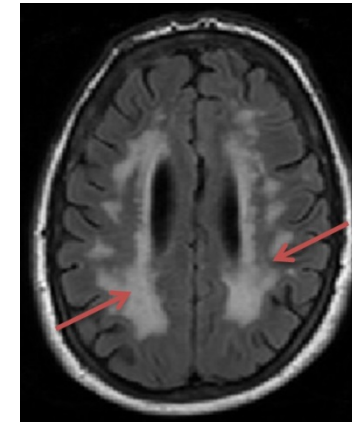
Multiple lacunar  
Infarcts (T1)



Microbleed (T2\*)



Microinfarct (FLAIR)



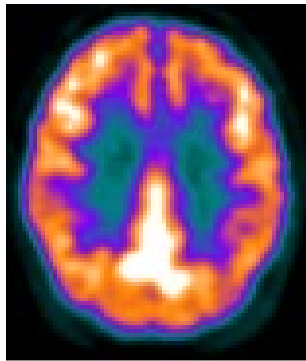
Extensive (>25%)  
WML (FLAIR)

# Dementia diagnosis in specialist dementia diagnostic services

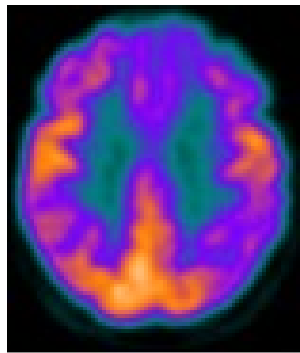
- Offer structural imaging to rule out reversible causes of cognitive decline and assist with subtype diagnosis, unless dementia is well established and the subtype diagnosis is clear
- If the dementia subtype is uncertain and vascular dementia is suspected, use MRI

# Diagnosing Alzheimer's disease

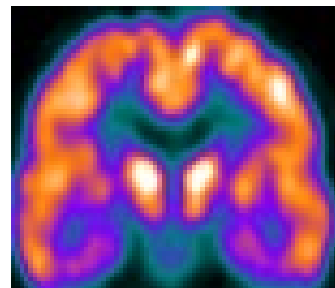
If the diagnosis is uncertain and Alzheimer's disease is suspected, consider using **FDG-PET** (fluorodeoxyglucose-positron emission tomography) - or **perfusion SPECT** (single-photon emission CT) if FDG-PET is unavailable



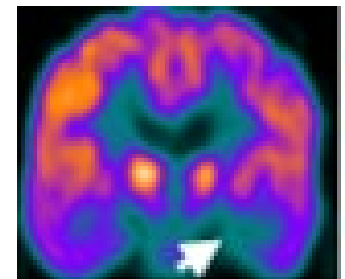
Control



AD



Control

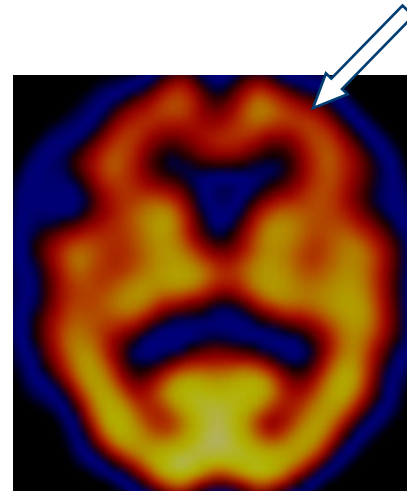


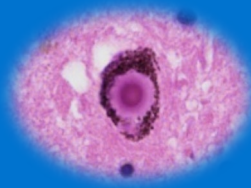
AD

# Diagnosing frontotemporal dementia

If the diagnosis is uncertain and frontotemporal dementia is suspected, use either:

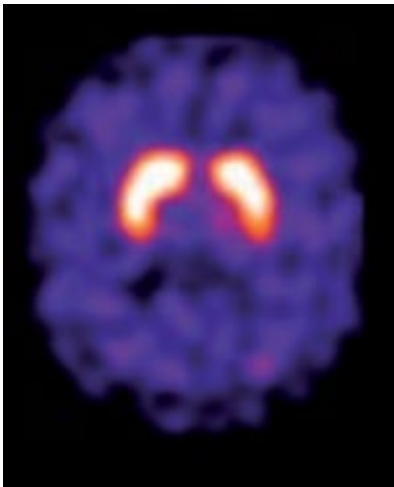
- FDG-PET or
- perfusion SPECT



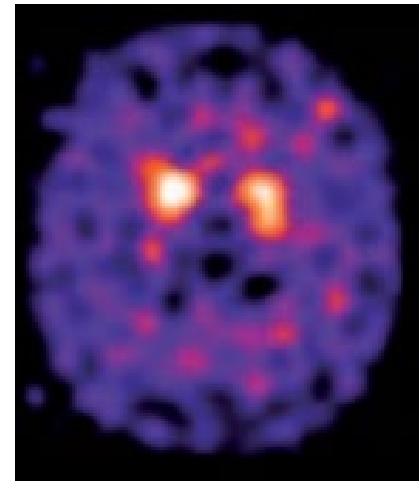


# Diagnosing dementia with Lewy bodies

- If the diagnosis is uncertain and dementia with Lewy bodies is suspected, use dopaminergic ( $^{123}\text{I}$ -FP-CIT) SPECT

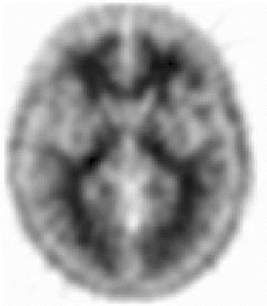


Normal

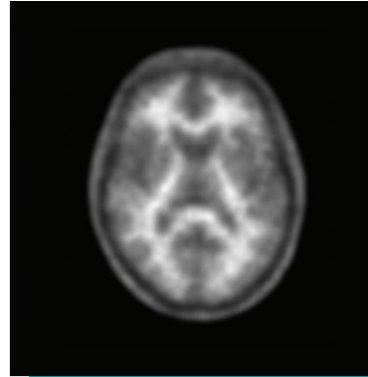


Dopamine deficit in DLB

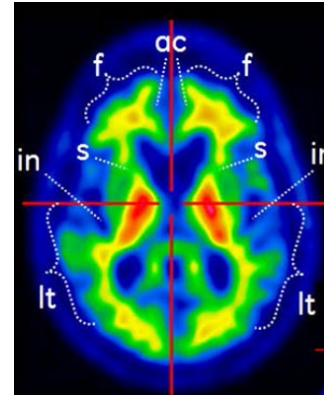
# Amyloid imaging in Dementia



**Flurbetapir  
(Amyvid)**

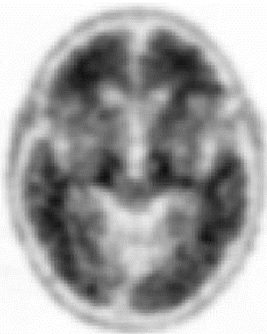


**Flurbetaben  
(NeuraCeq)**

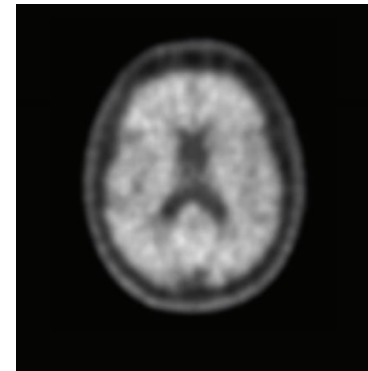


**Flutemetamol  
(Vizamyl)**

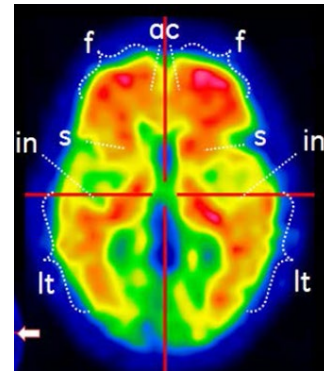
**Negative scan:  
normal**



**Flurbetapir  
(Amyvid)**

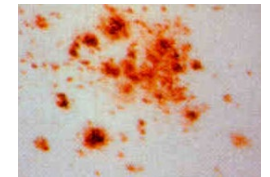


**Flurbetaben  
(NeuraCeq)**



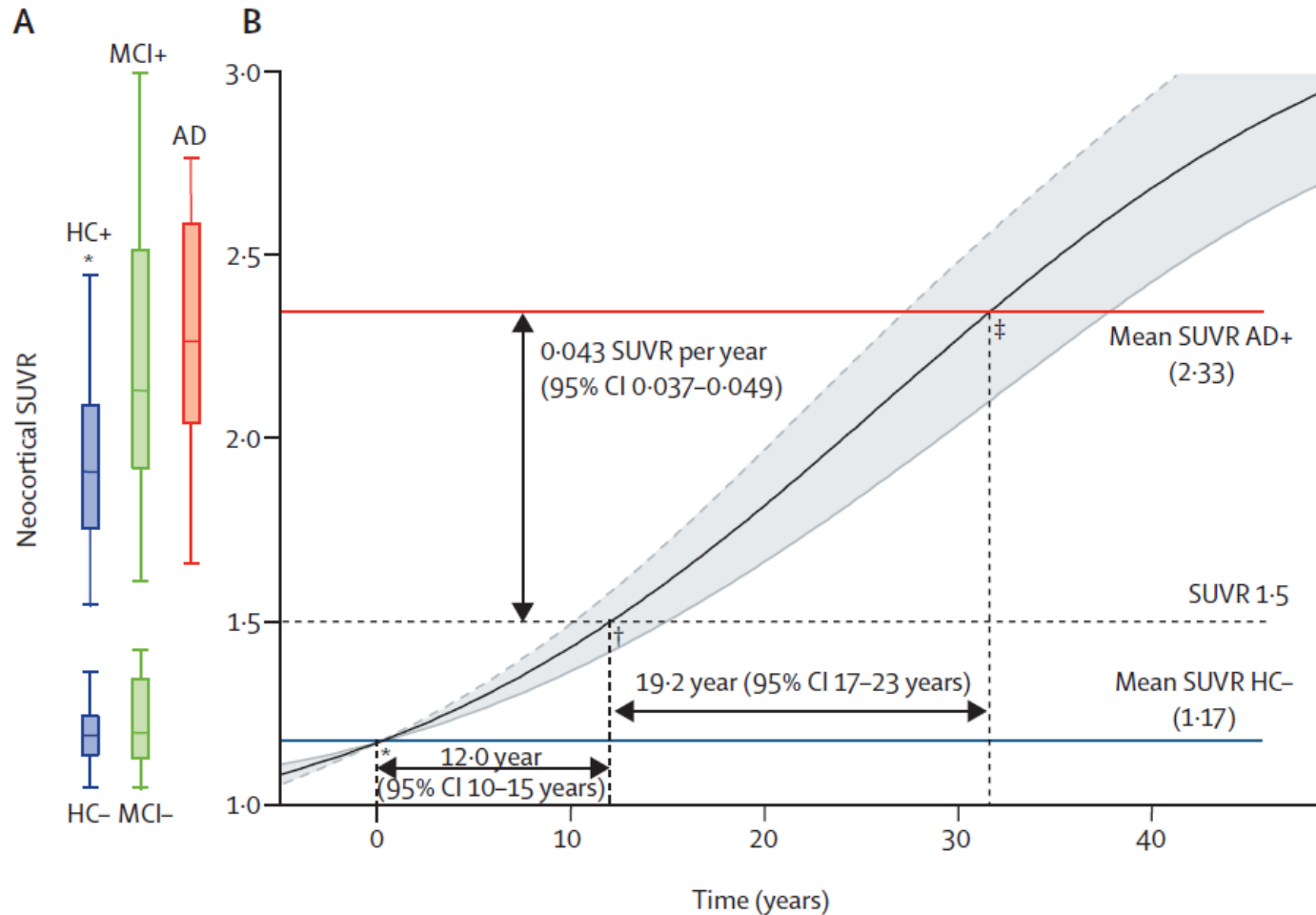
**Flutemetamol  
(Vizamyl)**

**Positive scan:  
Amyloid present  
(AD, DLB, old age)**





# Amyloid $\beta$ deposition and cognitive decline in Alzheimer's disease: a prospective cohort study



ORIGINAL ARTICLE

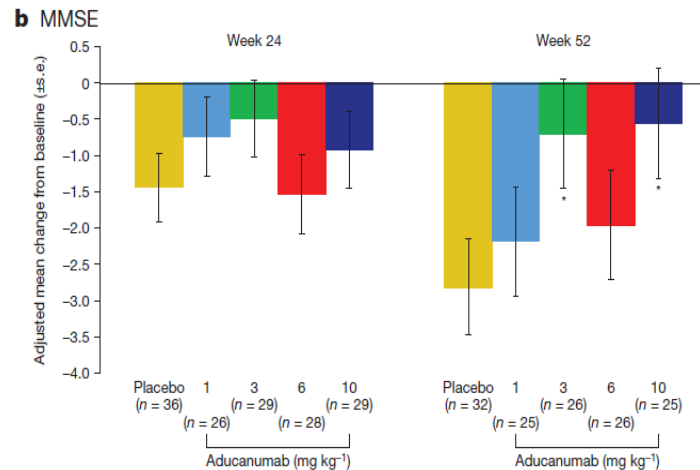
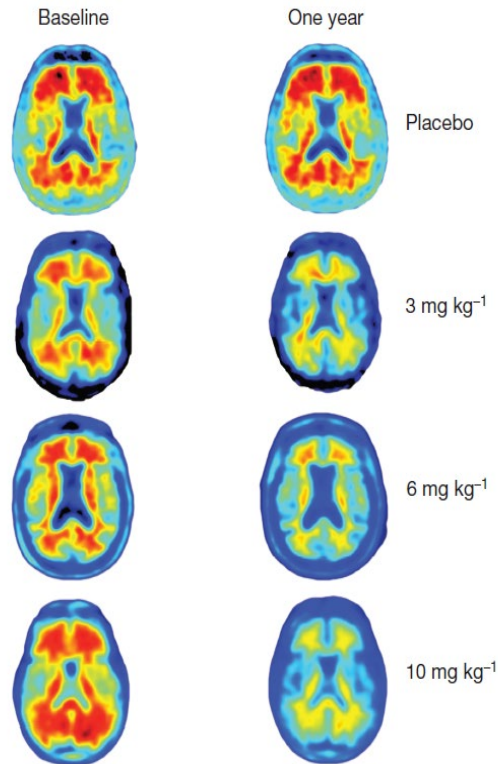
# Two Phase 3 Trials of Bapineuzumab in Mild-to-Moderate Alzheimer's Disease

Stephen Salloway, M.D., Reisa Sperling, M.D., Nick C. Fox, M.D., Kaj Blennow, M.D.,  
William Klunk, M.D., Murray Raskind, M.D., Marwan Sabbagh, M.D.,

- Negative study
- Over a third (36%) of Apo E4 non-carriers entered into the study had normal amyloid PET scans
- Current anti-amyloid studies usually require presence of amyloid on imaging or in spinal fluid for inclusion (stratification)

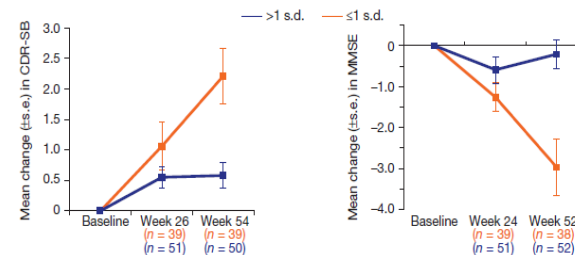
# The antibody aducanumab reduces A $\beta$ plaques in Alzheimer's disease

Jeff Sevigny<sup>1\*</sup>, Ping Chiao<sup>1\*</sup>, Thierry Bussière<sup>1\*</sup>, Paul H. Weinreb<sup>1\*</sup>, Leslie Williams<sup>1</sup>, Marcel Maier<sup>2</sup>, Robert Dunstan<sup>1</sup>, Stephen Salloway<sup>3</sup>, Tianle Chen<sup>1</sup>, Yan Ling<sup>1</sup>, John O'Gorman<sup>1</sup>, Fang Qian<sup>1</sup>, Mahin Arastu<sup>1</sup>, Mingwei Li<sup>1</sup>, Sowmya Chollate<sup>1</sup>, Melanie S. Brennan<sup>1</sup>, Omar Quintero-Monzon<sup>1</sup>, Robert H. Scannevin<sup>1</sup>, H. Moore Arnold<sup>1</sup>, Thomas Engber<sup>1</sup>, Kenneth Rhodes<sup>1</sup>, James Ferrero<sup>1</sup>, Yaming Hang<sup>1</sup>, Alvydas Mikulskis<sup>1</sup>, Jan Grimm<sup>2</sup>, Christoph Hock<sup>2,4</sup>, Roger M. Nitsch<sup>2,4§</sup> & Alfred Sandrock<sup>1§</sup>



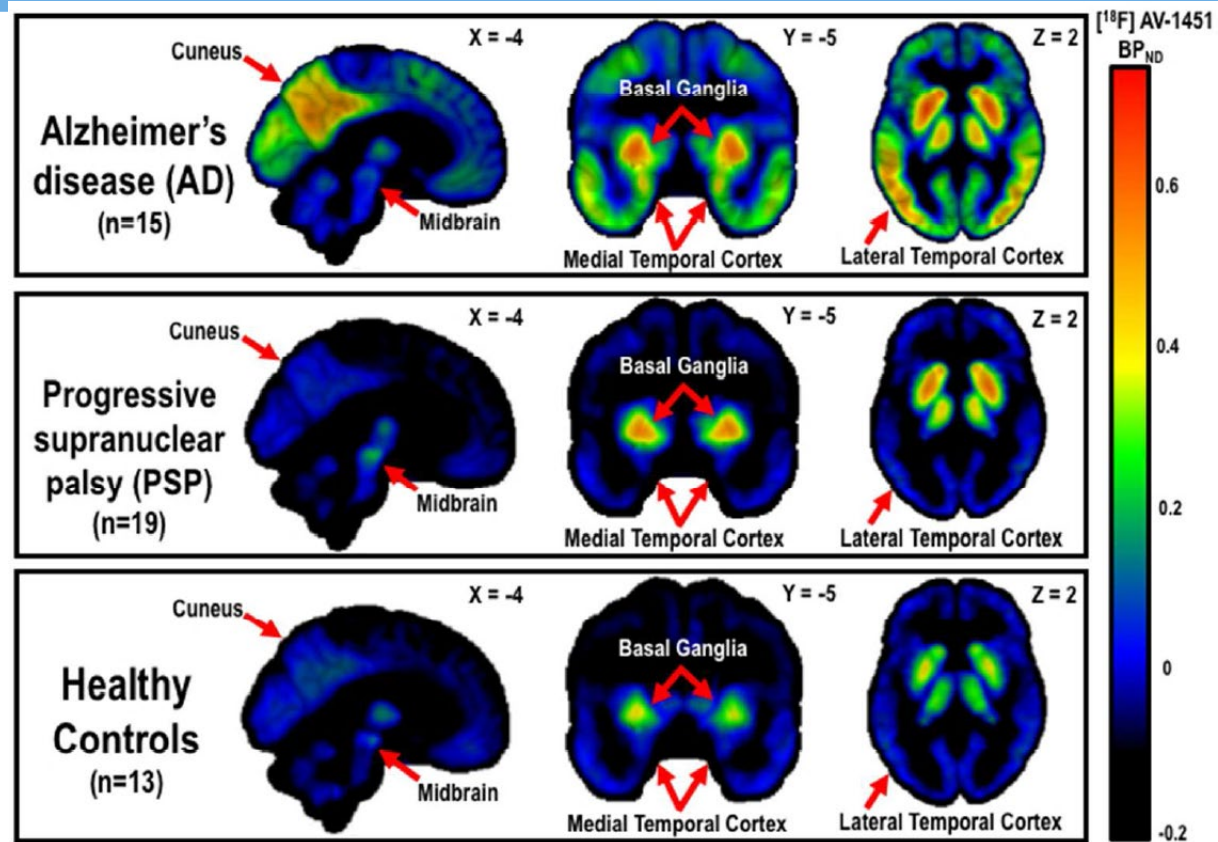
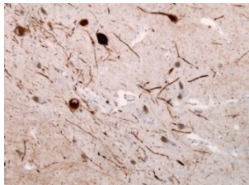
Dose-response  $P < 0.05$  at week 52 based on a linear contrast test

ARIA:  
 5% - Placebo  
 6% - 1mg  
 13% - 3mg  
 37% - 6mg  
 47% - 10mg



# Tau imaging with AV1451 in Alzheimer's disease (AD) and progressive supranuclear palsy (PSP)

## Tau Tangles



Clearly differentiates AD from PSP with differences in keeping with known and distinct regional distributions

# Summary

- Brain imaging is in clinical use to help diagnose all the common types of dementia
- It is increasing being used as a marker for selecting people for trials, and as an outcome measure
- The UK has some of the best research imaging in the world for dementia, MRC funded PET-MR and 7T MR network
- Imaging has a central role in many research studies in those with and at risk of developing dementia