



Neuroimaging in Epidemiology

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HPA 540/STAT 507

Outline



- Introduction to Neuroimaging.
- Neuroimaging in Epidemiology: Alzheimer's disease
- Epidemiology in Neuroimaging: Psychiatric Neuroimaging

Neuroimaging

- Neuroimaging involves use of technology to study structure and function of the human brain.

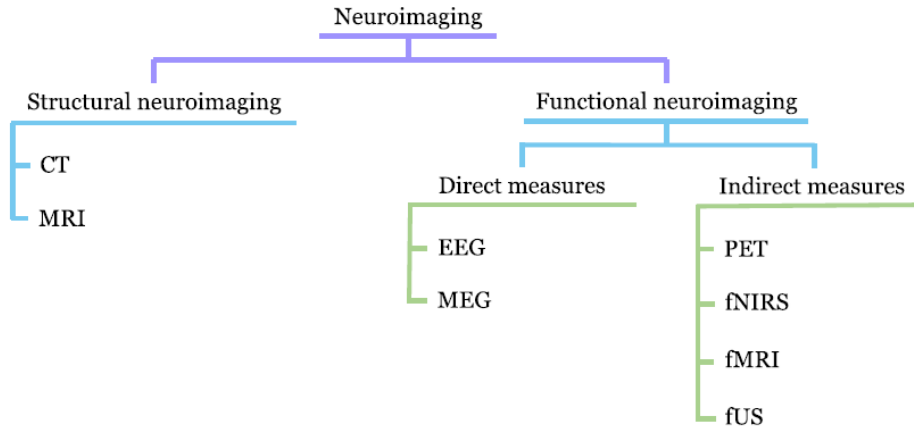


Fig 1: Two main categories of neuroimaging.
(Ref. *Tensors for data processing* (2022), Yipeng Liu)



Fig 2: Patient undergoing a CT scan
(Image taken from US FDA's website on CT)

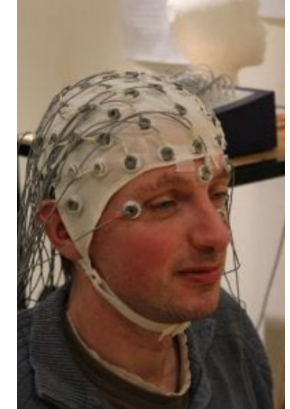
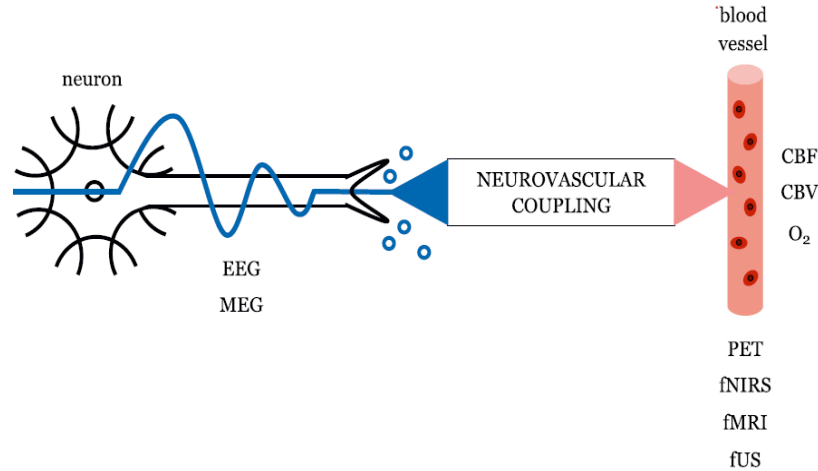


Fig 3: EEG
Electrodes placed on scalp to measure brain activity.
(Image taken from blog post by SciU, Indiana University)

Structural and Functional Neuroimaging

- Electroencephalogram (EEG)
- Magnetoencephalography (MEG)



- Positron emission tomography (PET)
- Functional near-infrared spectroscopy (fNIRS)
- Functional Magnetic Resonance Imaging (fMRI)
- functional Ultrasound (fUS)

Fig 4: Neuroimaging modalities in relation to neurovascular coupling.
(Ref. *Tensors for data processing* (2022), Yipeng Liu)

Functional neuroimaging modalities

- Trade-off between **spatial and temporal resolution** is common in neuroimaging.
- fMRI is one of the most popular modality due to its non-invasive nature and high spatial resolution.

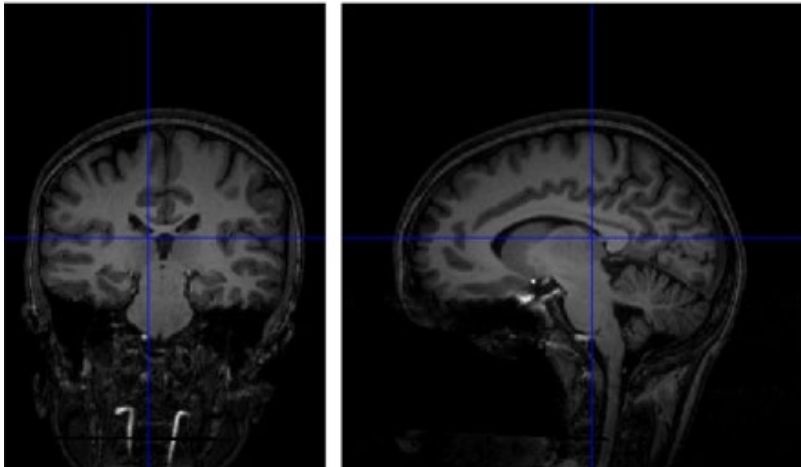


Fig. a: High spatial resolution and low temporal resolution anatomical image of sub-01

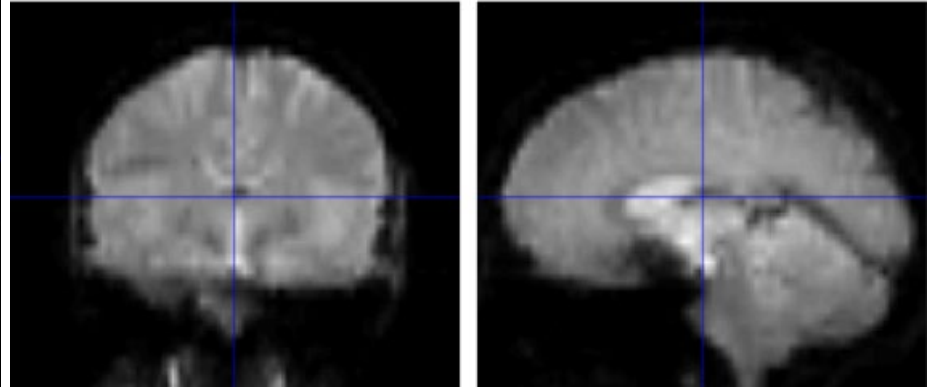


Fig. b: One of the low spatial resolution functional time frame of sub-01. There are 147 such time frames captured for sub-01.

Functional neuroimaging modalities

- Modalities that measure neuronal activity at best resolutions are invasive.

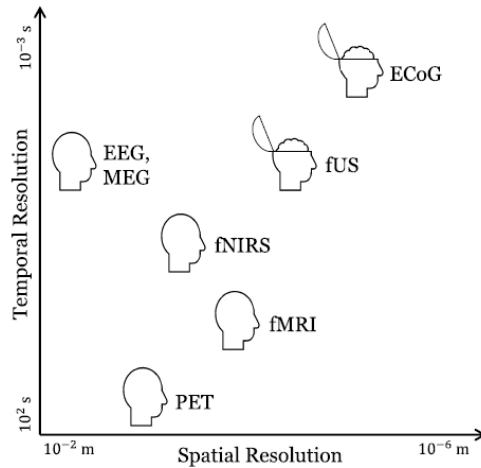
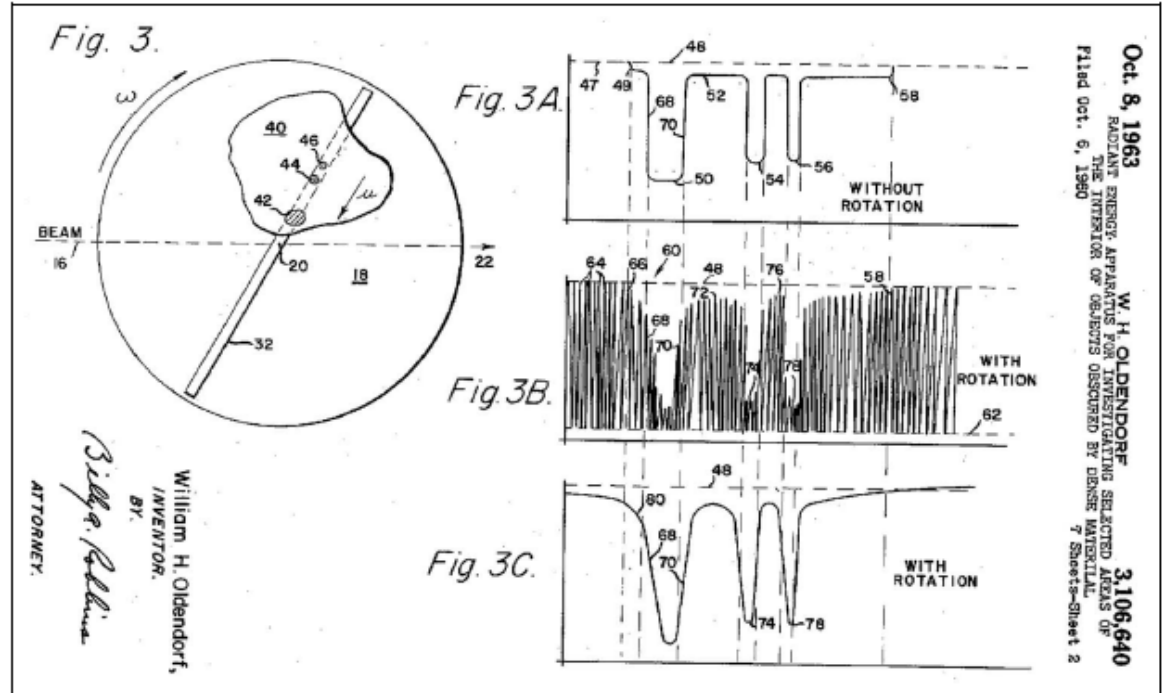
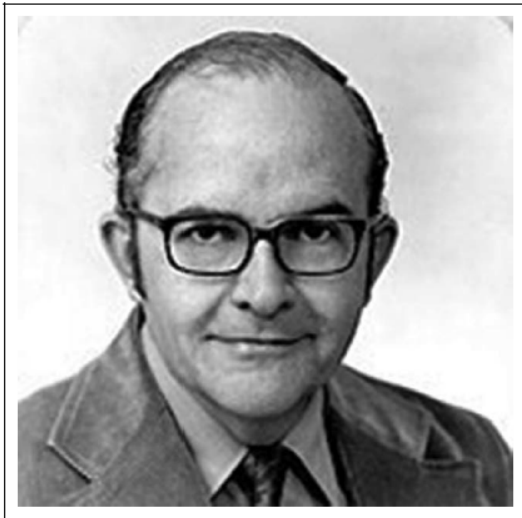


Fig : Spatial resolution of different Neuroimaging modalities
(Ref. *Tensors for data processing (2022)*, Yipeng Liu)

William Oldendorf



Alzheimer's disease

- Alzheimer's is the most common form of dementia.
- Progressive decline in cognitive function.
- Alzheimer's affects parts of the brain that control thought, memory, and language.
- In 2020: 5.8 million Alz. Americans. This is expected to triple by 2060! - huge financial burden.
- **There is no definite diagnostic test for AD**

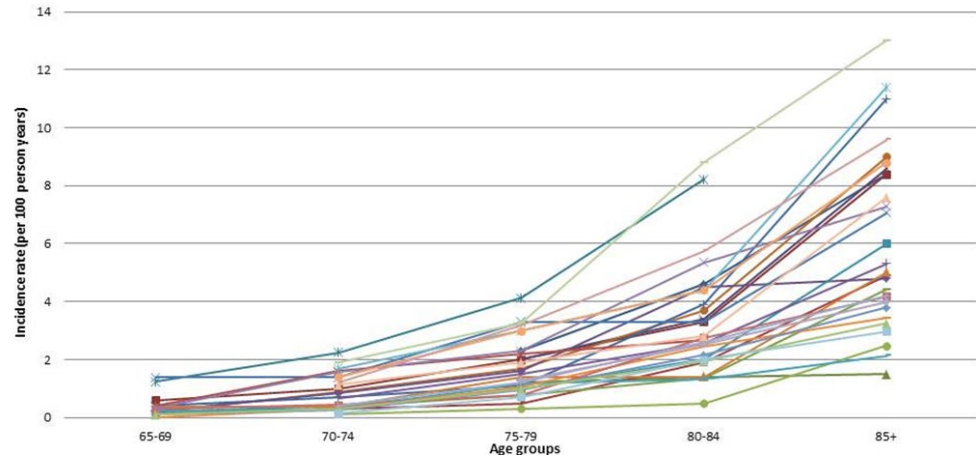


Fig : Incidence rates of Alzheimer disease (per 100 person-years) across studies. (Reitz, C., Brayne, C. & Mayeux, R. *Epidemiology of Alzheimer disease*. Nat Rev Neurol 7, 137-152 (2011).)

Biomarkers

- Biomarkers are measurable indicators of what's happening in the body. These can be found in blood, other body fluids, organs, and tissues.
- E.g. Increased cholesterol levels in the blood is a biomarker for heart attack risk.

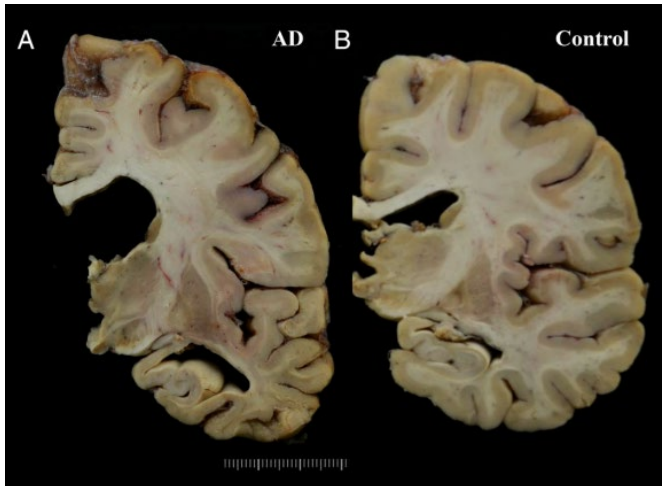


Fig: Brain atrophy is a biomarker for AD
(Renpei Sengoku, *Aging and Alzheimer's disease pathology*),
Neuropathology (2020) Vol 40 -1, Pg 22-29)

Biomarkers in Alzheimer's disease research

- There is no definite diagnostic test for AD, but biomarkers can help.
- Amyloid plaques and neurofibrillary tangles are pathological hallmarks of an AD brain.

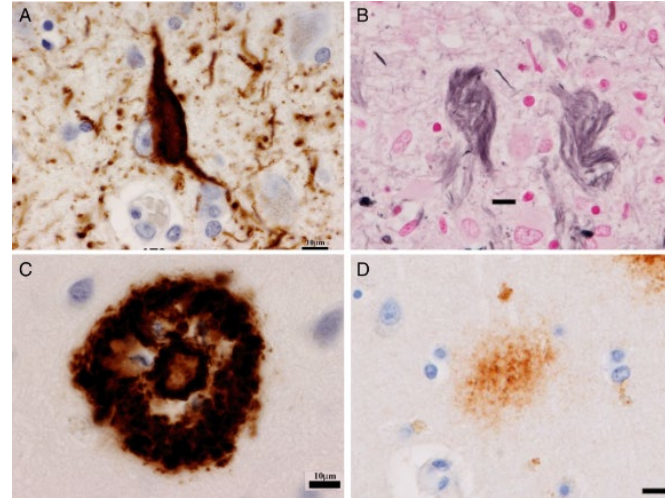
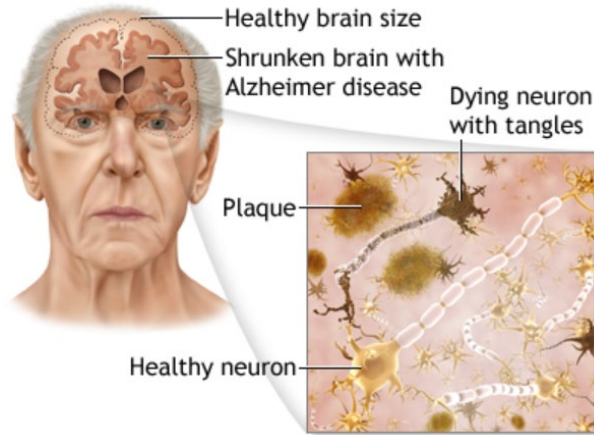


Fig: A, B - neurofibrillary tangles

C, D - plaques

(Renpei Sengoku, *Aging and Alzheimer's disease pathology*,
Neuropathology (2020) Vol 40 -1, Pg 22-29)

Imaging based biomarkers



- There are three types of AD biomarkers: genetic biomarkers, plasma biomarkers and imaging biomarkers.
- Definite diagnosis of AD can happen only after death through brain autopsy.
- The primary contribution of these biomarkers is that they make a stronger **case definition**.
- Stronger case definition implies more reliable epidemiological studies.



Magnetic resonance imaging (MRI)

- MRI uses magnetic fields and radio waves to produce detailed images of body structures, including the size and shape of the brain and brain regions.
- Evidence of shrinkage may support a diagnosis of Alzheimer's.
- MRI also provides a detailed picture of brain blood vessels to rule out vascular diseases.

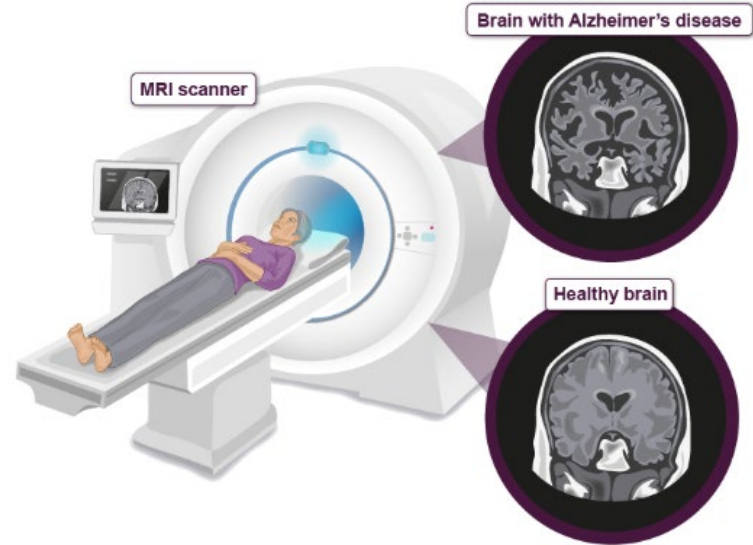


Fig: MRI scanner
(Taken from Alzheimer's research UK blog post)

- In Alzheimer's disease, the hippocampi are often affected first.
- A doctor will use an MRI to see if there are visible changes to these structures, which can help to diagnose Alzheimer's.

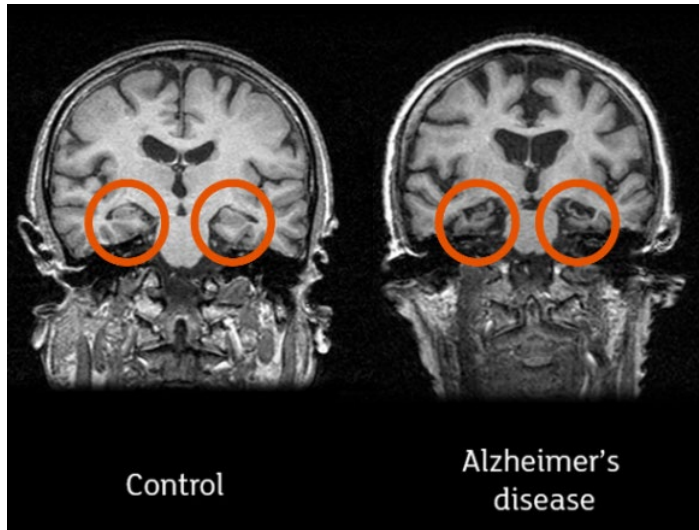


Fig: Hippocampus structure in AD vs control
(Images credit: Professor John O'Brien, University of Cambridge and Newcastle University)

Positron emission tomography (PET)

- PET uses small amounts of a radioactive substance, called a tracer, to measure specific activity — such as energy use — or a specific molecule in different brain regions.

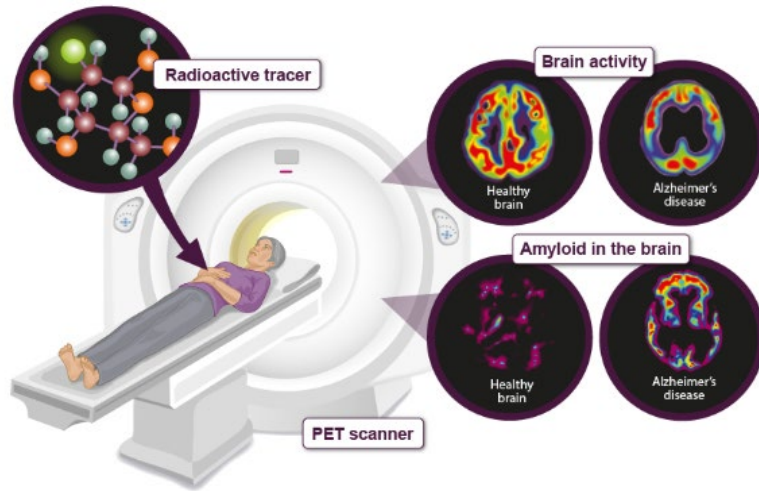


Fig: PET scanner
(Taken from Alzheimer's research UK blog post)

Types of PET scan: Fluorodeoxyglucose (FDG) PET scan

- Fluorodeoxyglucose (FDG) PET scans measure energy use in the brain.
- Studies show that people with dementia often have abnormal patterns of decreased glucose use in specific areas of the brain.

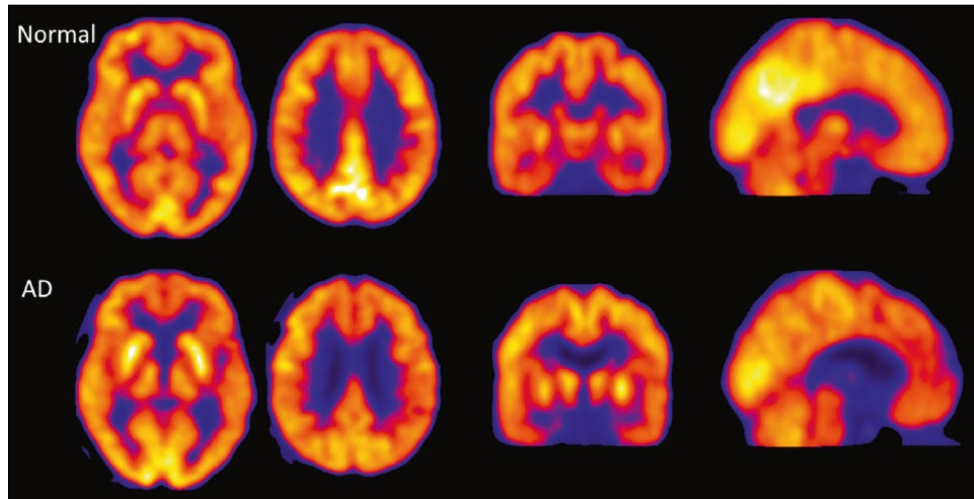


Fig: FGD PET scans of AD vs control
(Chouliaras and O'Brien, *The use of neuroimaging techniques in the early and differential diagnosis of dementia*, Molecular Psychiatry (2023))

Types of PET scan: Tau PET scans

- Tau PET scans detect the abnormal accumulation of the tau protein.
- Tau PET scans may be used by doctors to monitor progression of Alzheimer's.

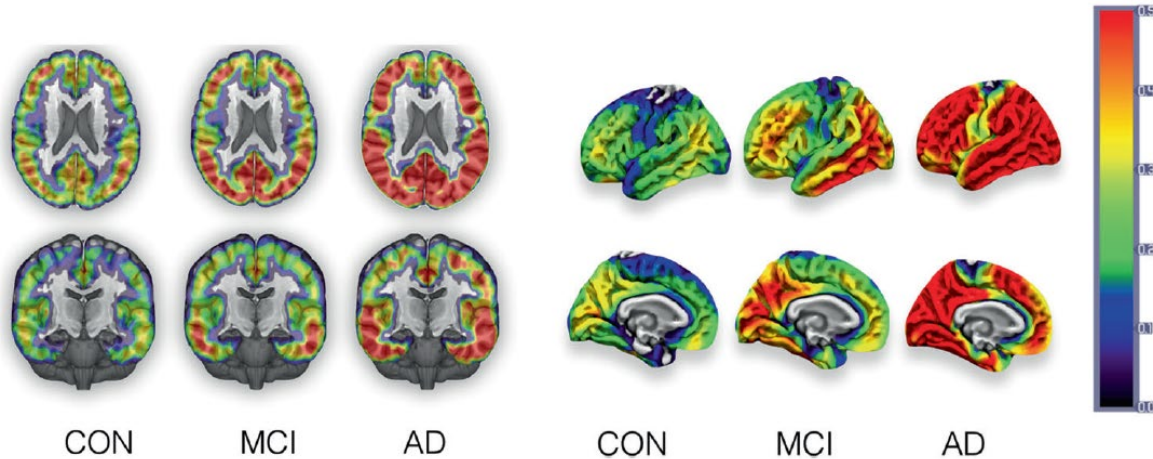


Fig: Tau PET scans of AD vs control (Chouliaras and O'Brien, *The use of neuroimaging techniques in the early and differential diagnosis of dementia*, Molecular Psychiatry (2023))

Psychiatric Neuroimaging



- Most mental health conditions are diagnosed subjectively.
- There are relatively few attempts at using imaging data to classify mental health disorders.
 - Imaging methods are expensive
 - **Primary obstacle: Psychiatric imaging studies rarely involve population sampling methods to characterize psychiatric issues.**

Solution: Use epidemiological methods in Imaging!

Epidemiology in Psychiatric Neuroimaging



- Descriptive epidemiological studies play the most important role in
 - Identification of risk factors for mental health conditions
 - Detecting trends in frequency of disease
 - Understand public health implications

Leads to better psychiatric practices and neuroimaging research.

More contributions to Psychiatry



- Analytical epidemiology focuses on
 - Risk and protector factors of diseases
 - Test hypothesis on cause-effect relationships.
- Such a study established that:
 - *Schizophrenia is part of a spectrum of disorders, which also includes schizoaffective disorder and schizotypal and paranoid personality disorders, which potentially share common genetic basis*
- Several epidemiological studies have shown that future adult-onset schizophrenia patients have, as a group, lower IQ and worse social abilities in childhood and adolescence
 - Important because it supports the *neurodevelopmental hypothesis of schizophrenia*