PET imaging in neurodegenerative disease

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Neuroimaging Modalities

- PET (Positron Emission Tomography)
  - Injection of radioactive drug
  - Gives information about a specific target within brain (Different scans for Amyloid, Tau, etc)

- MRI (Magnetic Resonance Imaging)
  - Magnetic field and radio waves
  - Gives information about brain structure or brain function

- Hybrid PET-MRI scanners allow simultaneous collection of these brain scans

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PET can measure multiple AD targets

- Amyloid PET
  - Amyloid plaques
  - Used for research since 2004
  - Three FDA approved PET scans (2012)

- Tau PET
  - Neurofibrillary tangles
  - Multiple research PET scans being investigated
  - First promising research scan 2013

- Fludeoxyglucose (FDG) PET
  - Glucose (sugar) uptake
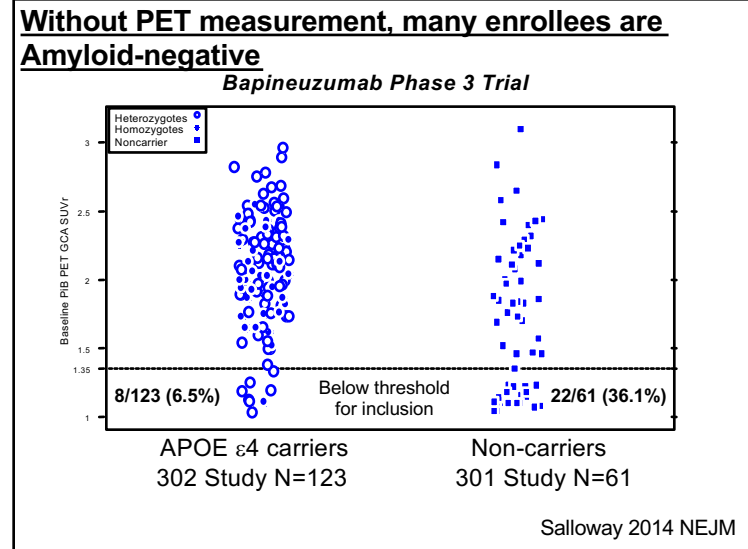 - Measure of neuron health
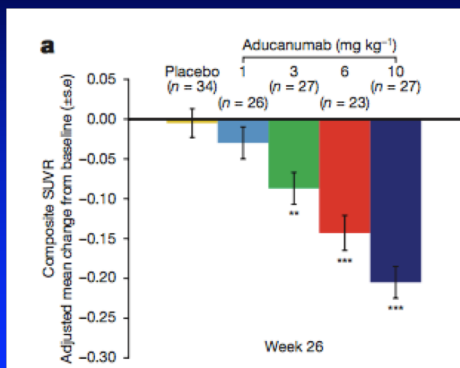 - In use for decades

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Amyloid PET scans

Tangles (Tau Protein)

Plaques (Amyloid Beta Protein)
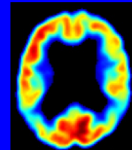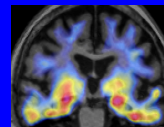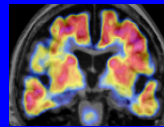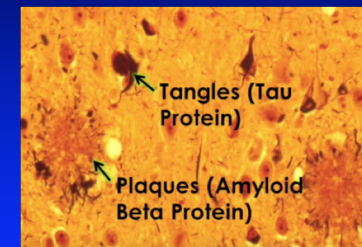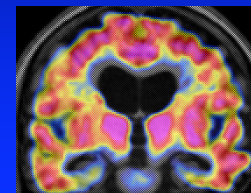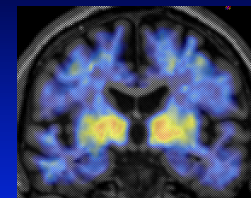
Amyloid PET in AD clinical trials

1. **Participant Selection**

2. **Examine drug engagement of anti-amyloid therapies**

Without PET measurement, many enrollees are Amyloid-negative

Bapineuzumab Phase 3 Trial

Heterozygotes
Homozygotes
Noncarrier

Baseline PIB PET GCA SUVr

3
2.5
2
1.5
1.35
1

8/123 (6.5%) Below threshold for inclusion **22/61 (36.1%)**

APOE ε4 carriers
302 Study N=123

Non-carriers
301 Study N=61
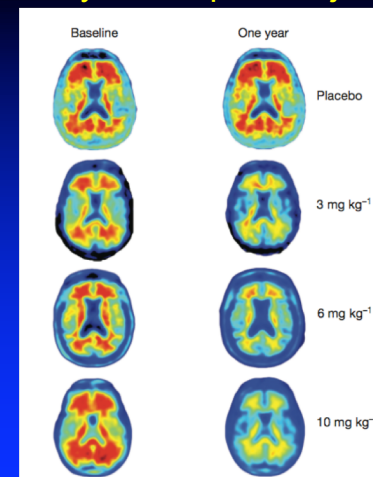
Salloway 2014 NEJM

PRIME Study: Anti-Amyloid therapy

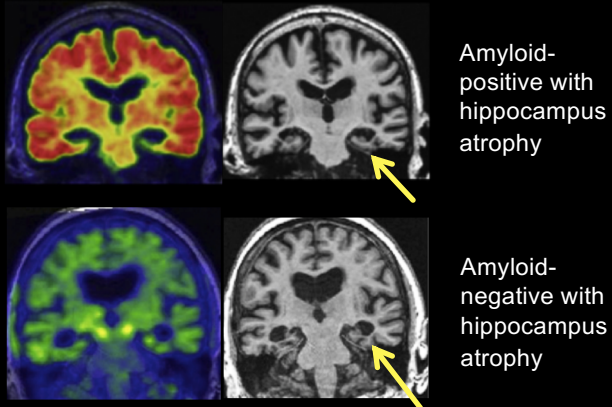*Reductions in Amyloid PET measured over time*

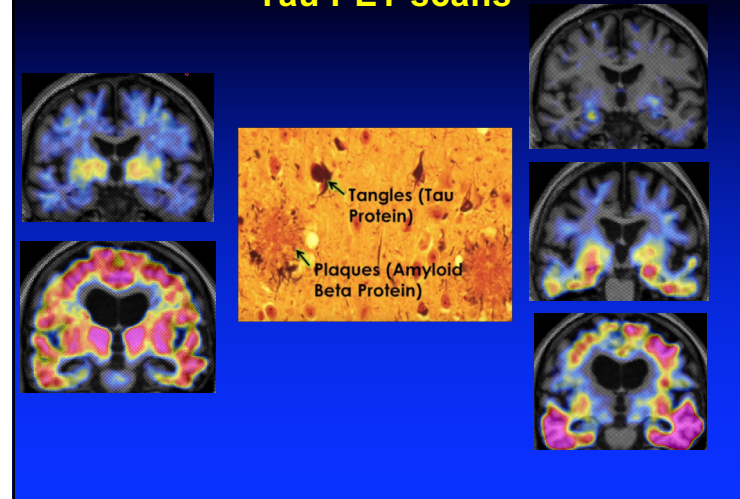
Sevigny 2016 Nature

PRIME Study: Example Subjects
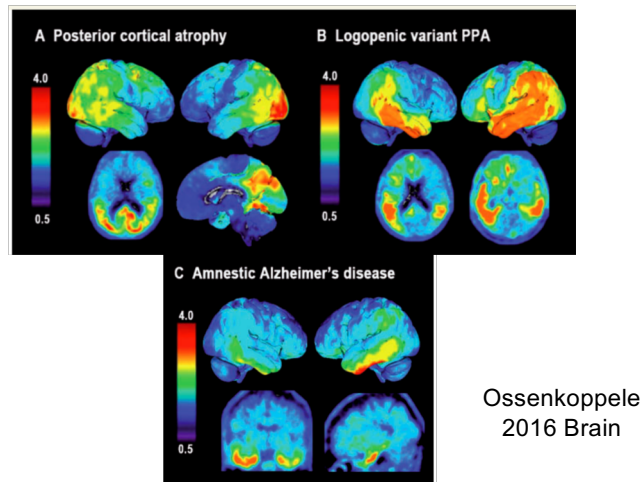

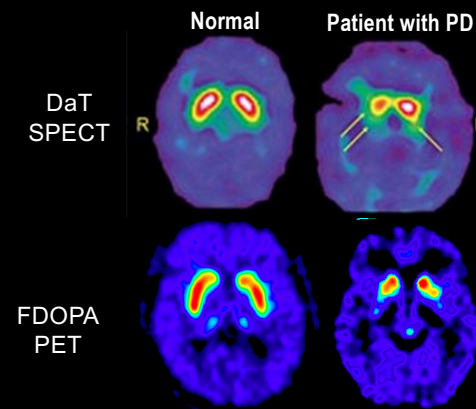Sevigny 2016 Nature

Combine Amyloid PET with Structural MRI scan

Amyloid-positive with hippocampus atrophy

Amyloid-negative with hippocampus atrophy

Tau PET scans

Tangles (Tau Protein)

Plaques (Amyloid Beta Protein)

Tau pattern aligns with clinical symptoms

A Posterior cortical atrophy
B Logopenic variant PPA
C Amnestic Alzheimer's disease

Ossenkoppele 2016 Brain

Dopamine imaging in Parkinson's Disease

Normal   Patient with PD

DaT SPECT

FDOPA PET

→Need for alpha-synuclein PET scans

Summary

- PET imaging allows visualization of specific brain targets relevant for neurodegenerative disease
- Amyloid PET is widely used in clinical trials
- Combining PET and MRI can help understand underlying disease
- Tau PET is a new promising research tool
- Other PET targets are important and under development (alpha-synuclein, synaptic density, neuroinflammation)

Thank you!

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