

Basis of Therapeutic Trials in Early Alzheimer's Disease

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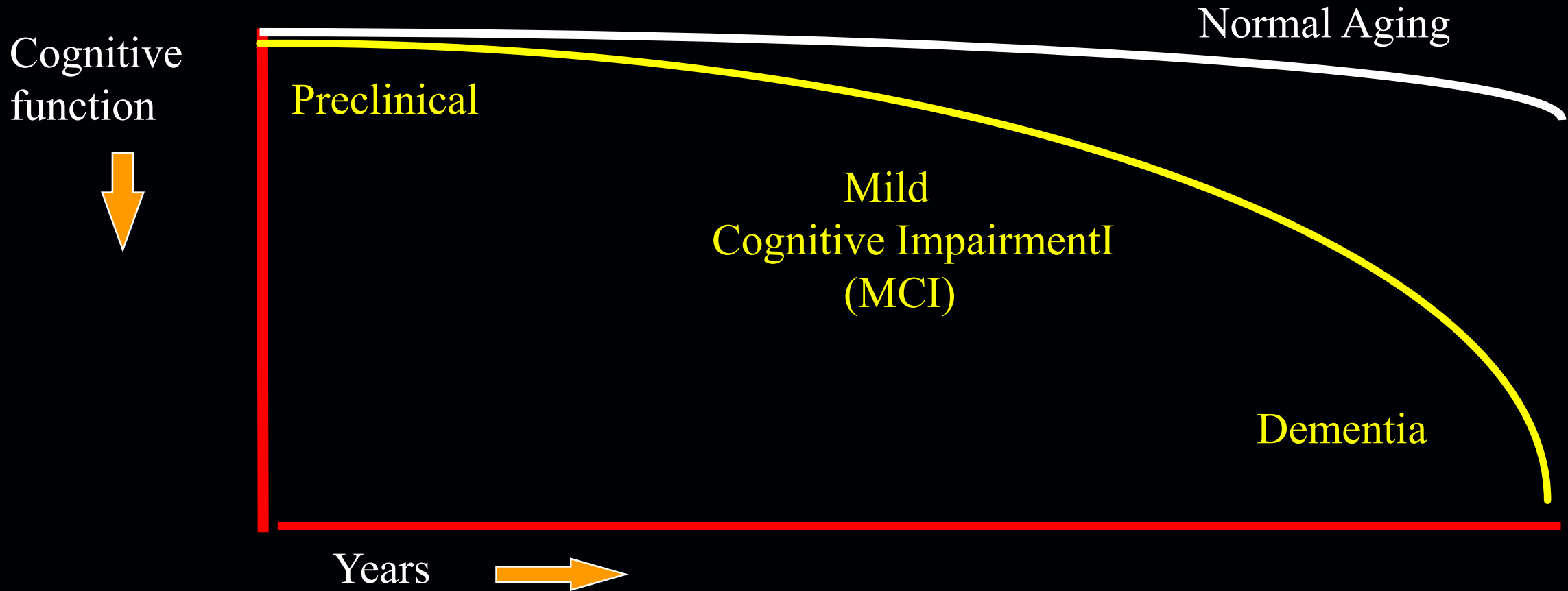
Harvard Medical School

The proverbial tip of the iceberg....

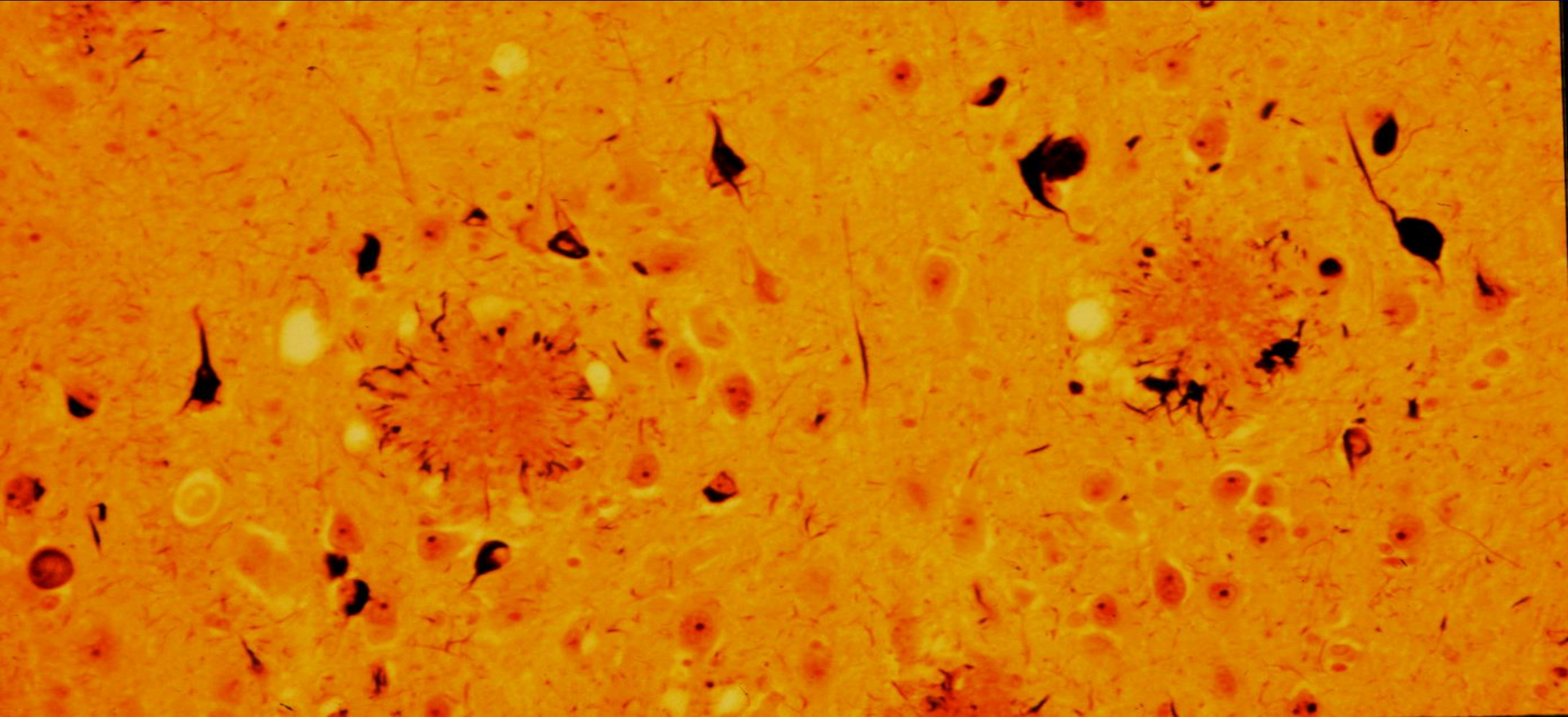


Image courtesy of
Ralph Clevenger

The Continuum of Alzheimer's Disease

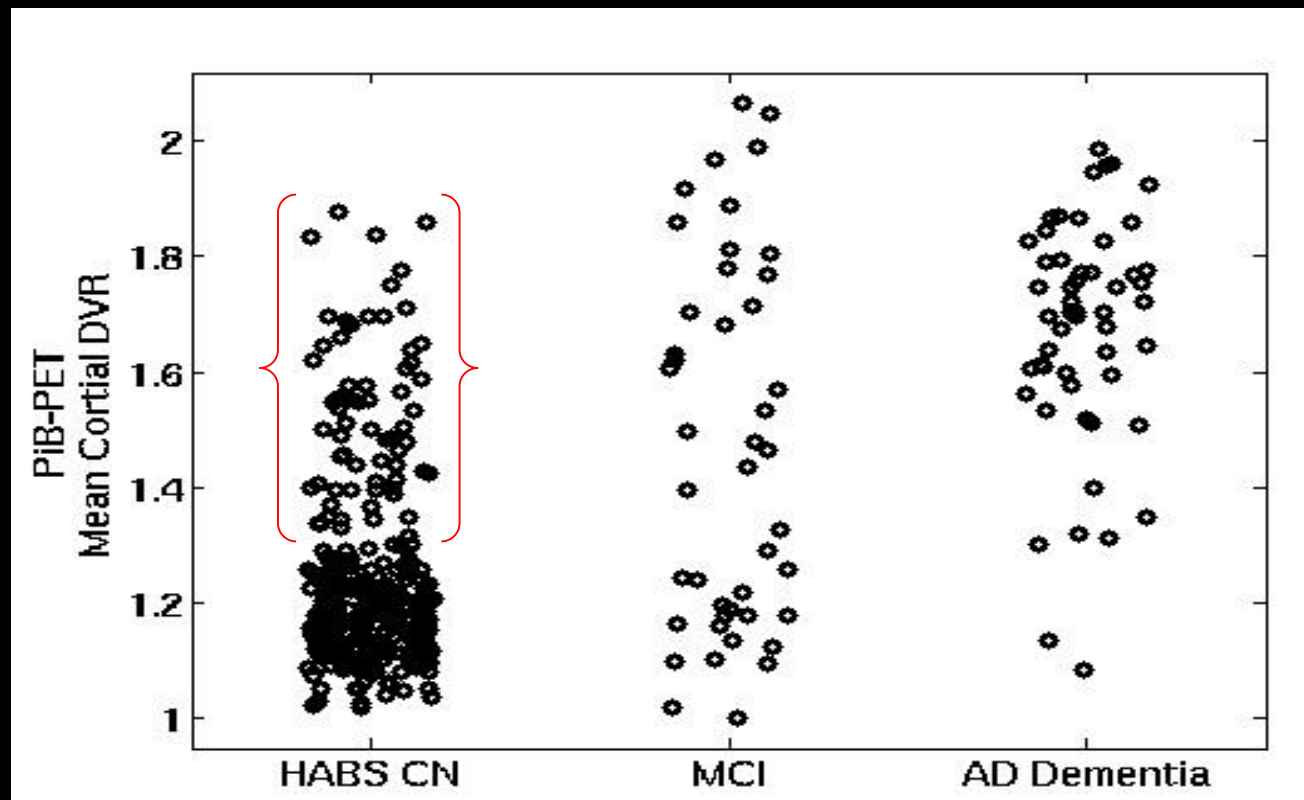
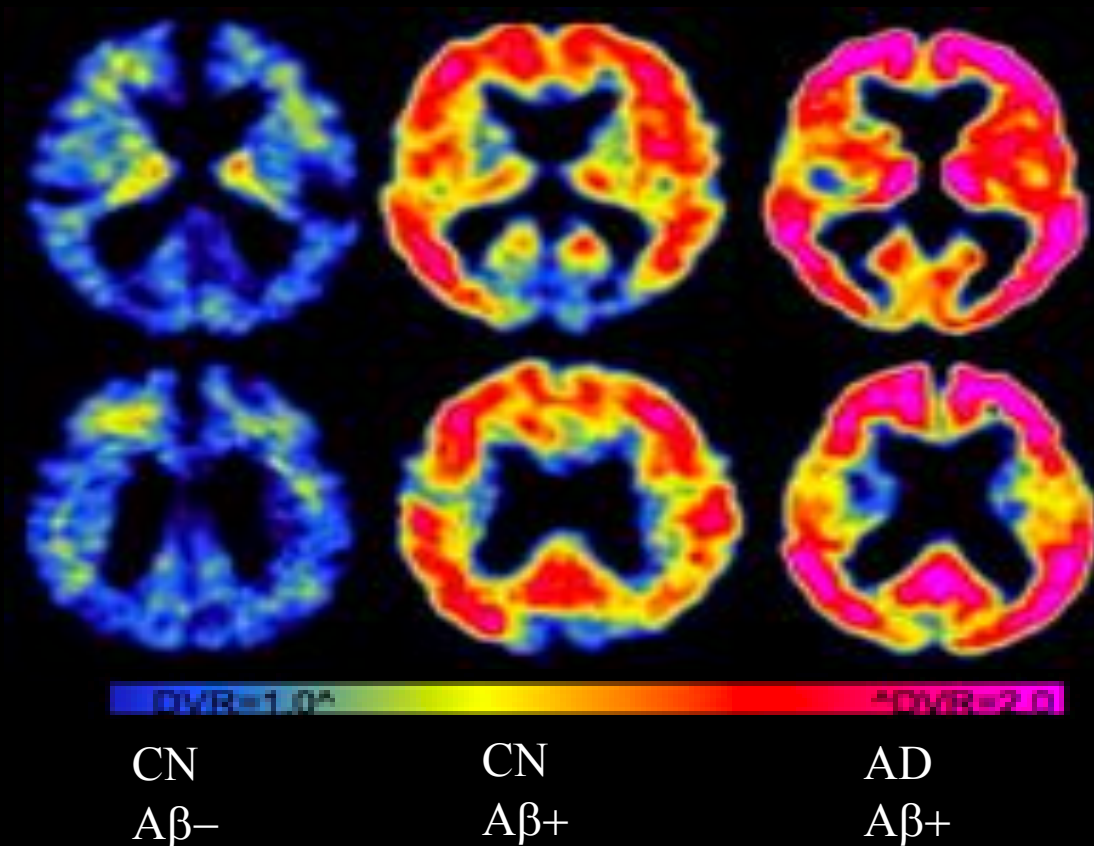


Pathology of Alzheimer's Disease



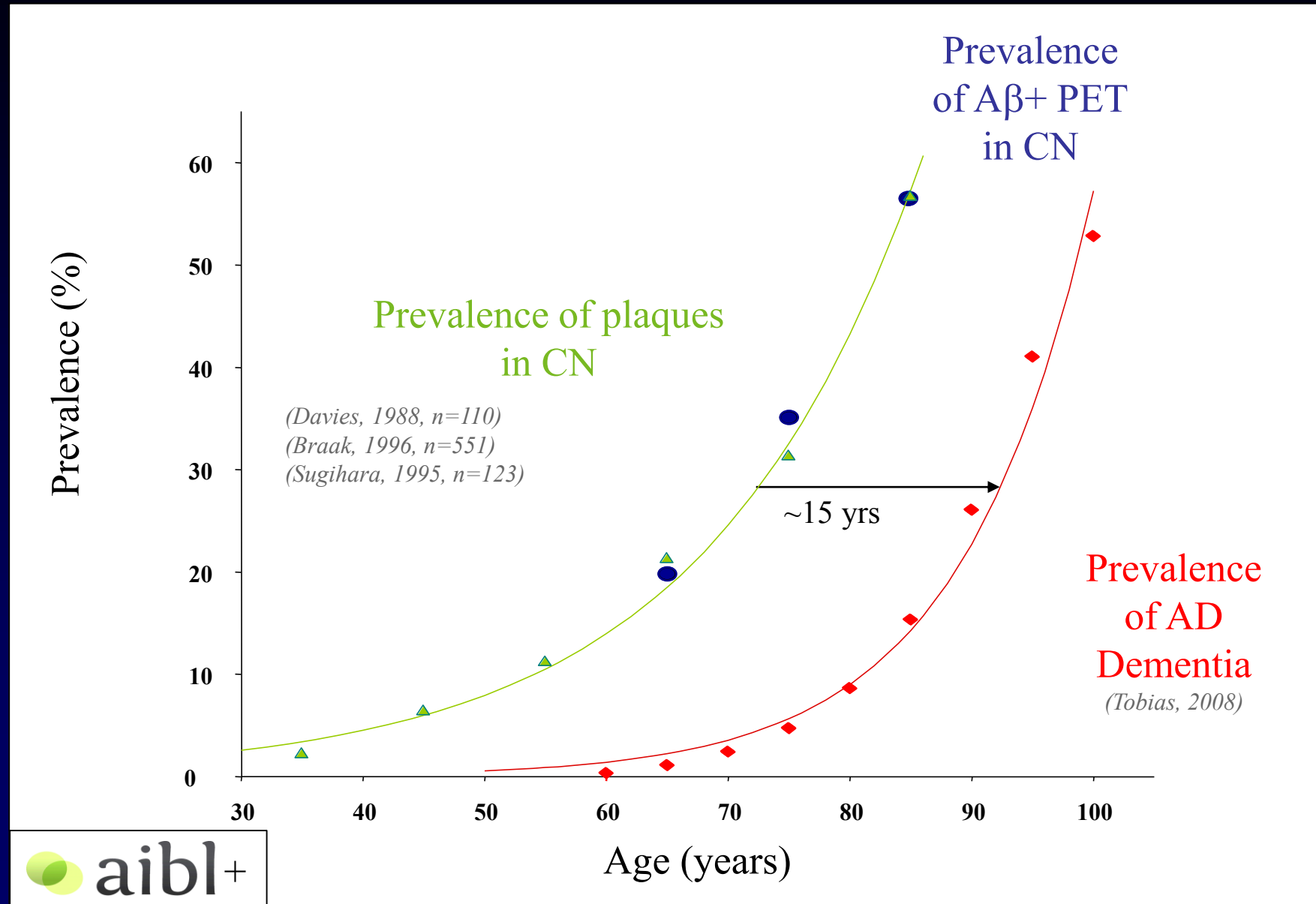
How do we detect evidence of Alzheimer's
disease changes in the living brain?

PET Amyloid Imaging Across the Spectrum of AD



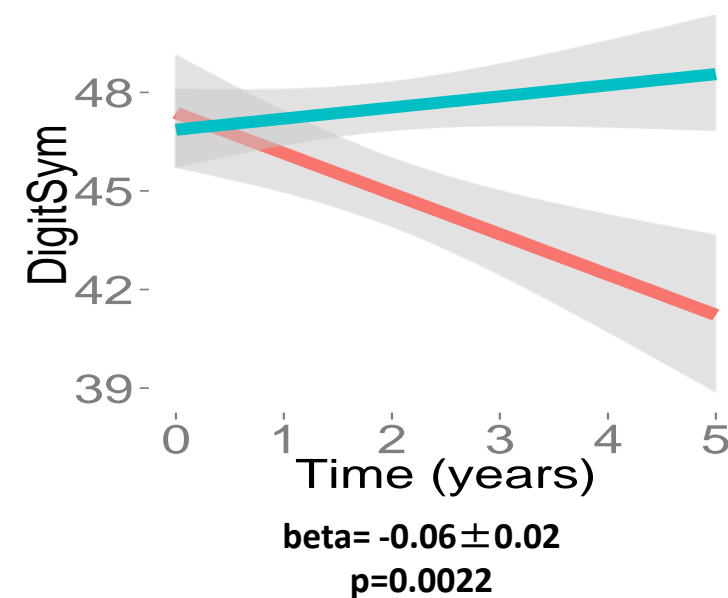
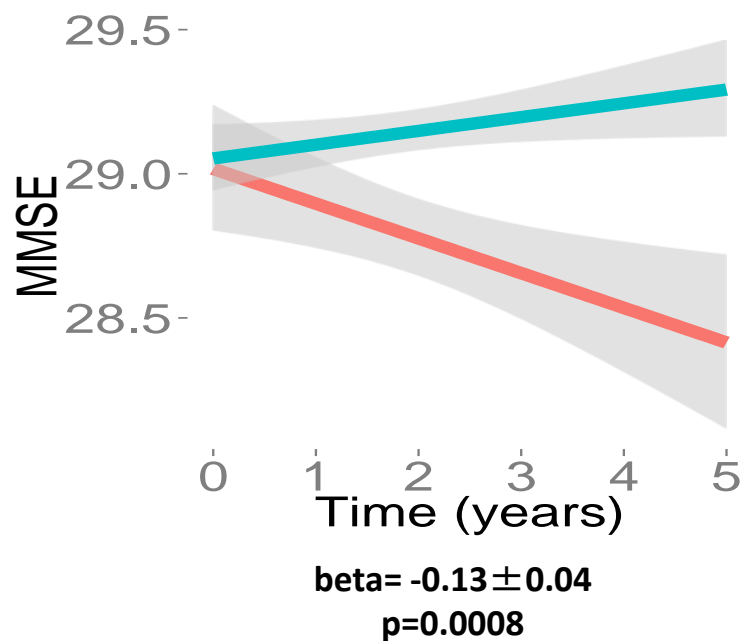
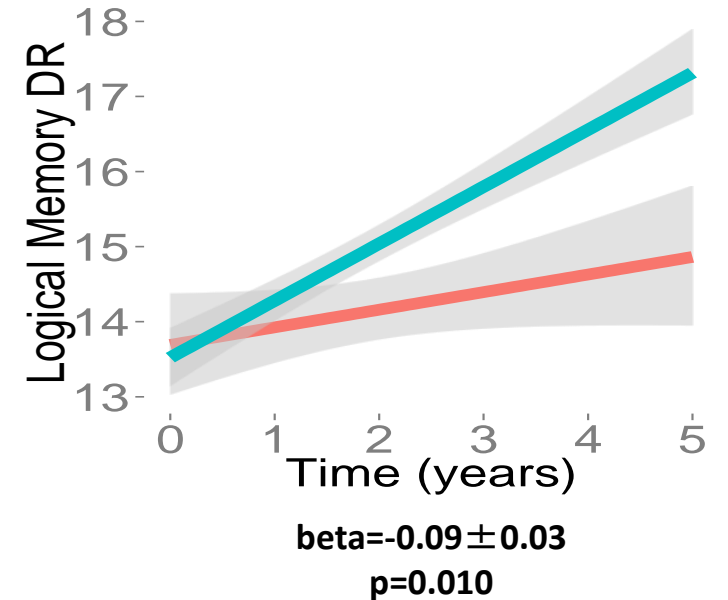
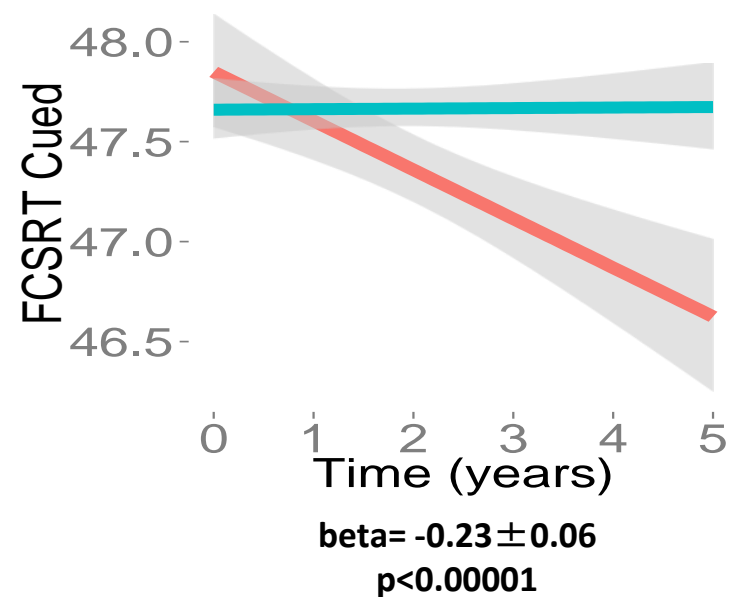
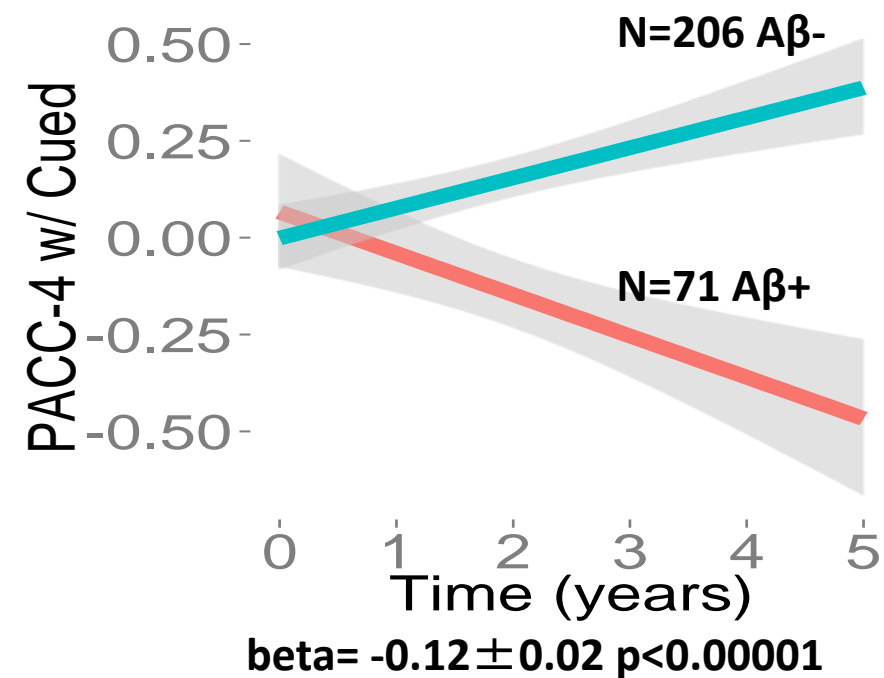
Harvard Aging Brain Study

Preclinical Alzheimer's Disease

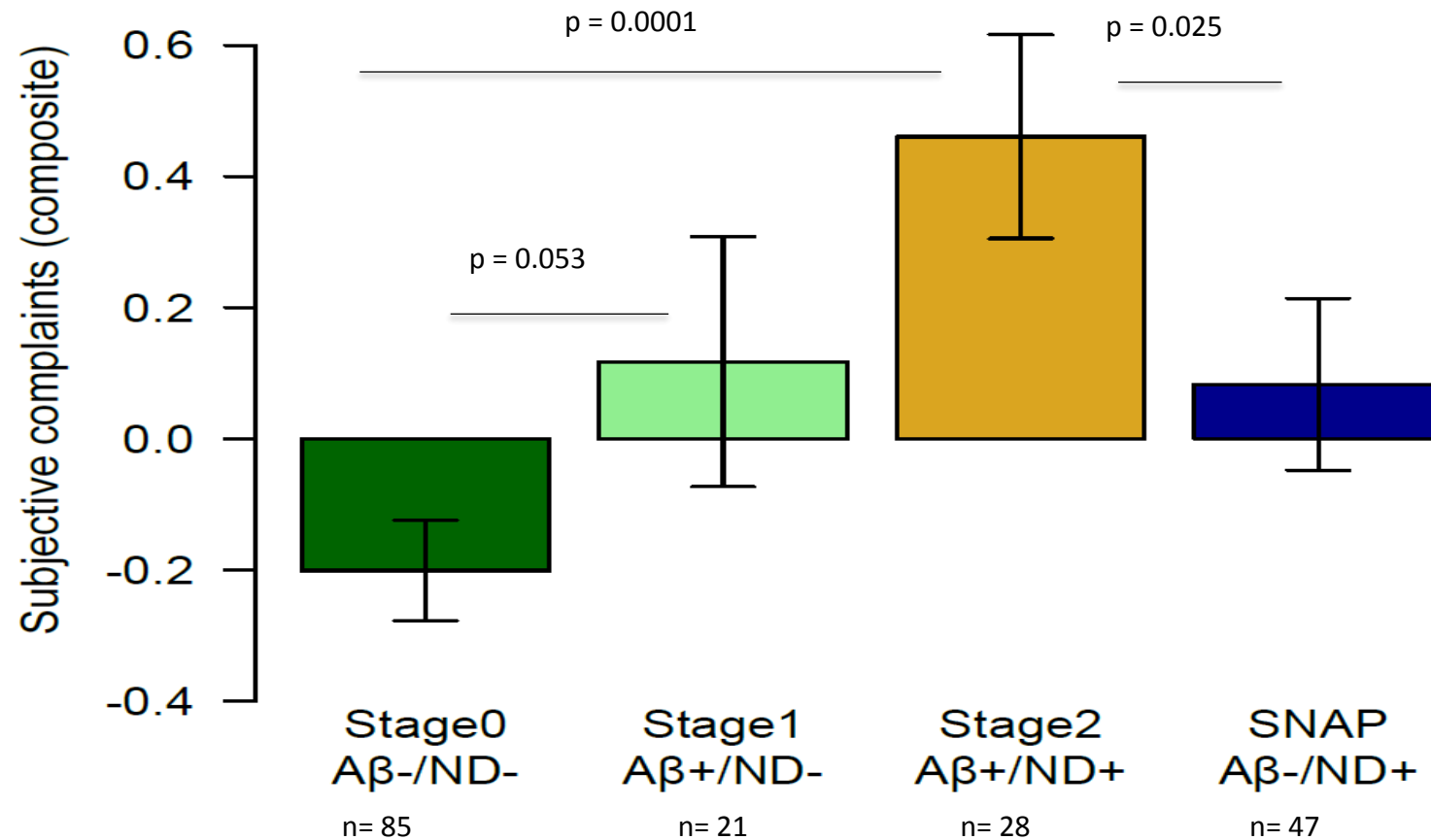


Adapted from Rowe C et al *Neurobiology of Aging* 2010

Preclinical Alzheimer Cognitive Composite (HABS)



Subjective cognitive concerns associated with advancing stages of preclinical AD

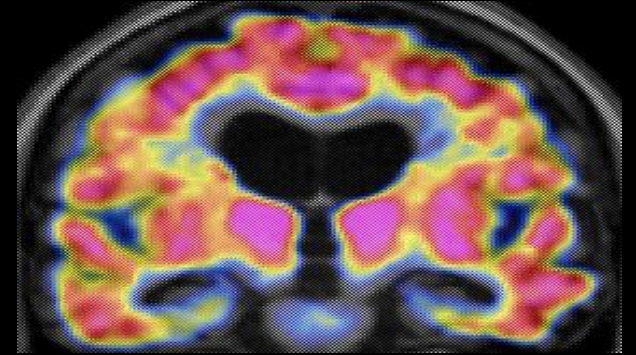
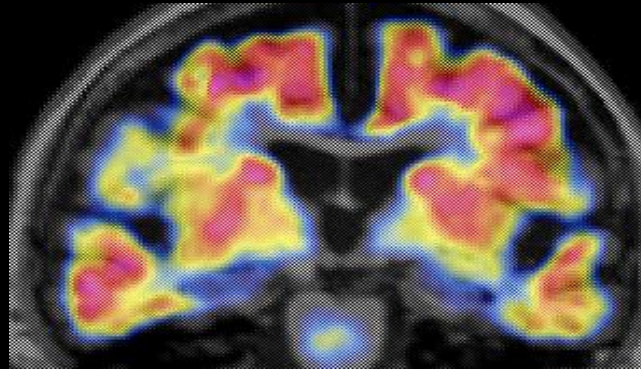
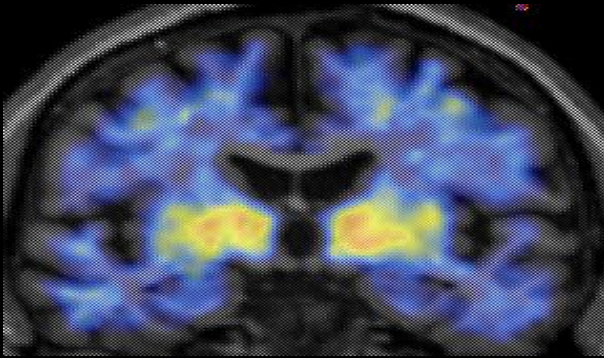


Harvard Aging Brain Study

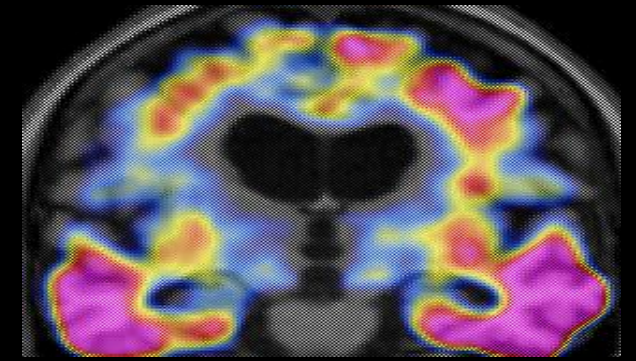
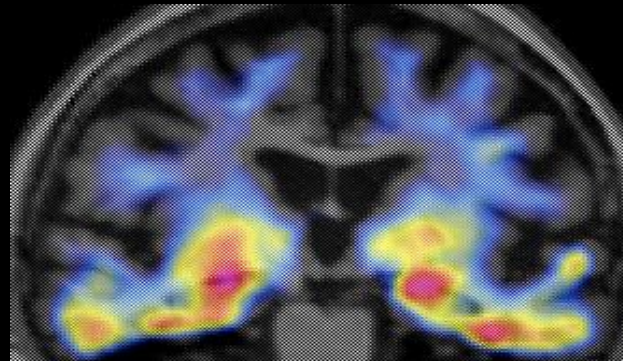
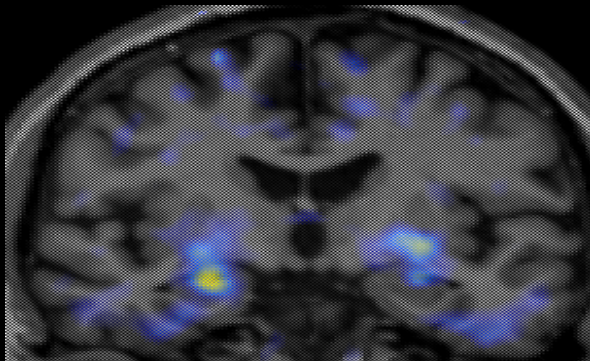
Amariglio et al. *Neurology* 2015

Amyloid and Tau PET Imaging

A β
(PiB)



Tau
(T807)

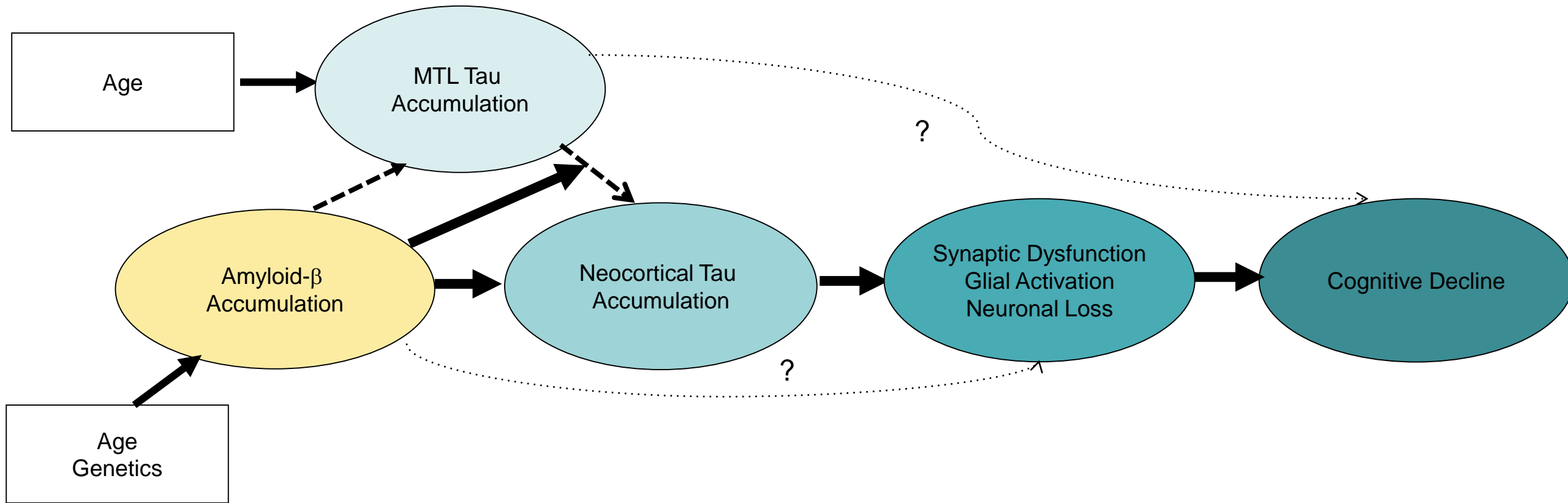


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AD Dementia

Hypothetical Interaction of Amyloid and Tau in Preclinical AD

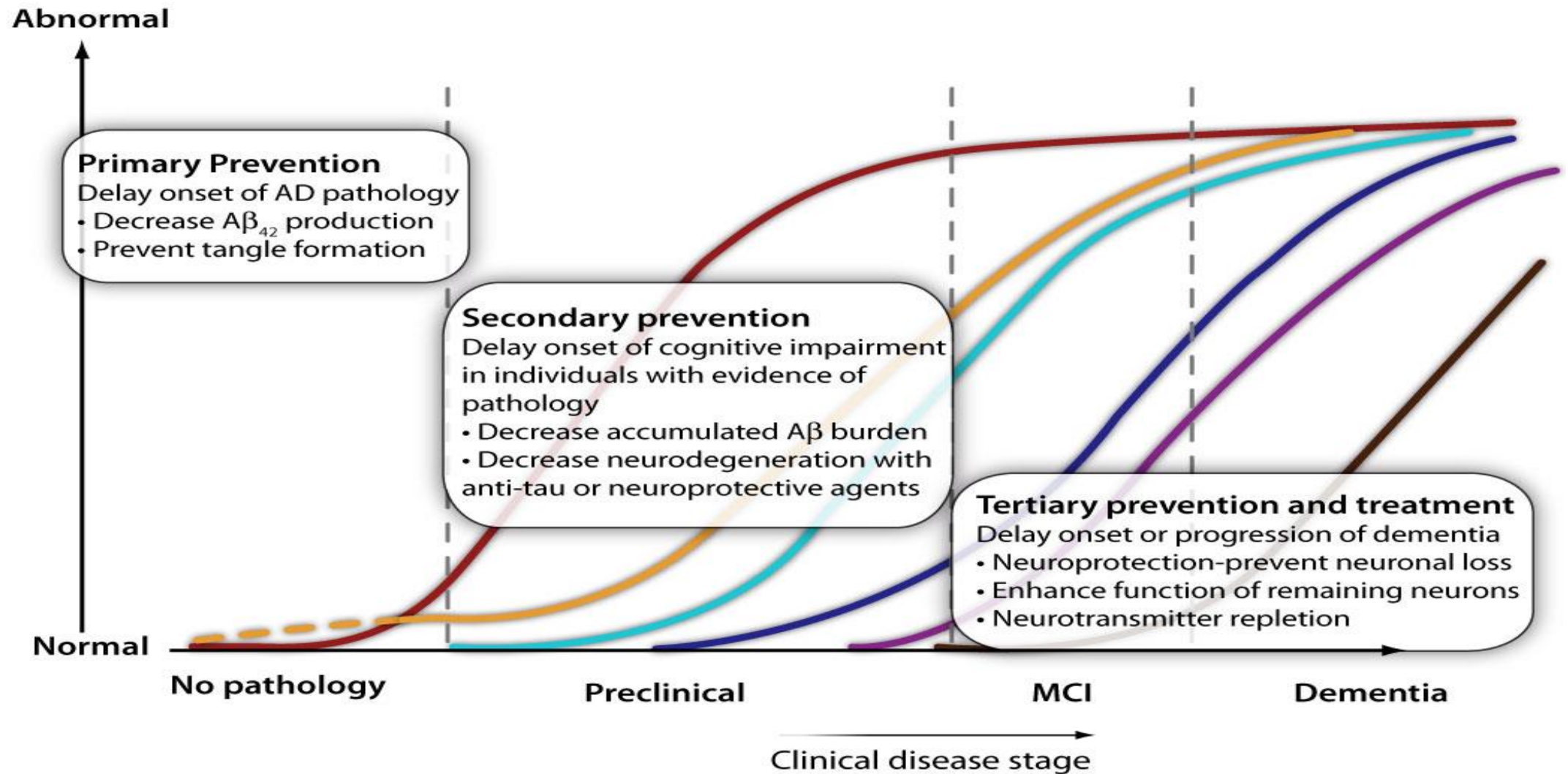


Does amyloid “fan the flames” of tau?



Why would we want to detect Alzheimer's
disease
a decade before dementia?

Testing the Right Target and the Right Drug at the Right Stage of Alzheimer's Disease



A4 Study - Anti-Amyloid Treatment in Asymptomatic AD

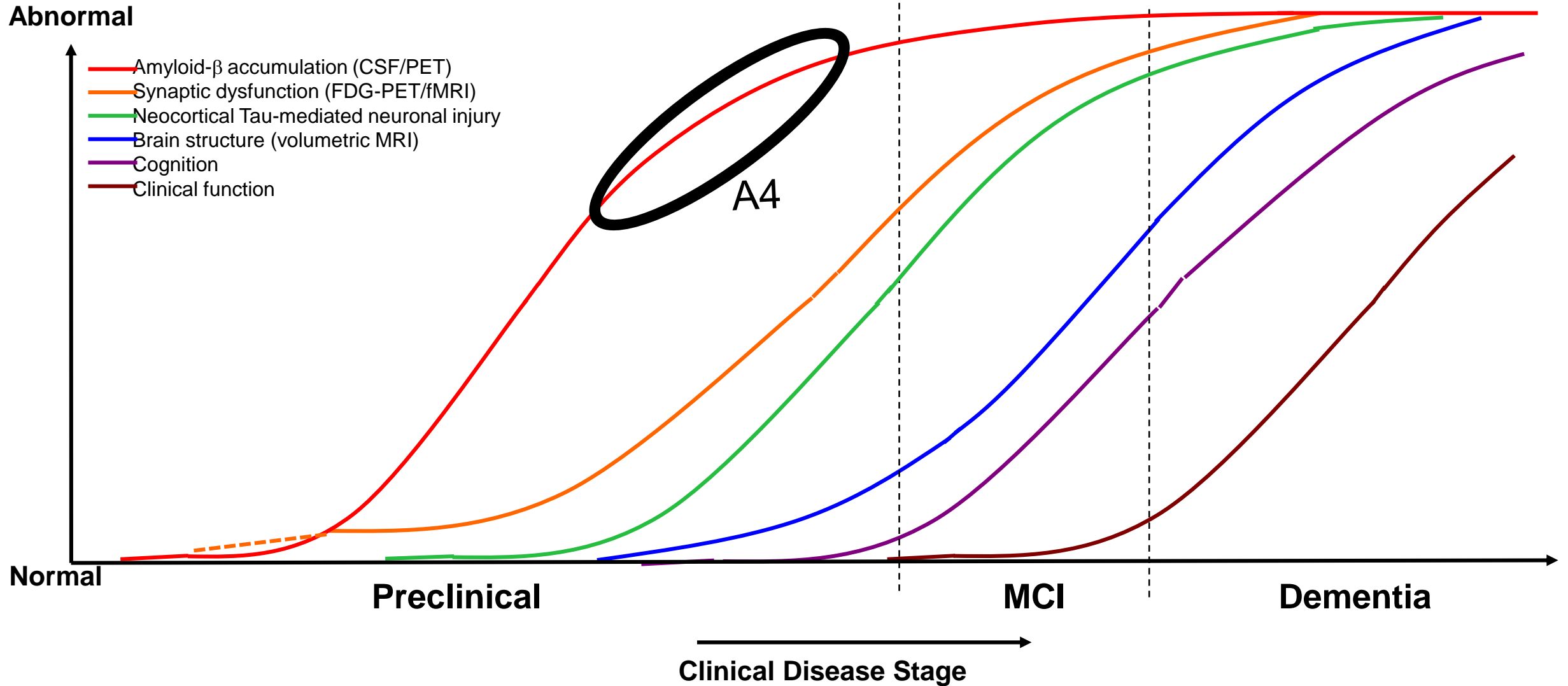


Figure adapted from Jack *et al.* 2010, Sperling *et al.* 2011



The A4 Study

NOW IS THE TIME

ABOUT THE A4 STUDY »

AM I ELIGIBLE?

FIND A LOCATION

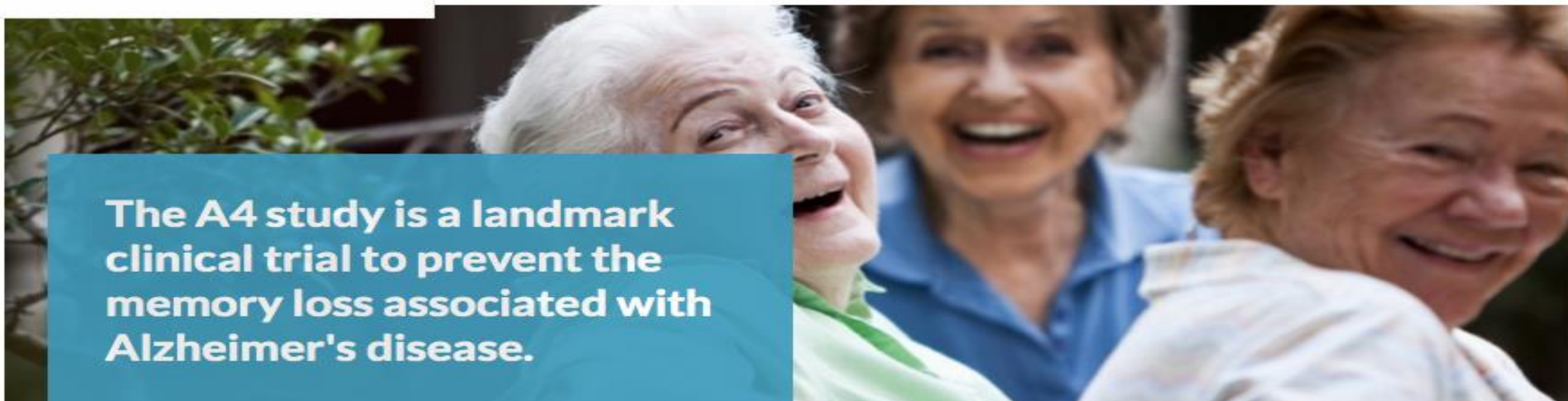


About the A4 Study

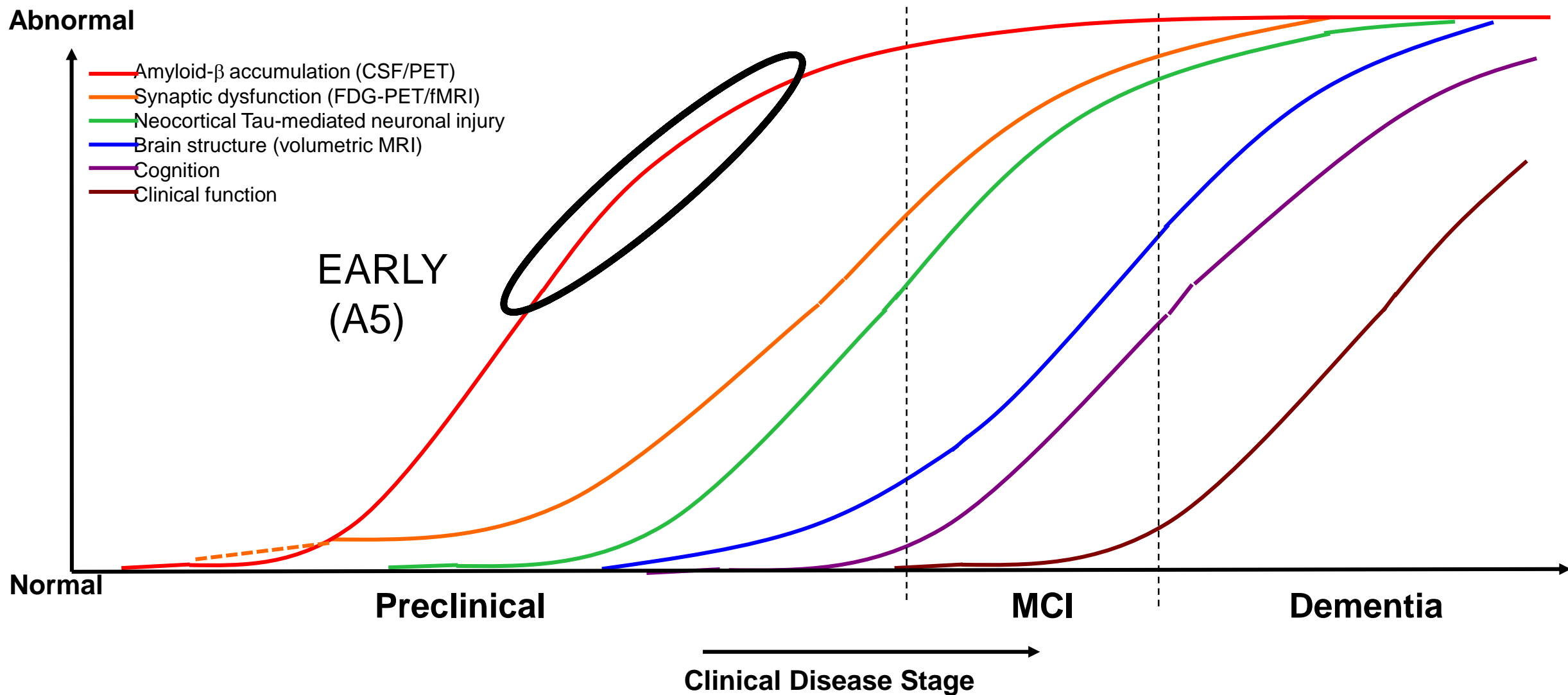
LEARN MORE

Watch the A4 Study Video

The A4 study is a landmark clinical trial to prevent the memory loss associated with Alzheimer's disease.

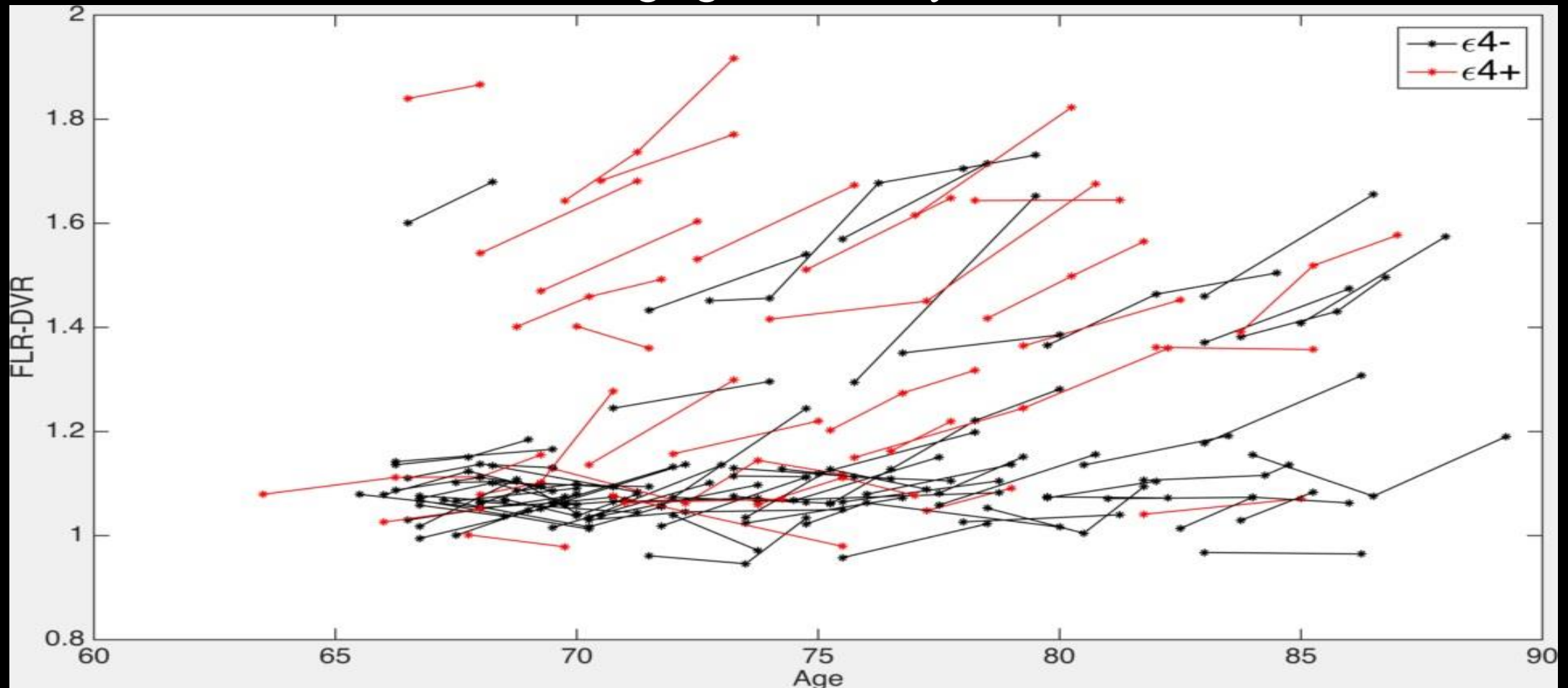


EARLY Study (“A5”) – BACE inhibitor



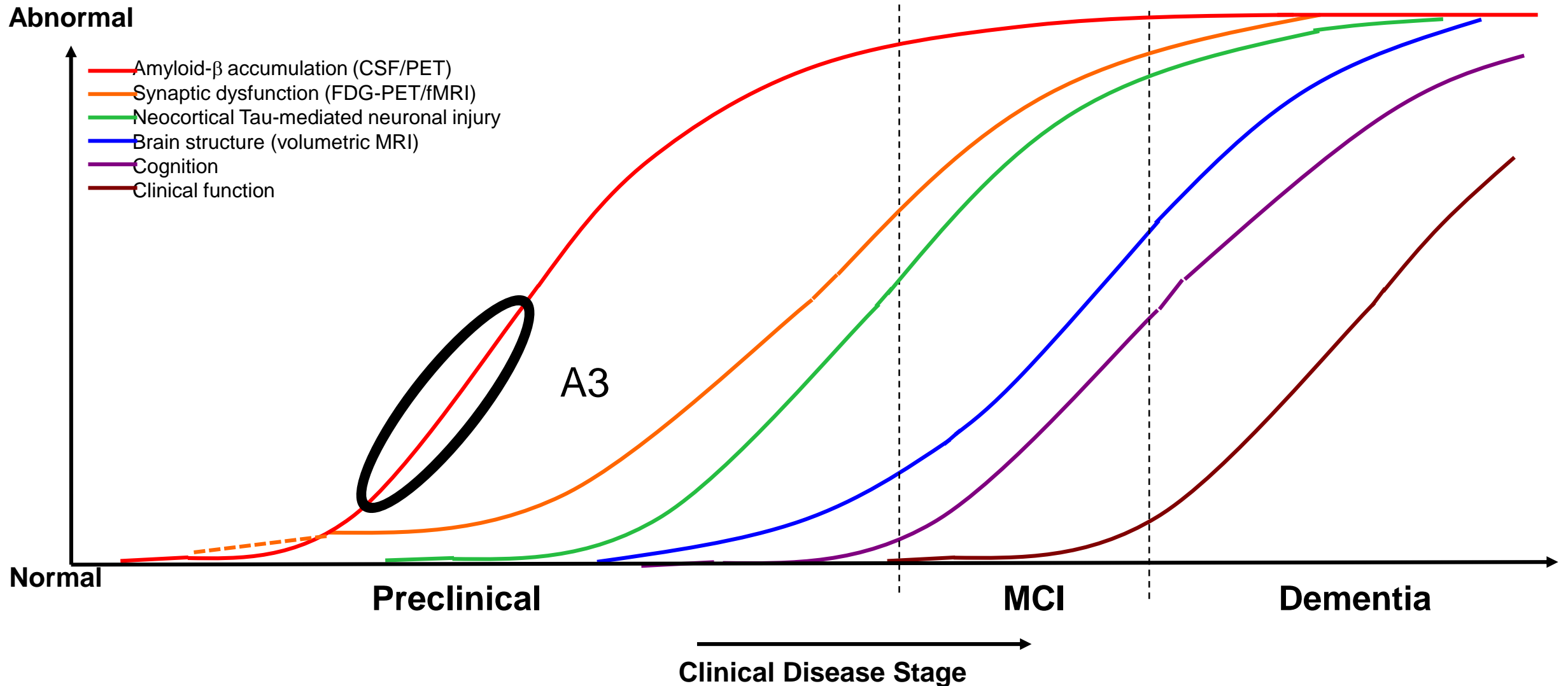
Longitudinal Amyloid- β Accumulation in Clinically Normal Elders

Harvard Aging Brain Study



A3 Study = Ante-Amyloid prevention of AD

Getting closer to Primary Prevention!





The Great Wave off Kanagawa – Hokusai circa 1832

Encouraging history from other fields

- Cholesterol Wars in Cardiology

- Good vs. bad cholesterol
- Secondary prevention trials in familial hypercholesterolemia and post-MI
- Reduction of cholesterol estimated to have reduced cardiac morbidity and mortality by 28%

- Delaying dementia by just 5 years would decrease Medicare costs by 50% (Alzheimer's Association 2010)

- Amyloid does not have to be “the” cause of AD merely “a” critical factor to impact the disease – May need combination therapy!

Resilience



Information

- Alzheimer's Association TrialMatch
<https://trialmatch.alz.org>
- A4 Study
A4STUDY.ORG
1-844-A4STUDY