Amyloid Imaging in Healthy Aging: Impact on Brain Function and Cognition

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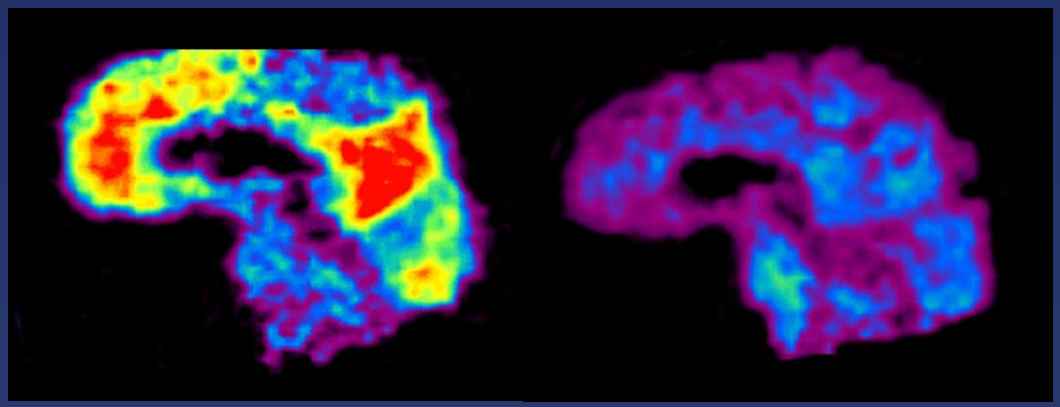
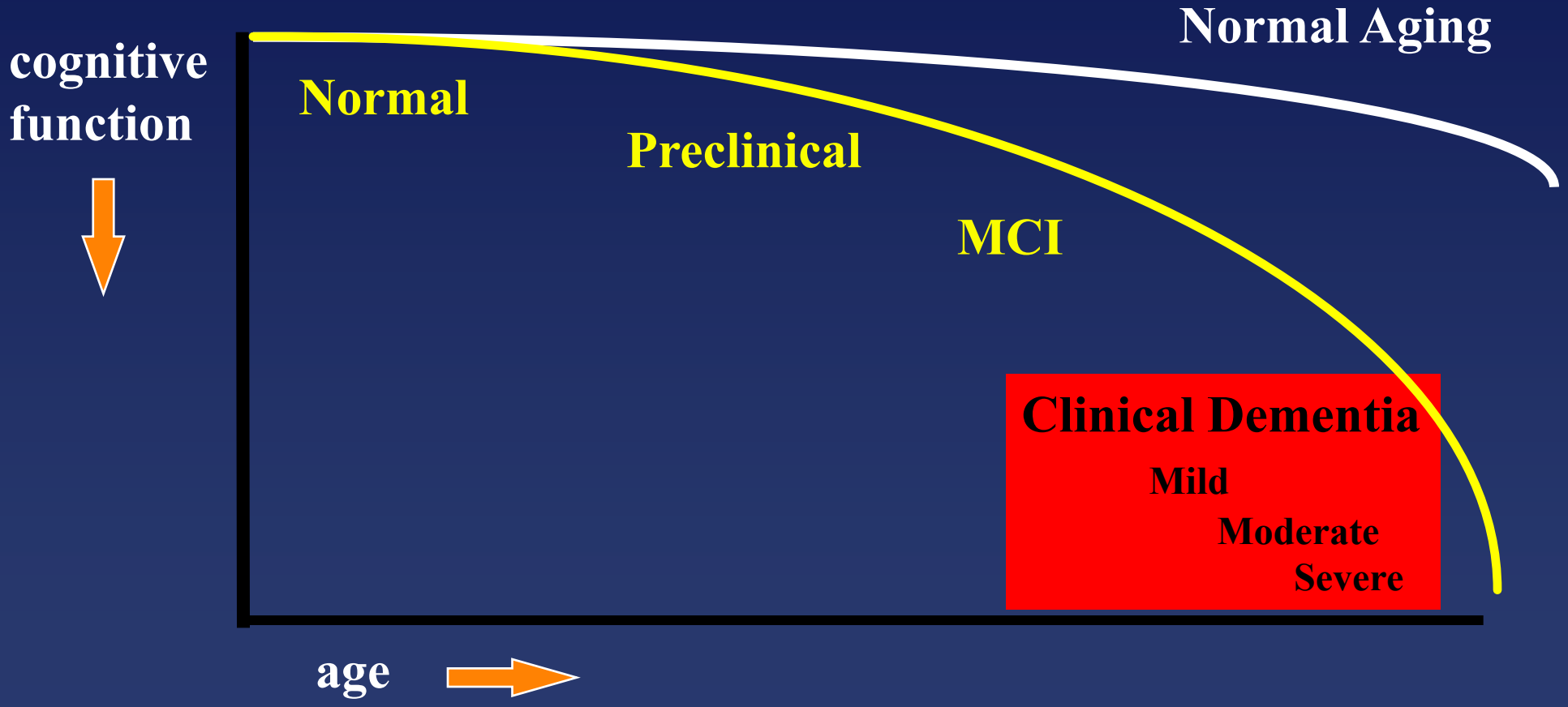


2nd Alzheimer's Public Education Forum
Miami, FL – January 19, 2014

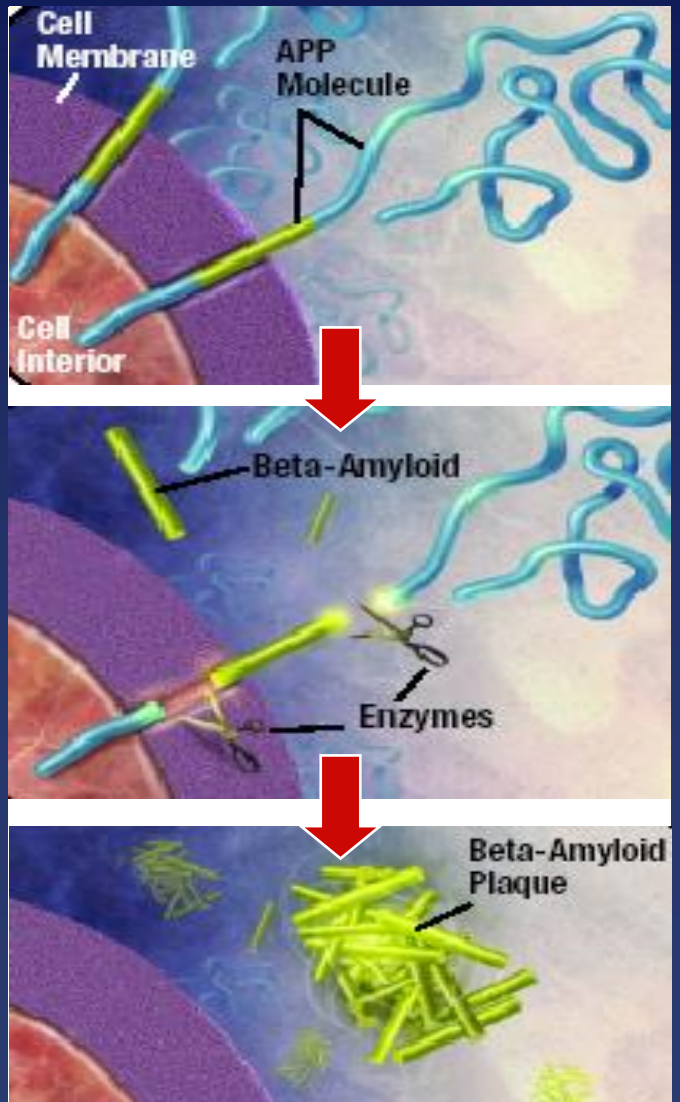
The Continuum of Alzheimer's Disease



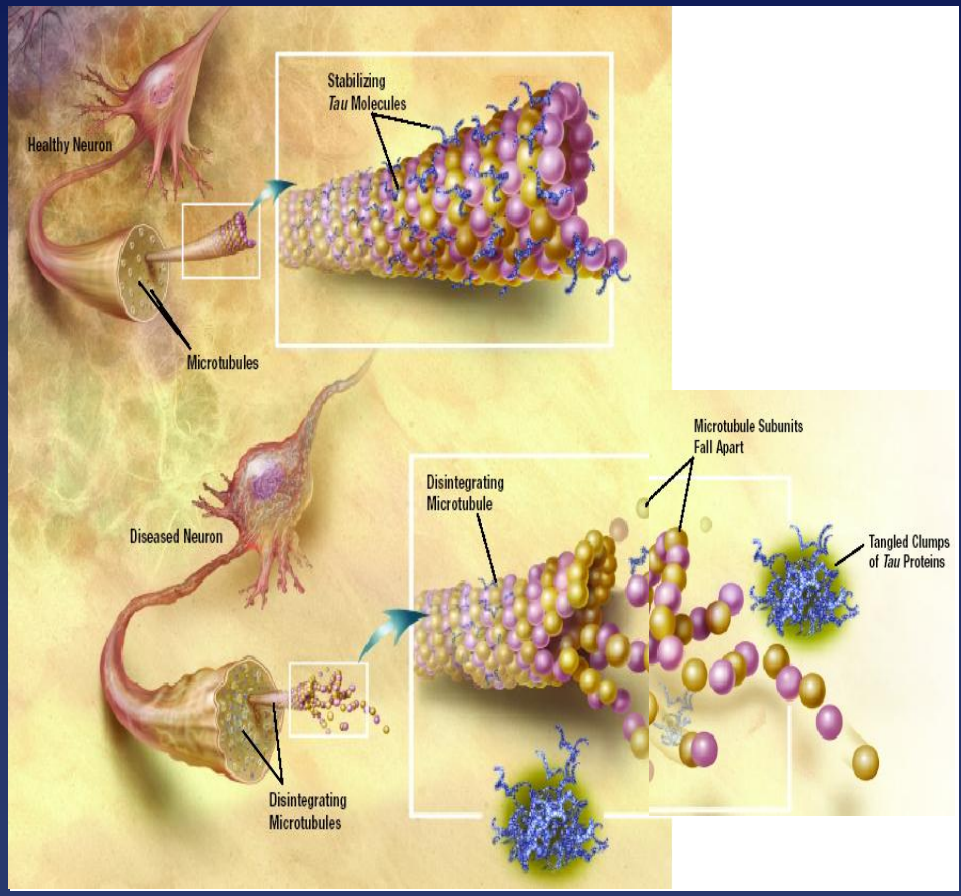
Sperling et al, Alzheimers Dement. 7: 280-292, 2011

Causes of Alzheimer's Disease

amyloid plaques damage nearby neurons

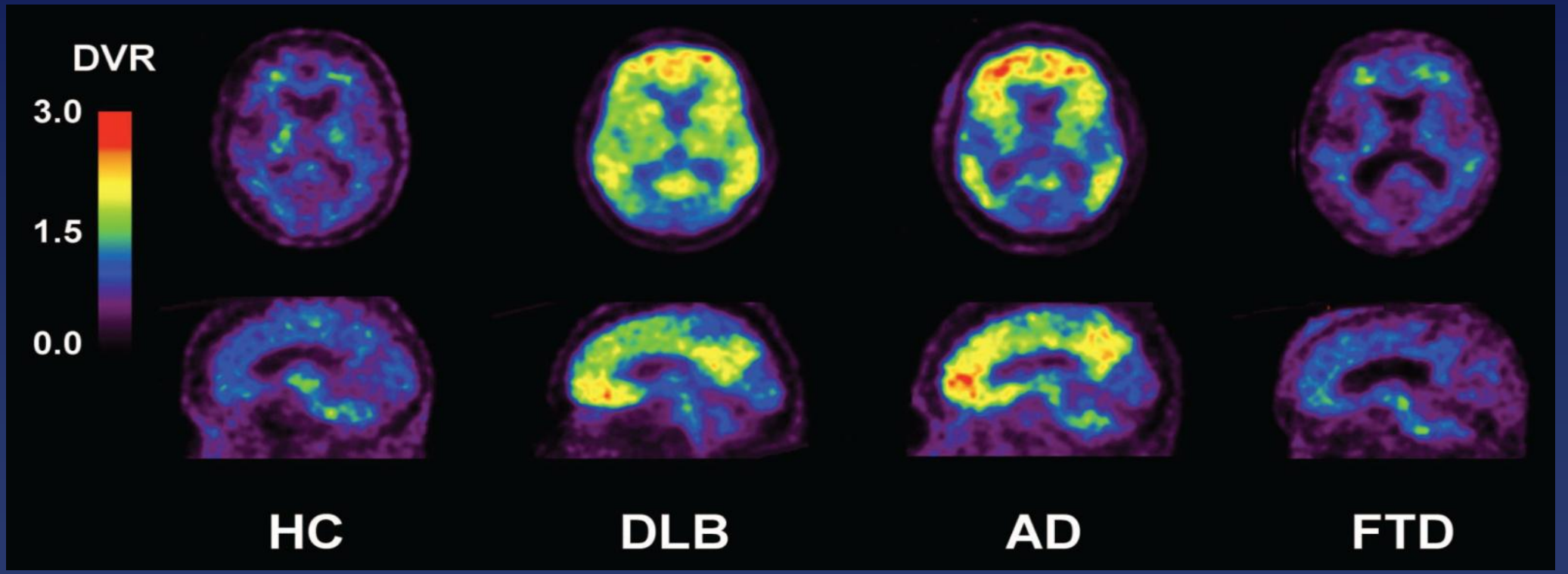


tau protein aggregates into tangles



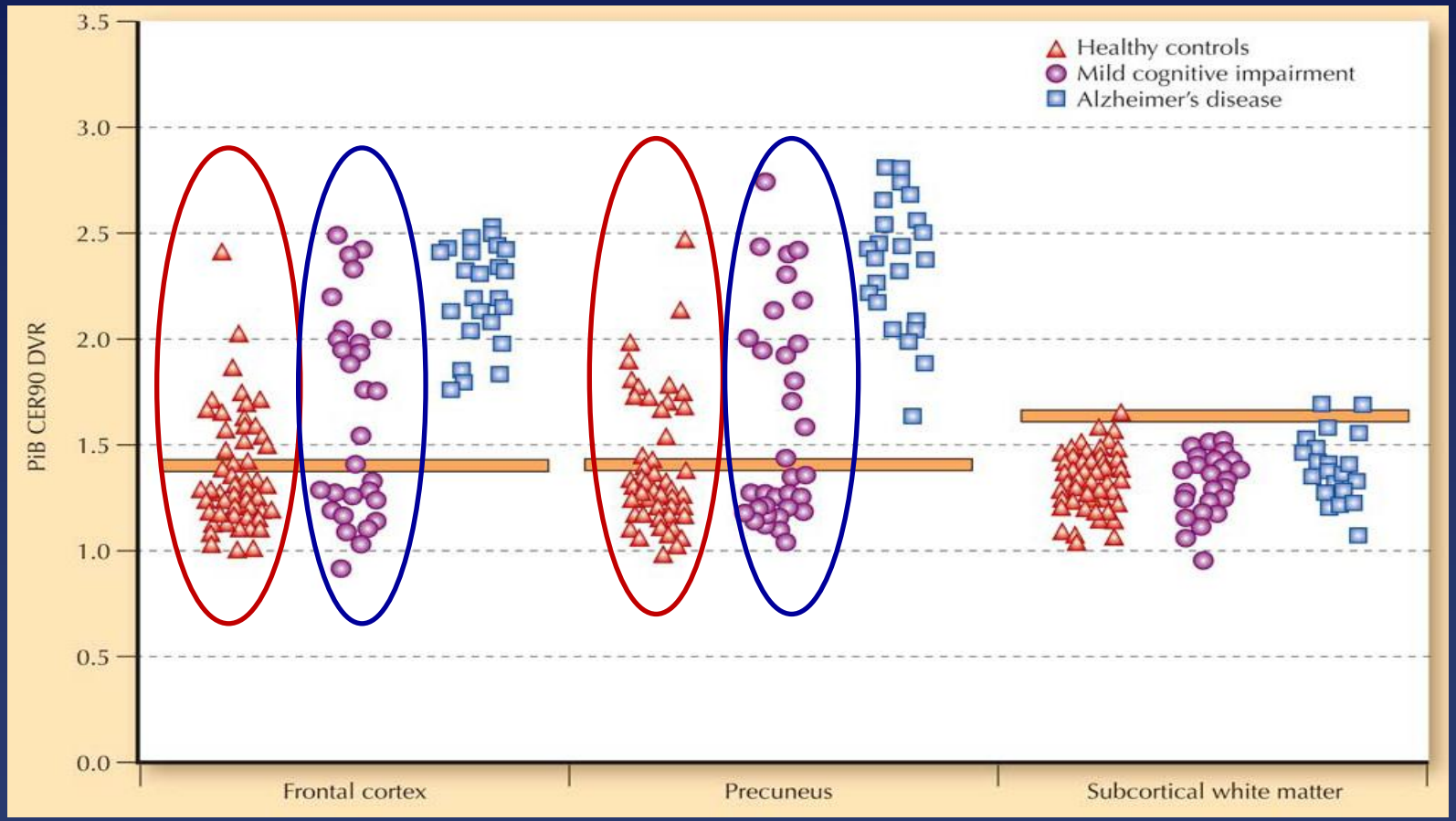
NIA Alzheimer's Disease: Unraveling the Mystery

And now we can image Amyloid Burden!



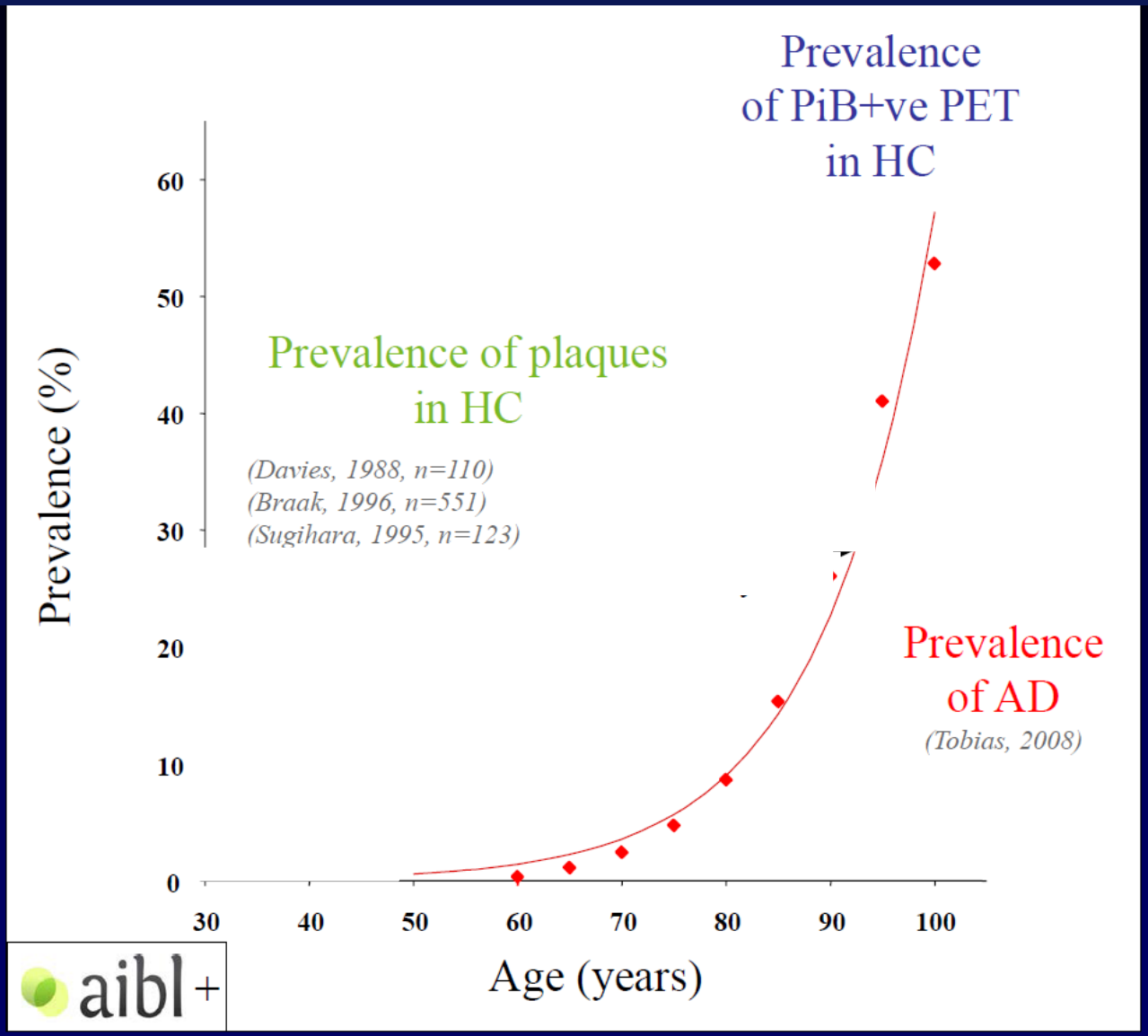
In the beginning there was PIB

(now there are several amyloid imaging agents available!)



Wolk and Klunk; Current Neurology and Neuroscience Reports 2009, 9:345–352

Amyloid Imaging Predicts Disease by 15 years!



Rowe C et al *Neurobiology of Aging* 2010

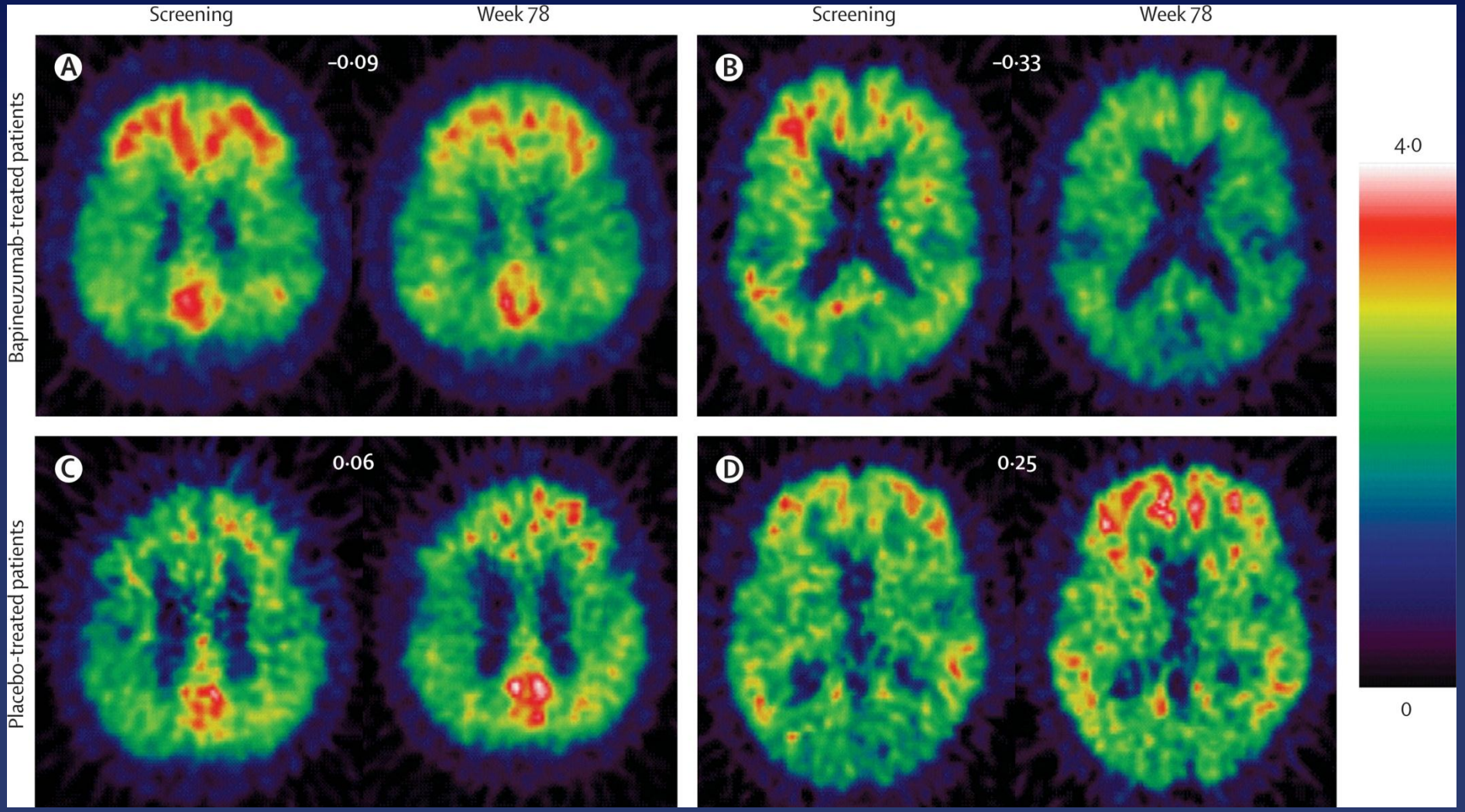
Can we fix it?
Does Anti Amyloid Therapy Work?

No . . .

And

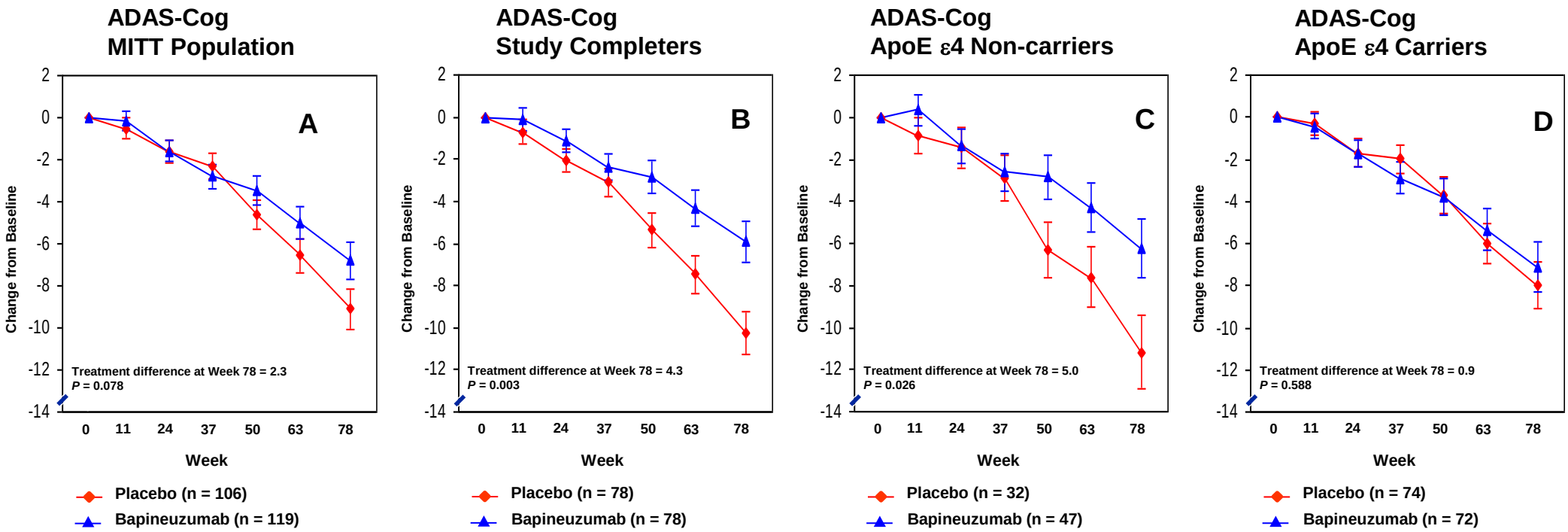
. . . Yes

Monoclonal Antibody Reduction of Fibrillar Amyloid Burden



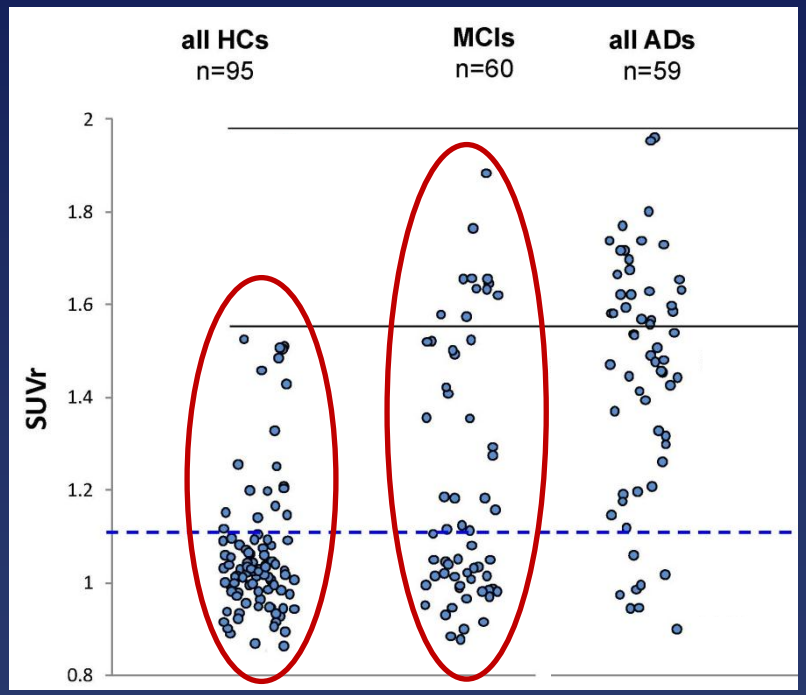
Rinne O *Lancet Neurology* 2010

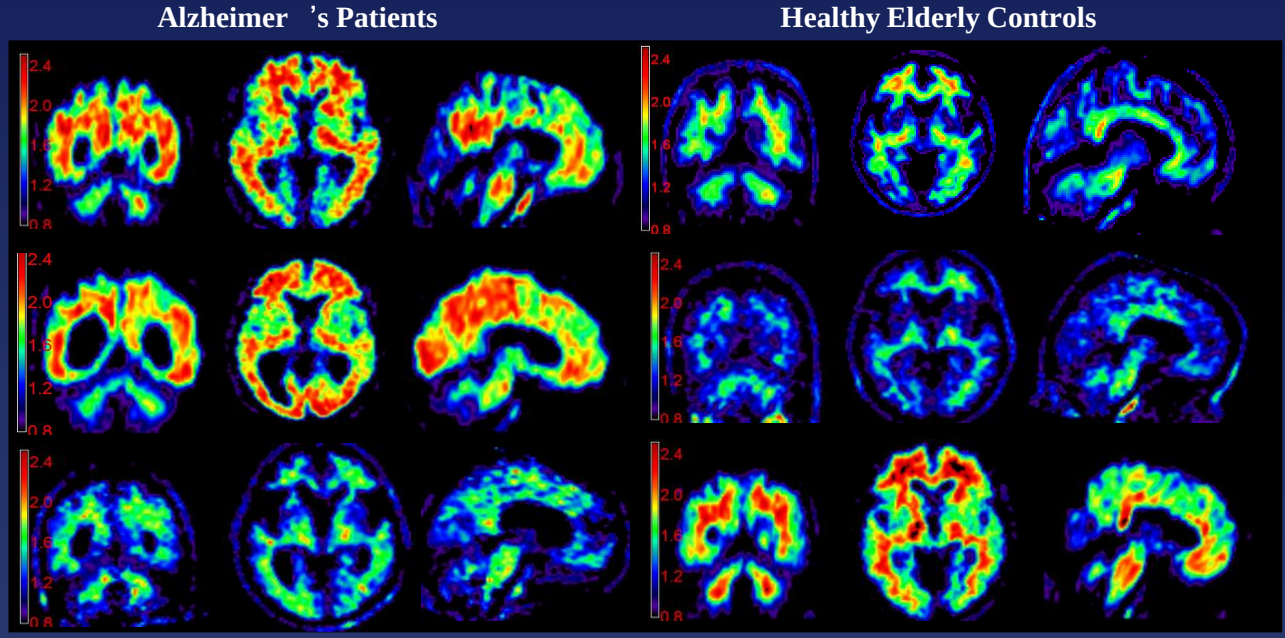
Bapineuzumab Phase 2 Trial: Results



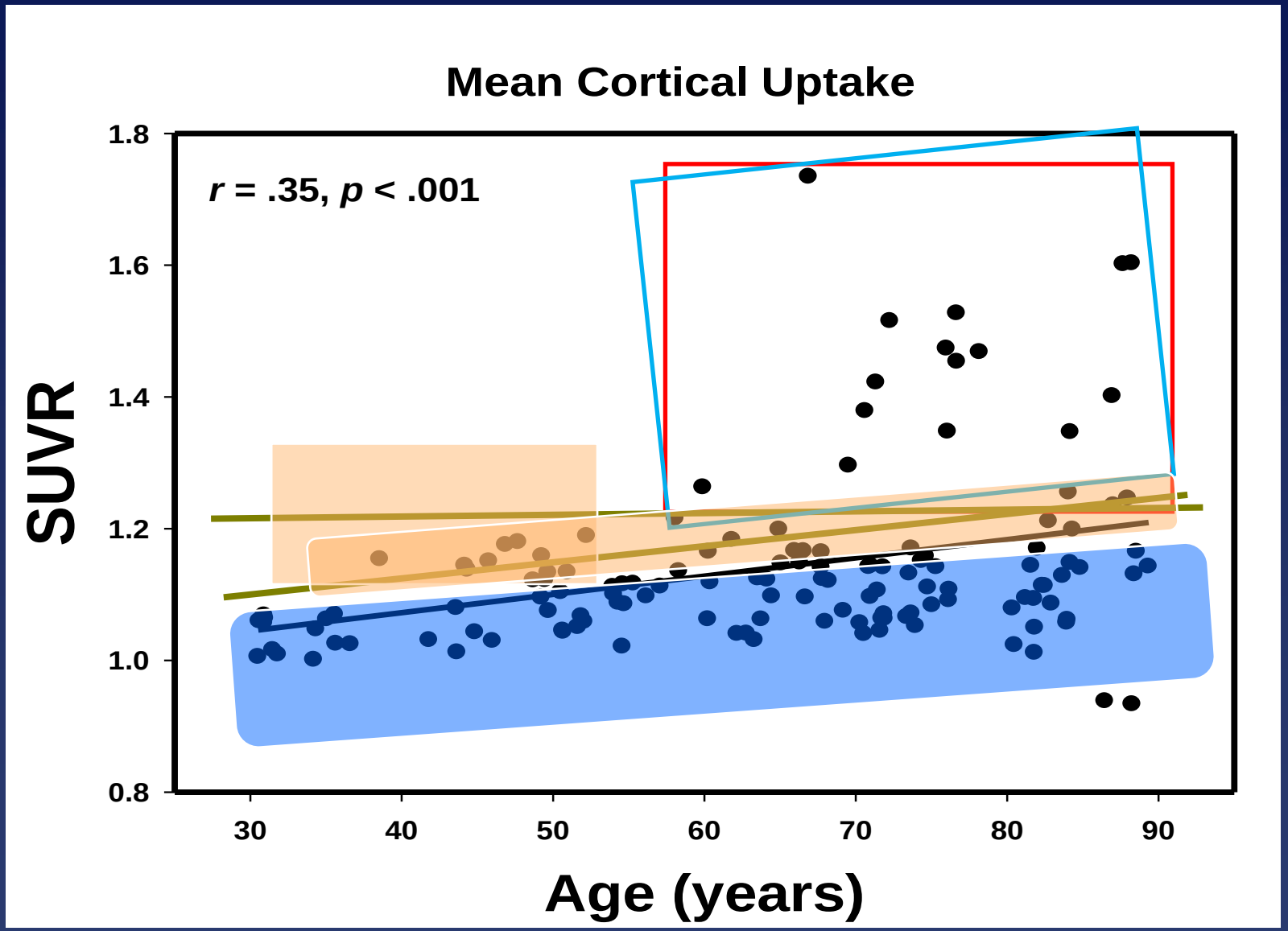
Salloway, Sperling et al. *Neurology* 2009

OK, so . . .
what does uptake in normals mean?





Amyloid in Healthy Aging Across the Lifespan



Rodrigue et al. Neurology 78:387-95, 2012

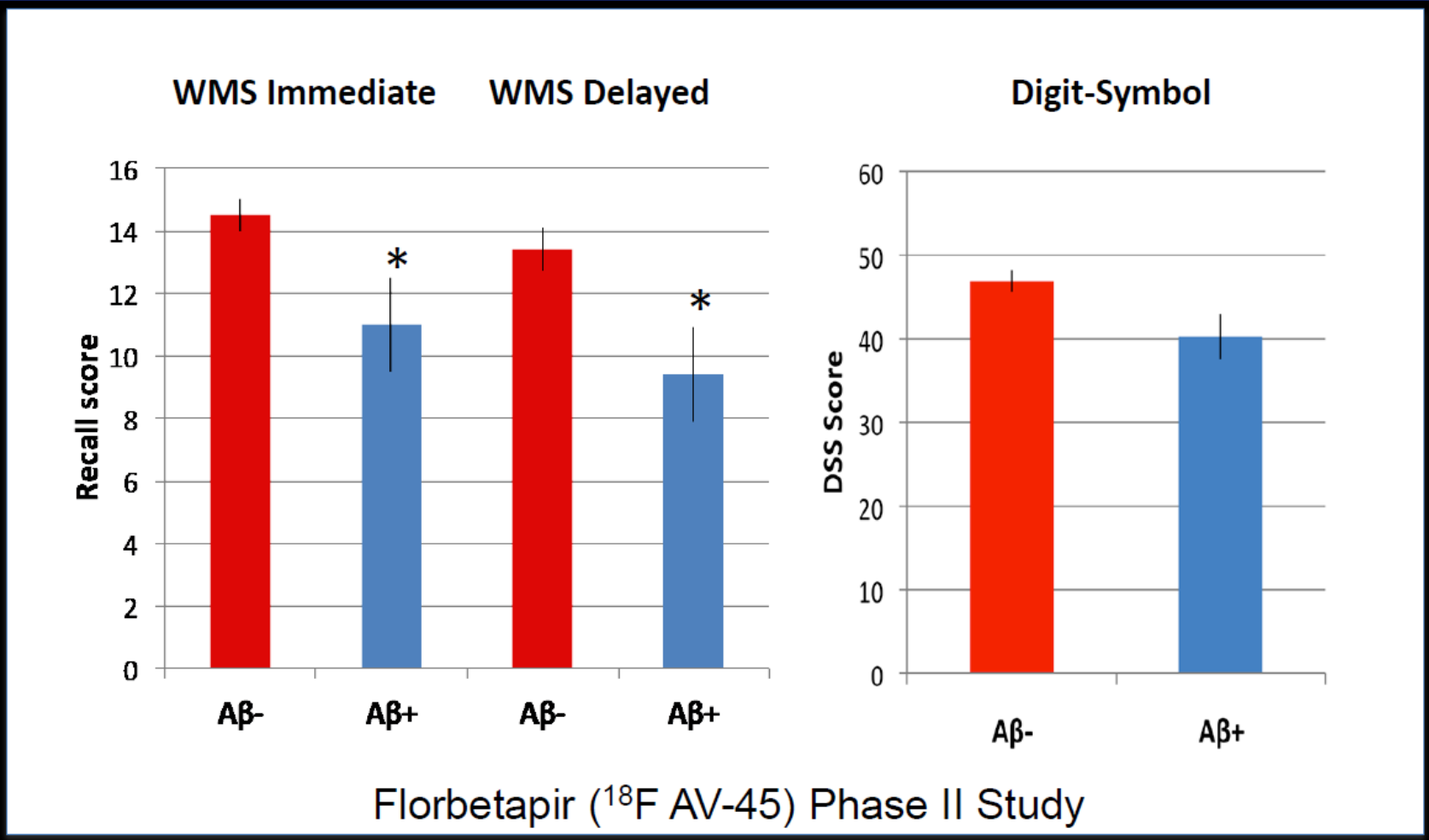
Does increased amyloid burden in healthy adults impact brain function?

Thinking Ability

Turning On Neurons

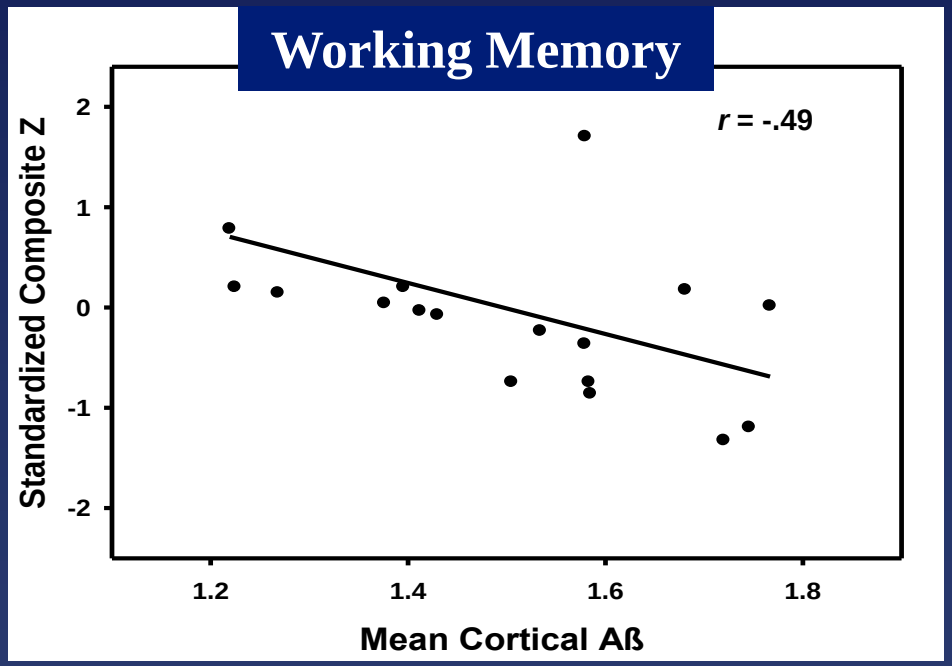
Connecting Neurons in a Network

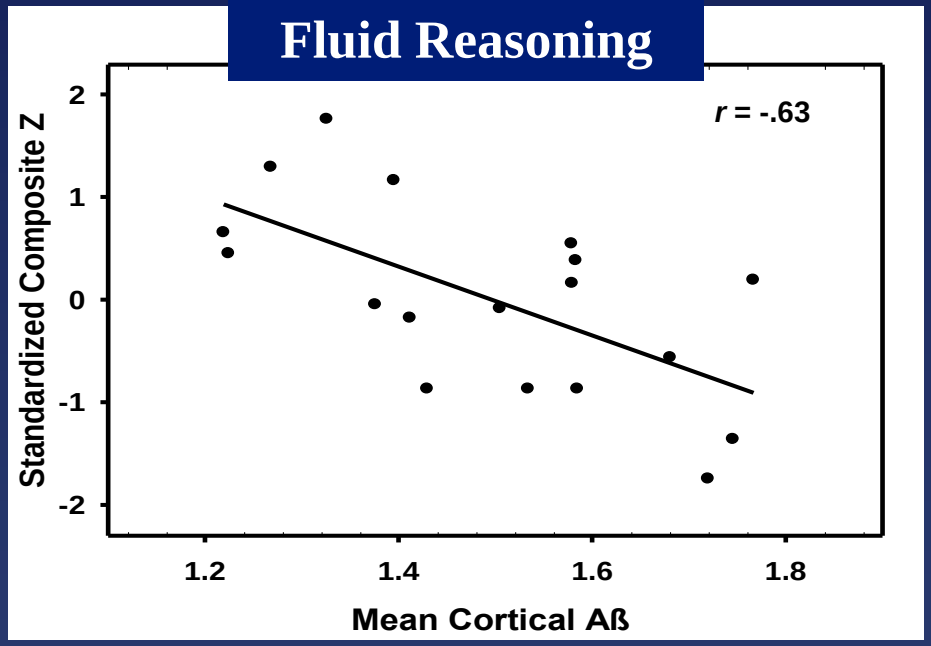
Cognition in normal subjects >age 70 is linked to amyloid



Sperling R et al *Neurobiology of Aging* 2012

Elevated Aβ and Cognition – Poorer Thinking



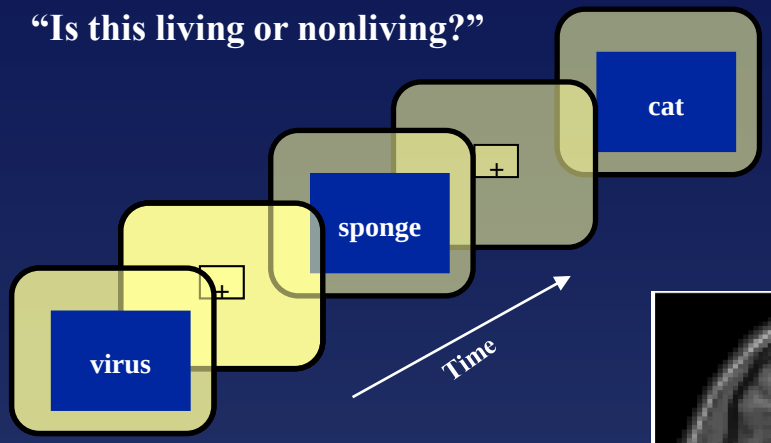


Rodrigue et al. Neurology 78:387-95, 2012

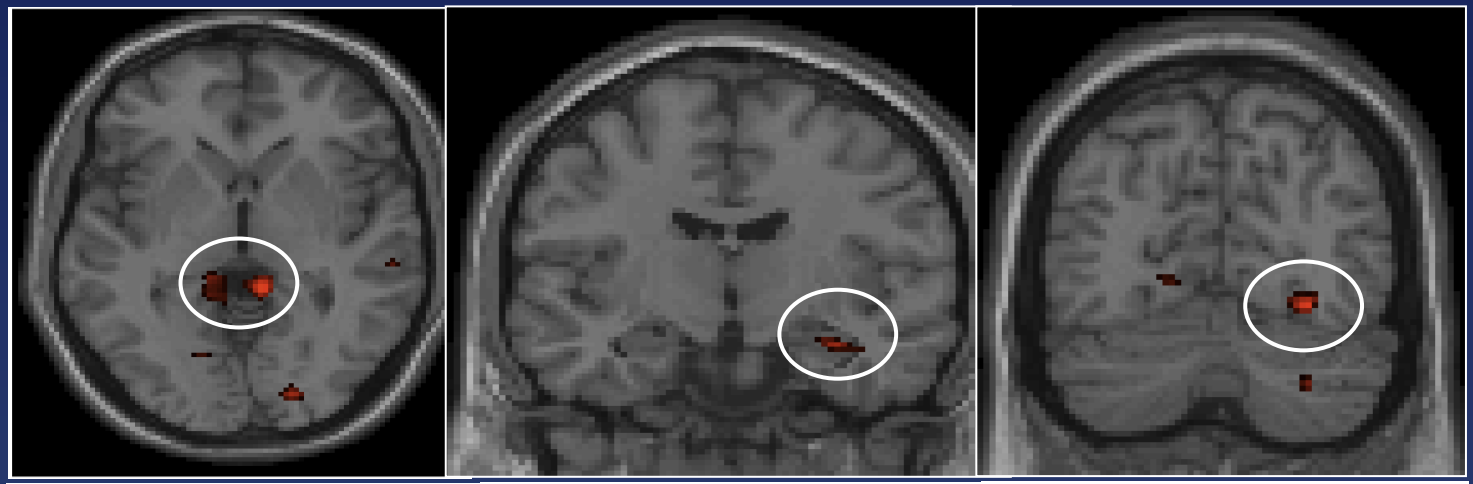
More Amyloid – Worse Brain Activation

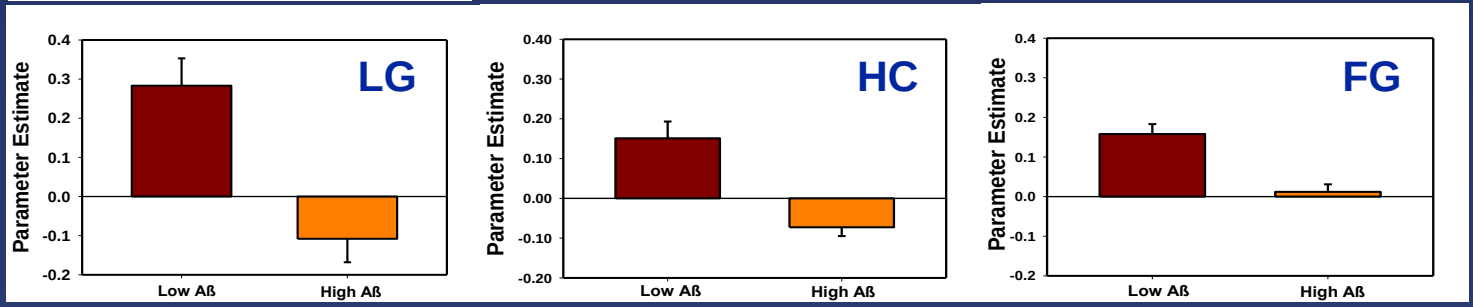
Functional Task: Semantic judgment

"Is this living or nonliving?"



High amyloid group shows decreased modulation to task difficulty (hard - easy)



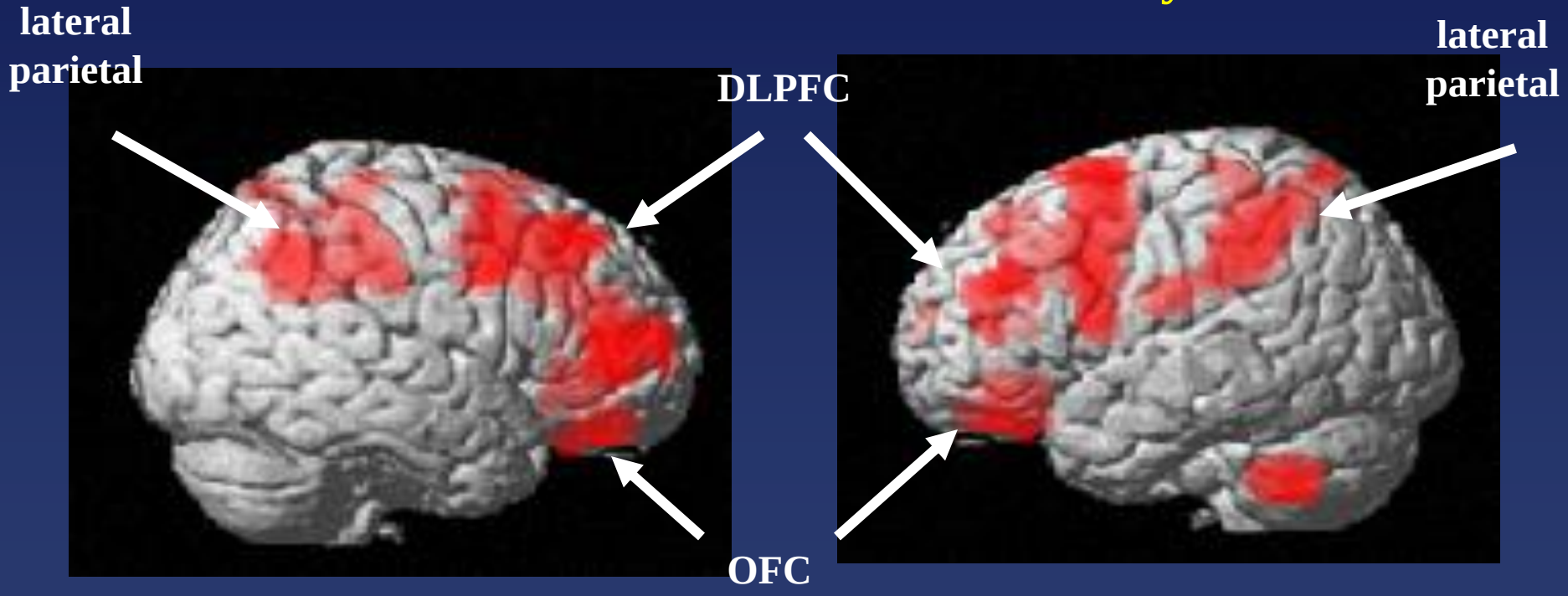


Rodrigue et al., ICAD (July 2010); SfN (Nov 2010)

More Amyloid – worse connectivity

Regions where increasing amyloid decreases

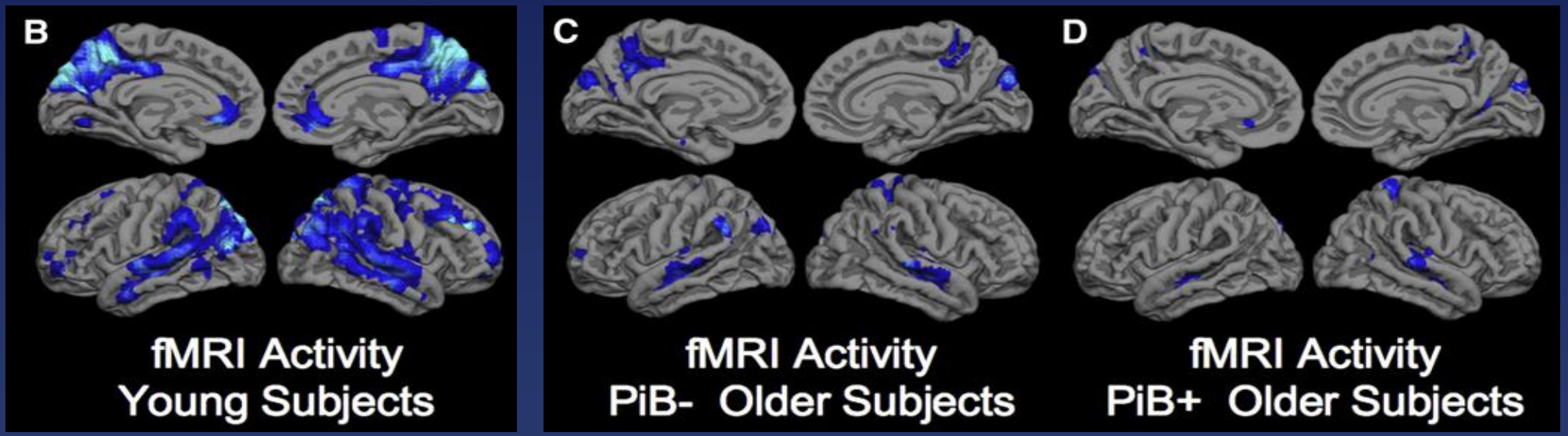
Default Mode Network connectivity



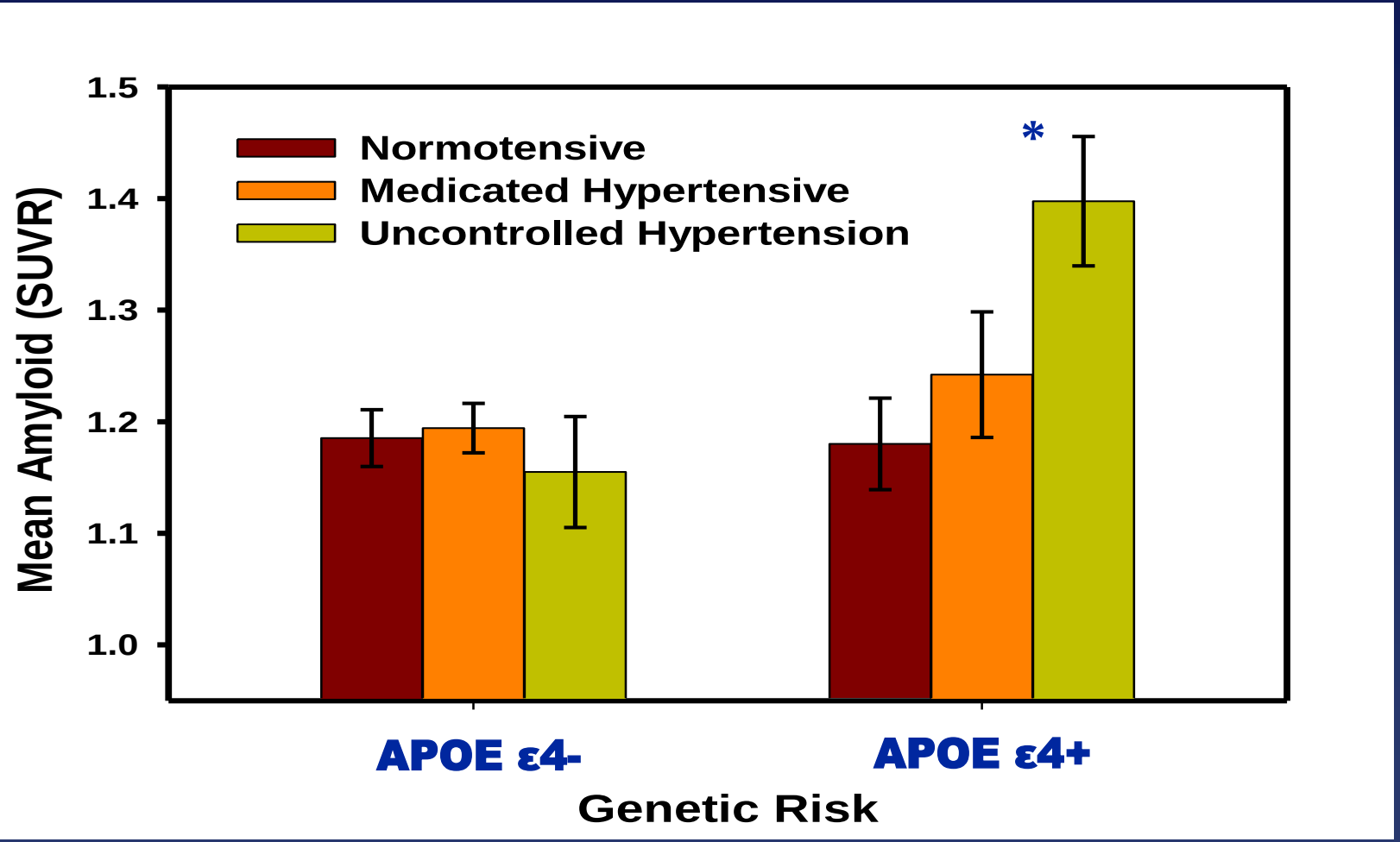
Devous et al., AAIC (July 2012)

Amyloid Impairs Default Mode Network Function in Older Persons without Dementia

Sperling et al; Neuron 63, 178–188, 2009



Other risk factors are associated with more amyloid



Age-adjusted means plotted

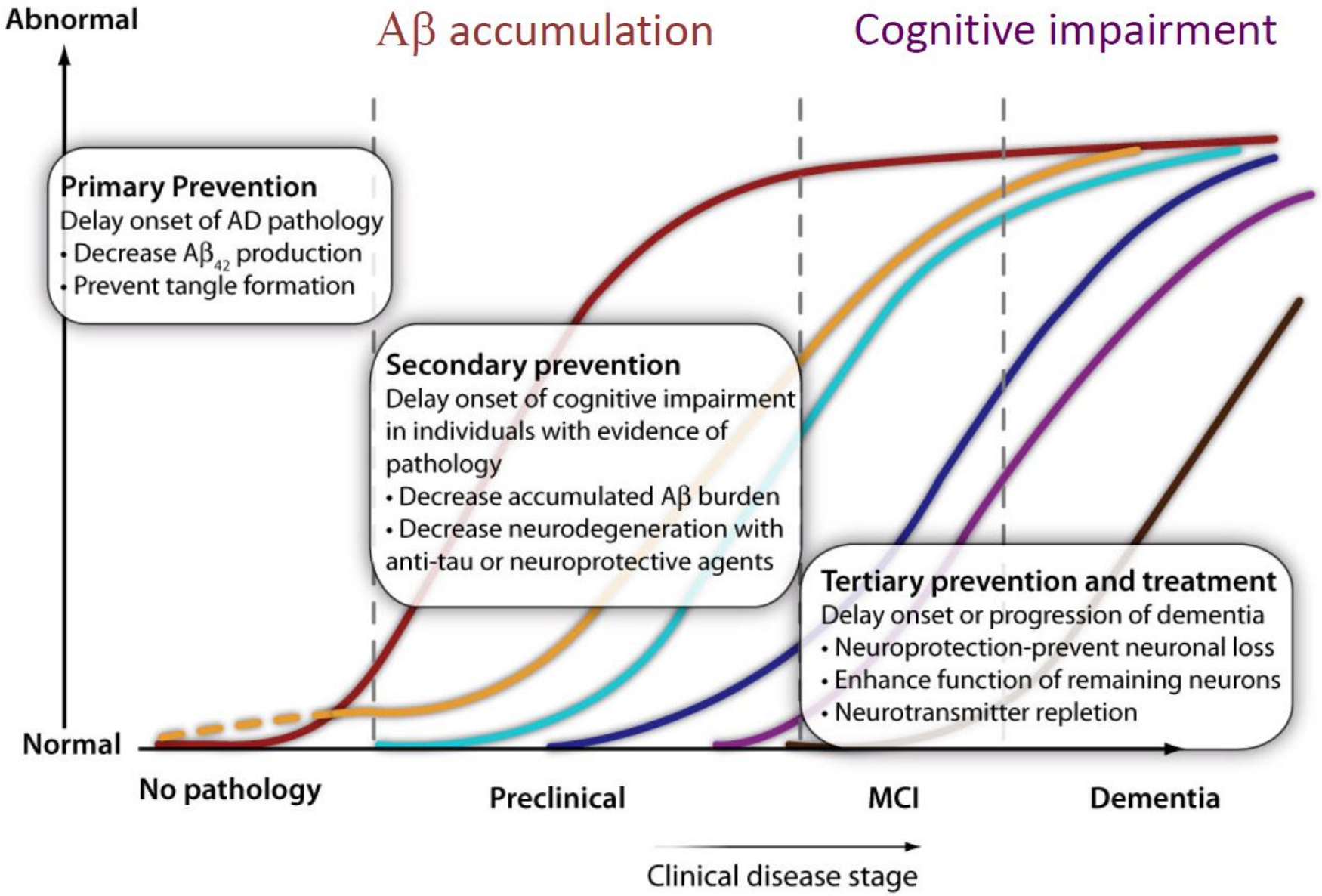
*Hypertension Group × APOE: $F(1, 113) = 9.52$, $p = .003$

Rodrigue et al., in prep.

Conclusions

- Amyloid increases with age even in healthy adults
- High amyloid is associated with faster progression
- Increased amyloid with age:
  - Impairs key types of thinking
  - Reduces the ability to activate neurons
  - Decreased brain network connectivity
- Aβ burden is associated with a range of neuronal abnormalities, and thus may offer the opportunity to identify at risk individuals for early intervention

Testing the Right Target and Right Drug at the Right Stage of AD



Sperling, Jack, Aisen *Science Trans Med* 2011

And, in fact, that is where clinical trials are going . . .

Anti-amyloid treatment in Asymptomatic* AD
A4 Trial

Reisa Sperling, M.D.

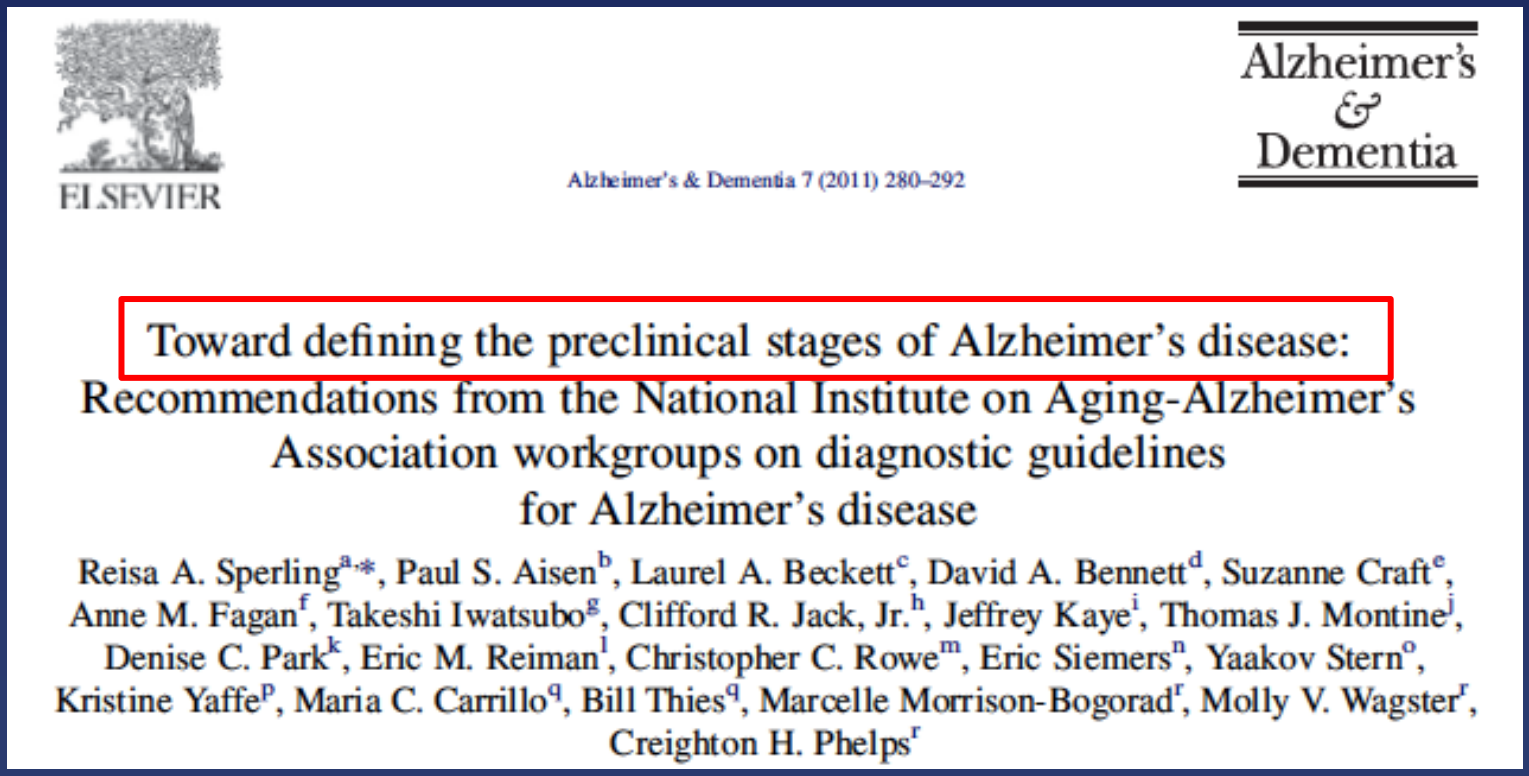
Paul Aisen, M.D.

A4 Specific Aims

- **To determine if treatment with an anti-amyloid drug will slow the rate of cognitive decline in normal elderly *who are at risk for decline to MCI or AD because of their amyloid.***
- **To see if removing amyloid will also improve other biomarkers of degeneration – is there a "critical window" for treatment?**

The future of clinical trials, and in the end, the treatment of Alzheimer's Disease, is in asymptomatic at risk individuals

where risk assessment is based on biomarkers!!



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Alzheimer's & Dementia 7 (2011) 280–292

Alzheimer's & Dementia

Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

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- UT Sou[illegible]ester[illegible]Nuclear Medicine Center: C[illegible]rise Chin Fatt, Thomas[illegible]arris
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Thanks!