

Implications of a Biologically Based Definition of Alzheimer's Disease NAPA 7-25-17

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What is Alzheimers disease (AD)?

- Symptoms (syndrome) vs disease
 - Shortness of breath vs heart, lung disease
 - Effect vs cause
- Dementia vs Alzheimer's disease
 - Dementia – progressive loss of cognitive ability leading to significant functional impairment (loss of independence)
 - Alzheimers disease
 - Plaques
 - Tangles
 - Inflammation
 - Loss of neurons

Diagnosis of Alzheimer's disease

- Historic diagnosis (McKhann et al 1984): clinico-pathologic
 - Definite at autopsy
 - Probable or possible in life – syndromal definition
 - Definition “creep”
- Problems
 - Not all “AD” syndrome is AD (20%)
 - Some non AD syndromes are AD
 - Many AD are asymptomatic (up to 40%, depends on age)
- Solution - biomarkers

What is a biomarker?

- A measure of pathologic change that can be obtained in the living subject – biomarkers are proxies for specific pathologic changes in the brain
- Accepted Alzheimer's biomarkers are imaging or biofluid (CSF)*

Biomarkers are proxies for AD pathologic changes

Measures of brain $A\beta$ deposition – amyloid plaques

- Amyloid PET
- CSF AB 42

Measures of neurofibrillary tangles - pathologic tau

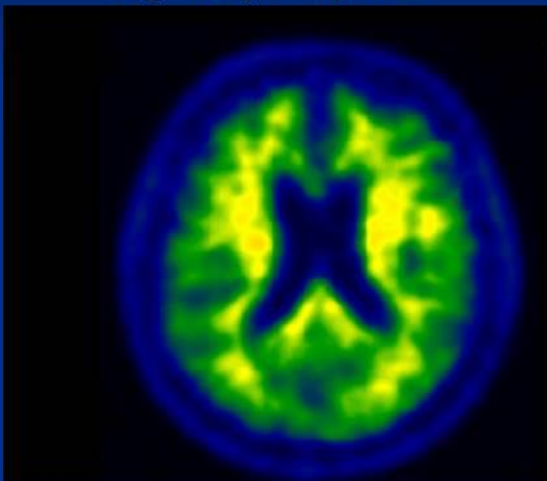
- CSF phospho tau
- Tau PET

Measures of neurodegeneration

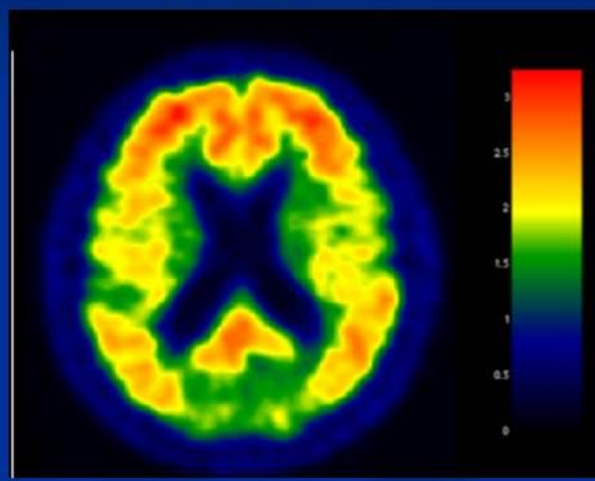
- FDG PET
- CSF total tau
- Structural MRI

Amyloid PET - plaques

Cognitively unimpaired

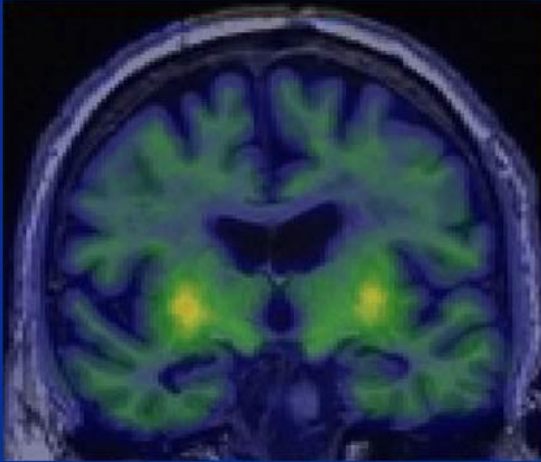


demented

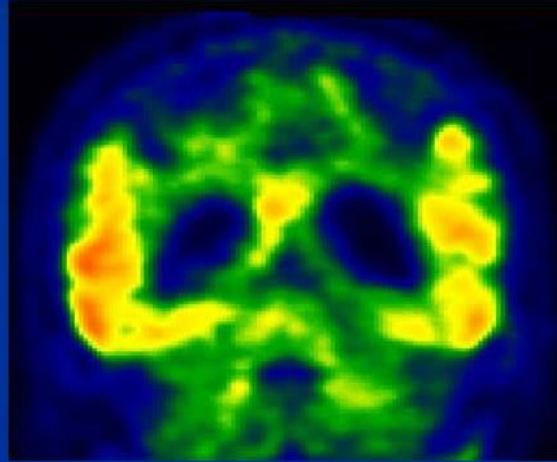


Tau PET - tangles

Cognitively unimpaired

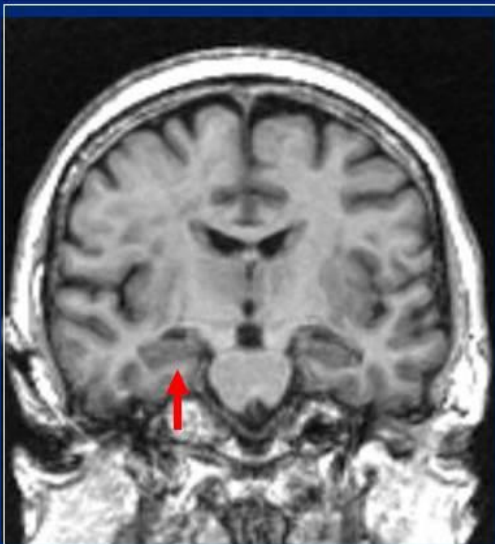


demented

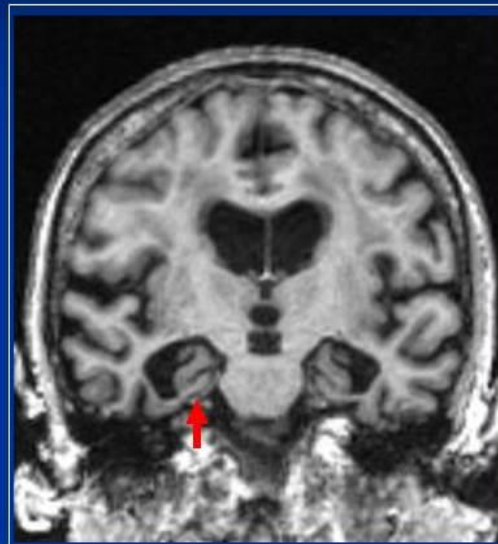


MRI – neurodegenerative brain atrophy

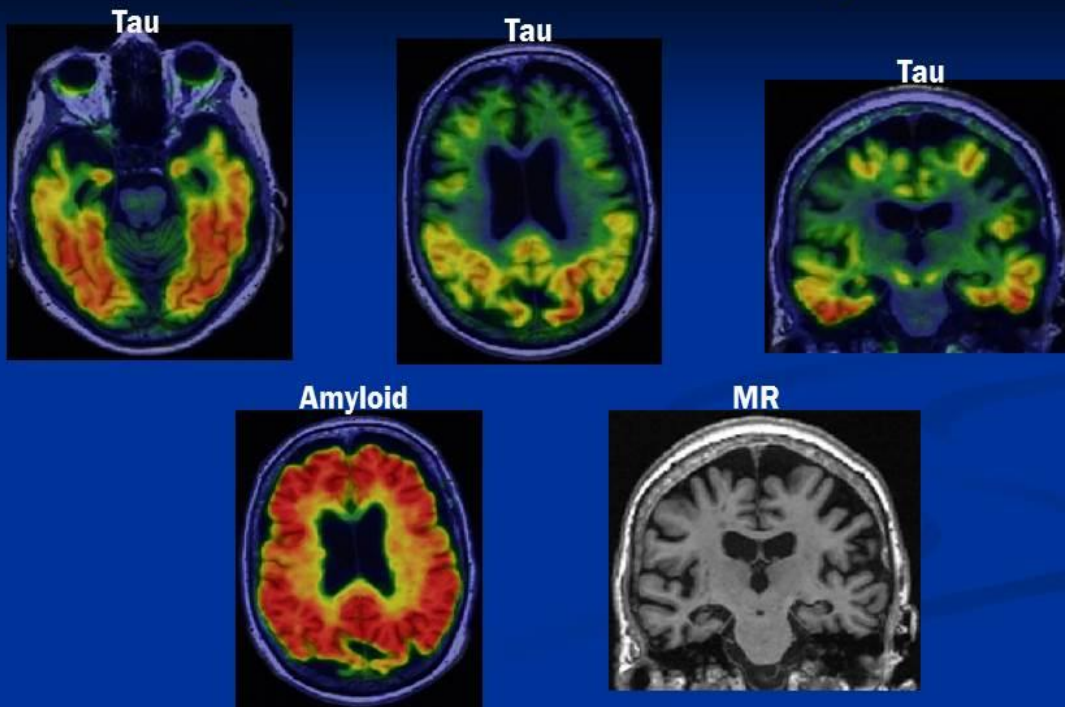
Cognitively unimpaired



demented



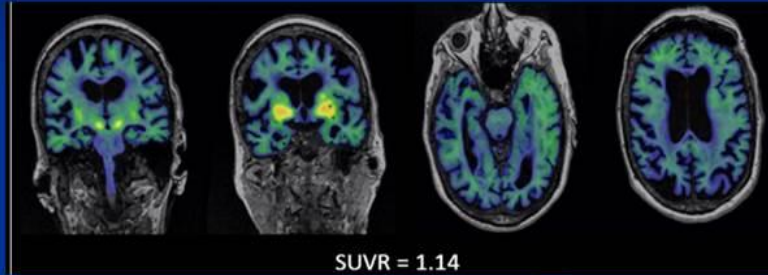
75 yo F, amnesic multi domain dementia: A+T+N+ profile



Diagnosis of Alzheimer's disease

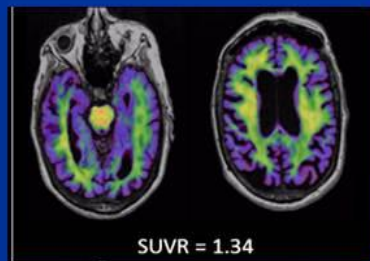
- Historic diagnosis (1984)
 - Definite at autopsy
 - Probable or possible in life – syndromal definition
- Problems – treatment discovery and application
 - Not all “AD” syndrome is AD (20%)
 - Some non AD syndromes are AD
 - Many AD are clinically asymptomatic (up to 40%, depends on age)

85 yo F, progressive memory problem, demented, clinical diagnosis "Alzheimer's disease"

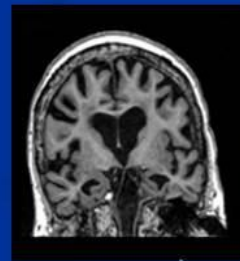


Tau PET

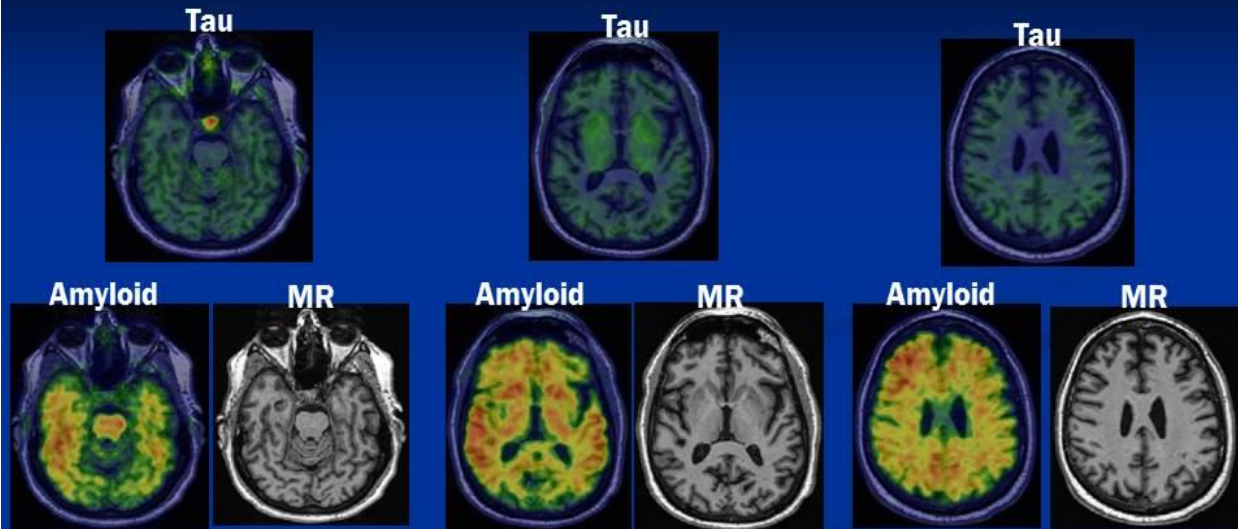
Amyloid PET



MRI



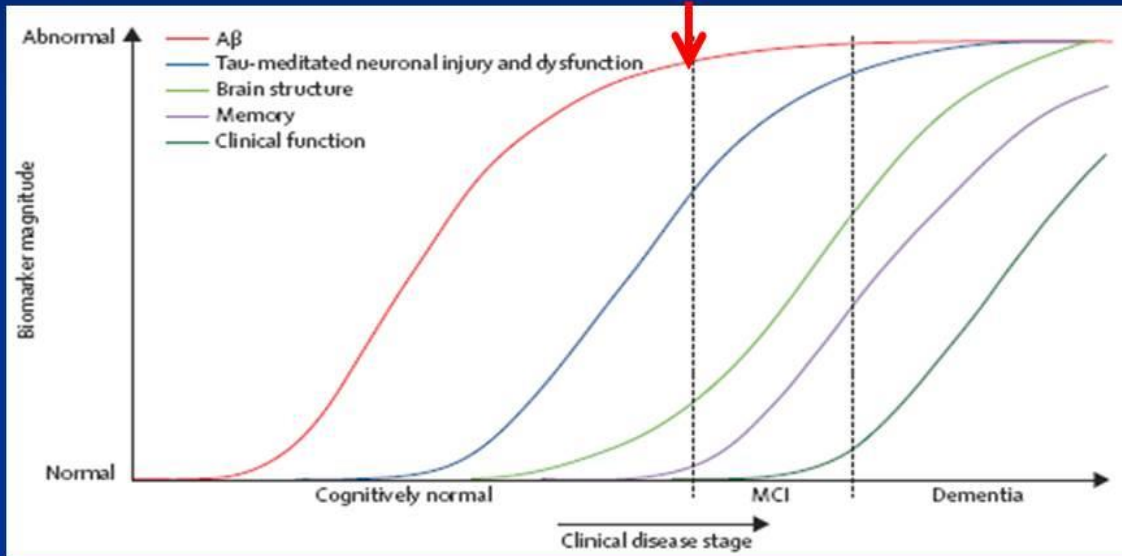
Cognitively unimpaired, 67 yo, M



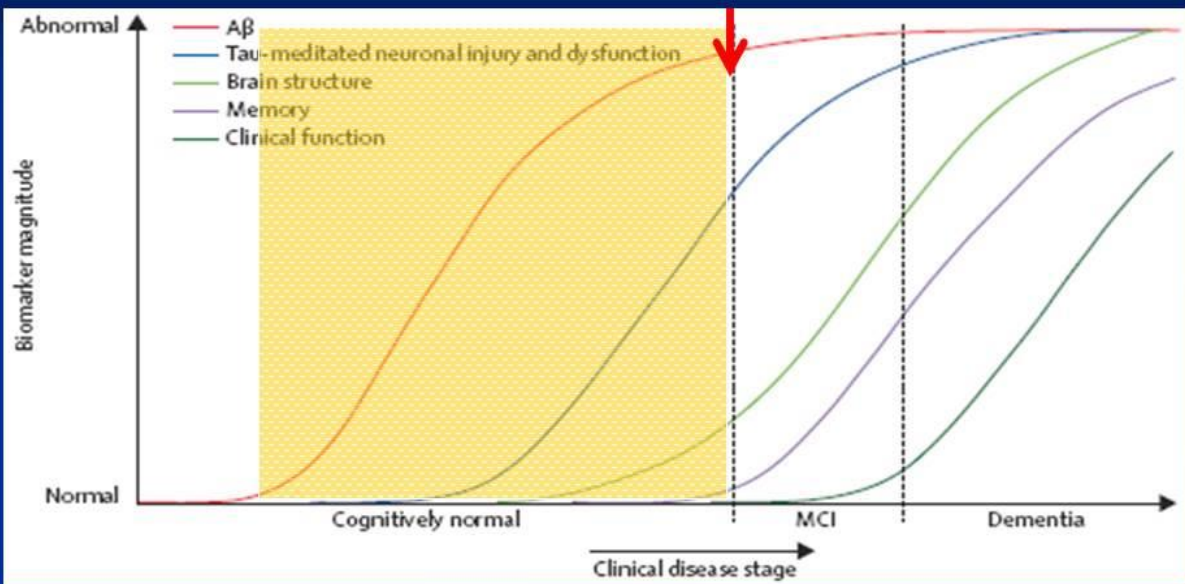
Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade

Lancet Neurol 2010

Clifford R Jack Jr, David S Knopman, William J Jagust, Leslie M Shaw, Paul S Aisen, Michael W Weiner, Ronald C Petersen, John Q Trojanowski



Prevention - biomarkers



Implications of biologically based (biomarker based) definition of Alzheimer's disease

- Specificity of biomarkers – AD treatment for those with AD
 - Clinical trials
 - Clinical practice
- Sensitivity of biomarkers – Prevention -- can not “treat” something that does “not exist”
 - Clinical trials
 - Clinical practice
- Prevalence - higher

NIA-AA Research Framework: Towards a Biological Definition of Alzheimer's Disease

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July 28, 2017 -- Advisory Council Meeting #25

The meeting was held on Friday, July 28, 2017, in Washington, DC. The Advisory Council spent the morning discussing information gaps across the three areas of research, clinical care, and long-term services and supports. There was also a presentation on the recently released National Academy of Sciences, Engineering, and Medicine (NASEM) report on preventing cognitive decline. Additional presentations included a presentation on planning and progress towards the October Care and Services Summit and federal workgroup updates. Material available from this meeting is listed below and is also available at <https://aspe.hhs.gov/advisory-council-alzheimers-research-care-and-services-meetings#Jul2017>.

Comments and questions, or alerts to broken links, should be sent to napa@hhs.gov.

General Information

Agenda	[HTML Version] [PDF Version]
Meeting Announcement	[HTML Version] [PDF Version]
Meeting Summary	[HTML Version] [PDF Version]
Public Comments	[HTML Version]

Presentation Slides

2017 National Plan Update and Non-Federal Recommendations	[HTML Version] [PDF Version]
Clinical Services Subcommittee Federal Update	[HTML Version] [PDF Version]
CommunityRx for Community-Residing People with Dementia and Their Caregivers	[HTML Version] [PDF Version]
Dementia Caregiving in the U.S.	[HTML Version] [PDF Version]
Development of the FY 19 NIH Bypass Budget for Alzheimer's Disease and Related Dementias	[HTML Version] [PDF Version]
Implications of a Biologically Based Definition of Alzheimer's Disease	[HTML Version] [PDF Version]
Increasing Opportunities for Choice and Control for Persons with Dementia	[HTML Version] [PDF Version]
Interventions to Prevent or Slow Cognitive Decline, MCI and Dementia in Individuals without Dementia	[HTML Version] [PDF Version]
Living Alone With Dementia	[HTML Version] [PDF Version]

Long-Term Services and Supports Committee Update	[HTML Version] [PDF Version]
Managing Chronic Conditions in People Living with Dementia	[HTML Version] [PDF Version]
Preventing Cognitive Decline and Dementia	[HTML Version] [PDF Version]
Research Summit on Dementia Care	[HTML Version] [PDF Version]
The Many Challenges of Alzheimer's Disease	[HTML Version] [PDF Version]

Videos

Welcome thru Clinical Care	[Video]
LTSS Research	[Video]
Public Comments thru Federal Workgroup Updates	[Video]
Recommendations thru Adjourn	[Video]

Last Updated: 06/27/2018