Mild Cognitive Impairment

And Its Progression to Dementia

Irina Anna Skylar-Scott, MD
Alzheimer's Disease Research Center
Participant Appreciation Day
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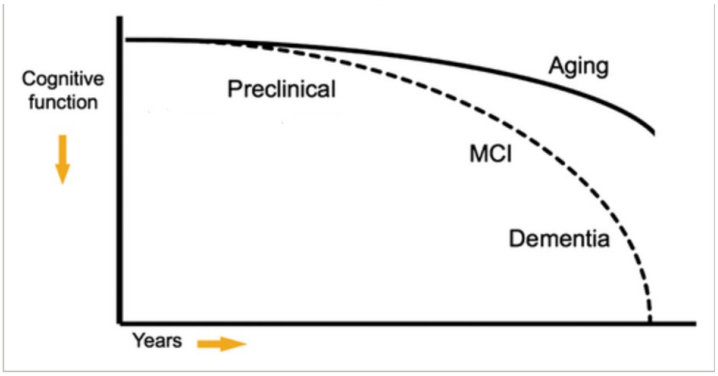
The Clinical Continuum



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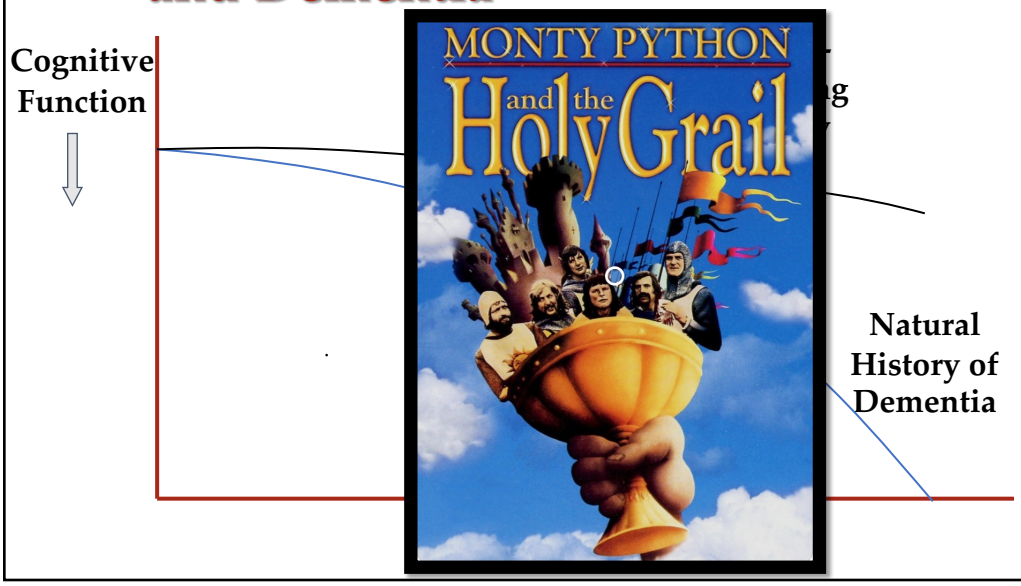
The Holy Grail: Treatment of MCI and Dementia



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Two take-home ideas:

- Mild cognitive impairment (MCI) and dementia are not normal aging
- MCI and dementia are not always synonymous with Alzheimer's disease, but they can be!
  - Severity
  - Syndrome
  - Pathological diagnosis

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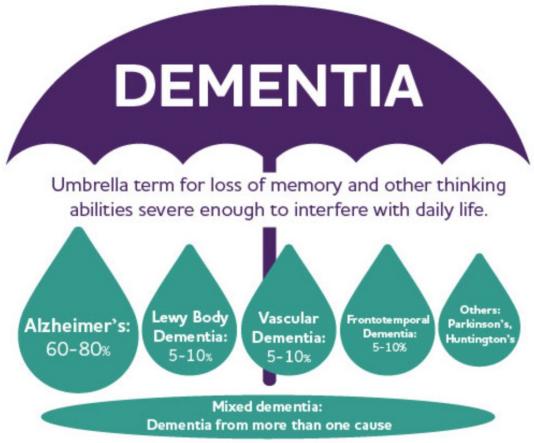
If I have MCI, will I progress to dementia?

- **MCI does not always lead to dementia**
  - MCI progression to dementia: 12% per year
  - MCI due to AD progression to dementia: 17-20% per year
- **MCI and dementia are umbrella terms**



Source: Alzheimer's Association

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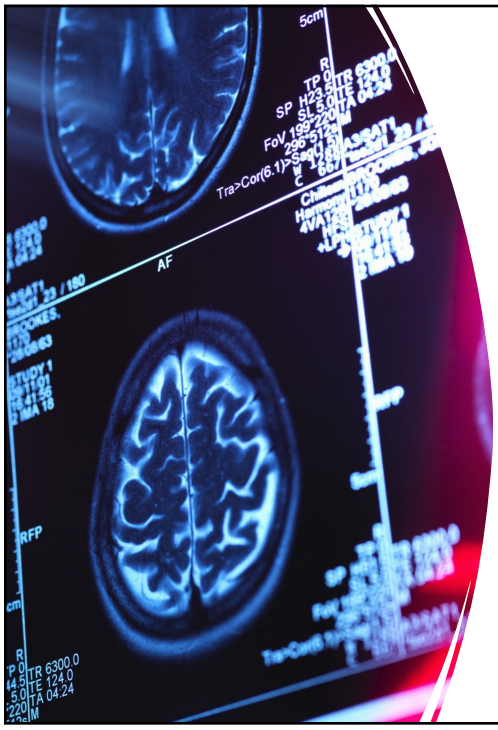

Mild Cognitive Impairment Criteria

- **Step 1: Establish clinical and cognitive criteria**
  - Cognitive concern reflecting a change in cognition reported by a patient, informant, or clinician (historical or observed evidence of decline over time)
  - Objective evidence of impairment in one more cognitive domains
    - Formal or bedside testing
  - Preservation of independence in functional abilities

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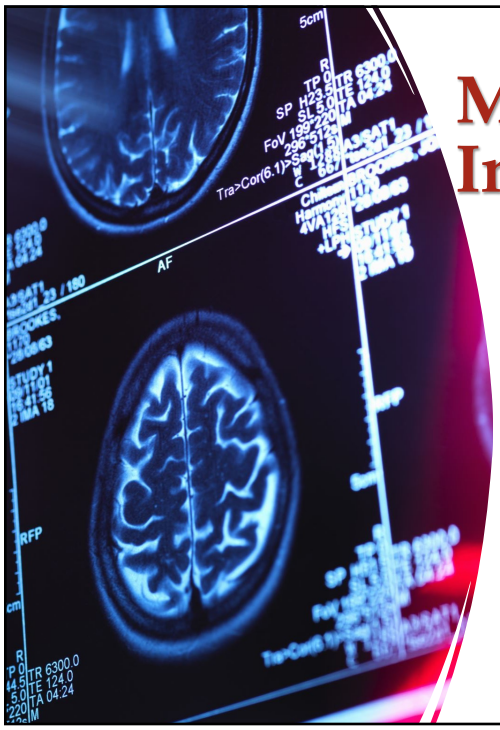

Mild Cognitive Impairment Criteria Part II

- **Step 2: Examine "pathophysiological" cause of MCI**
  - Look for vascular, traumatic, and medical causes of cognitive decline
  - Provide evidence of longitudinal decline (meaning decline over time), when feasible
  - Look for genetic factors, where relevant
  - Biomarkers (objective indicators of a medical state that are reproducible), where relevant
    - Examples of biomarkers: spinal fluid amyloid and tau, amyloid PET scan

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Dementia criteria part I

1. Interfere with the ability to function

2. Represent a decline from previous levels of functioning

3. Are not explained by delirium or major psychiatric disorder

4. Cognitive impairment is detected and diagnosed through a combination of (1) history-taking and (2) an objective cognitive assessment

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Dementia criteria part II

5. The cognitive or behavioral impairment involves a minimum of two of the following domains:

1. **Impaired ability to acquire and remember new information**
2. **Impaired reasoning and handling of complex tasks, poor judgment**
3. **Impaired visuospatial abilities**
4. **Impaired language functions (speaking, reading, writing)**
5. **Changes in personality, behavior, or comportment**

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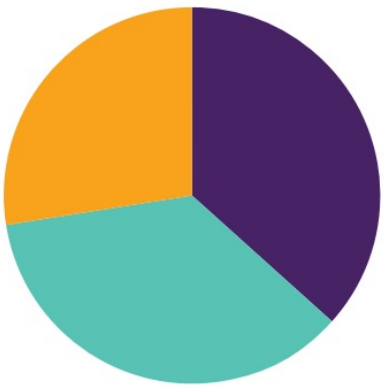
MCI and dementia by the numbers

- Number of people over age 65 in the US with MCI: 10-12 M
  - Number due to Alzheimer's disease: roughly 5 M
- Number of people over age 65 in the US with dementia: at least 6 M
  - Number due to Alzheimer's disease: 3.5-6 M

Number and Ages of People 65 or Older with Alzheimer's Dementia, 2021*



Total:
6.2 Million

- 65-74 years: 1.72 million (27.6%)
- 75-84 years: 2.25 million (36.1%)
- 85+ years: 2.27 million (36.4%)

Created from data from Rajan et al.[A1,216]

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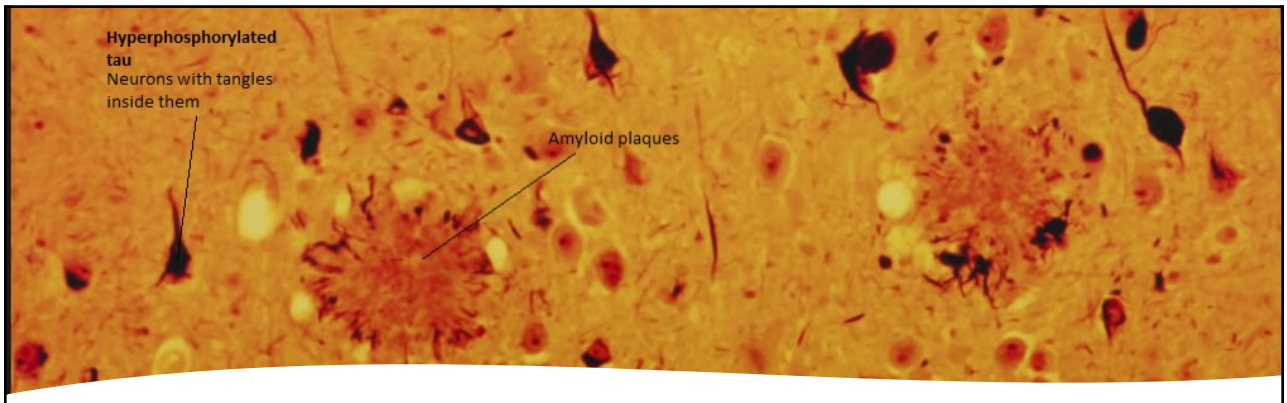

Alzheimer's disease: What's going on in our brains?

- β-amyloid plaques and neurofibrillary tangles (NFTs)
  - NFTs numerous within structures critical memory such as the hippocampus
  - By the time of MCI, 50-70% of memory network neurons are lost

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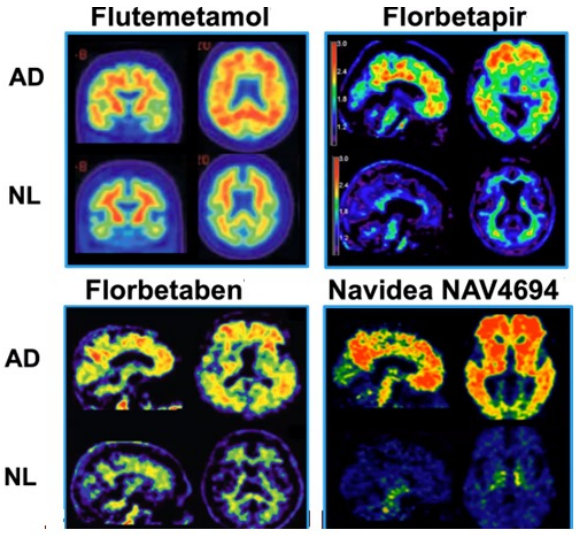
Amyloid PET



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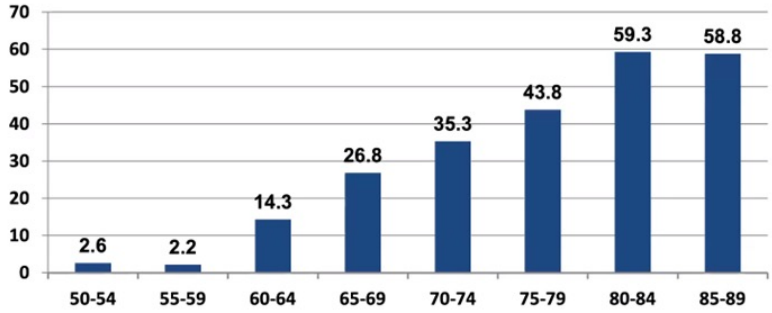
Amyloid Positivity in the US Population

- N= 1,646 without dementia, mean age: 70.8
- **21.1% prevalence for amyloidosis**

Roberts RO et. al. Neurology 2018



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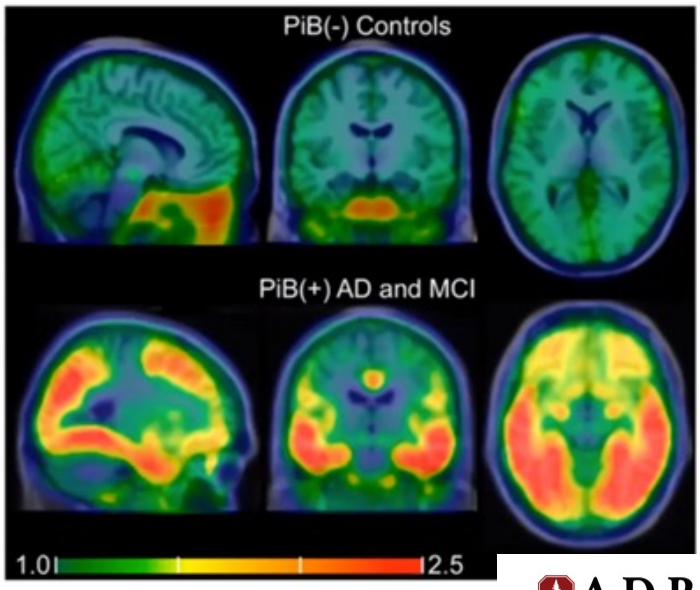
Tau PET



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FDA Approved Medications for AD dementia

1993	1997	2000	2001	2003	2021
tacrine (Cognex®)	donepezil (Aricept®)	rivastigmine (Exelon®)	galantamine (Razadyne®)	memantine (Namenda®)	Aducanumab (Aduhelm®)

- Cholinesterase-inhibitors (ChE-I): donepezil, rivastigmine, galantamine, tacrine* (*no longer clinically used)
  - All FDA approved for treatment of mild to moderate AD dementia
  - Donepezil also FDA approved for treatment of severe AD dementia (2006)
  - Galantamine available as a generic since 2/2009; donepezil since 12/2010
- NMDA (glutamate) receptor antagonist: memantine
  - FDA approved for treatment of moderate to severe AD dementia (generic 2015)

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Ladies and gentlemen, my mother thanks you, my father thanks you, my sister thanks you, and I thank you!

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