Mild Cognitive Impairment

And Its Progression to Dementia

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The Clinical Continuum
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
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

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
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

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
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

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.41,216
Alzheimer’s disease: What’s going on in our brains?

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

Amyloid PET
**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 2016

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**Tau PET**
FDA Approved Medications for AD dementia

<table>
<thead>
<tr>
<th>Year</th>
<th>Medication</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>1993</td>
<td>tacrine</td>
<td>(Cognex®)</td>
</tr>
<tr>
<td>1997</td>
<td>donepezil</td>
<td>(Aricept®)</td>
</tr>
<tr>
<td>2000</td>
<td>rivastigmine</td>
<td>(Exelon®)</td>
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<td>2001</td>
<td>galantamine</td>
<td>(Razadyne®)</td>
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<tr>
<td>2003</td>
<td>memantine</td>
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<tr>
<td>2021</td>
<td>Aducanumab</td>
<td>(Aduhelm®)</td>
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</tbody>
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- **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)

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