Moving Targets: An Update on Diagnosing Dementia in the Clinic

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Disclosures

- No relevant financial disclosures
Diagnosis
THE NEW CRITERIA FOR DIAGNOSING AD
Better understanding of the pathology of AD and subsequent clinical spectrum (including importance of age)

Better understanding of other common age-related neurodegenerative/non-neurodegenerative dementia syndromes (DLB/FTD/VaD/PPA)

Memory as the primary affected domain (PCA, logopenic aphasia)

Age cutoff

Discovery of mutations with deterministic implications (APP, PS1, PS2)

Heterogeneity of “Possible AD”
NIA-AD 2011

‘flexible enough to be used by both general healthcare providers... as well as specialized investigators involved in research or clinical trial studies’
<table>
<thead>
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<tbody>
<tr>
<td><strong>Probable (still probable)</strong></td>
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<tr>
<td>Progressive memory + 1 other domain</td>
<td>Amnestic vs Nonamnestic presentation + 1 other domain (Language/Visualspatial/Executive)</td>
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<td>Absence of systemic or neurological disorders that in and of themselves could account for the cognitive deficits</td>
<td>Absence of substantial concomitant CVD (includes isolated imaging findings), core symptoms of DLB, bvFTD, PPA (SD/ PNFA)</td>
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<td>Support by or Increased level of certainty</td>
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<td>Family history of similar disorder (especially with neuropathology)</td>
<td>Carrier of causative AD genetic mutation</td>
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<td><strong>Possible AD</strong></td>
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<td>presence of additional factor that can cause dementia but not considered the cause; ‘single, progressive, severe deficit identified in the absence of other identifiable causes’- Currently MCI</td>
<td>Etiologically mixed presentation (core symptoms +: stroke, features of DLB, evidence of another neurological disorder or medical comorbidity/medication possibly contributing)</td>
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<tr>
<td><strong>Laboratory Tests or Biomarkers (probable AD w evidence of AD pathophys)</strong>*</td>
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<tr>
<td>LP, EEG, CT brain</td>
<td>Amyloid markers (csf Aβ₄₂ , PET ligands); Downstream neuronal markers (CSF tau, FDG PET, MRI imaging)</td>
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<td>3 categories: clearly +, clearly -, indeterminate.</td>
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<td><strong>Possible AD w evidence of AD pathophys</strong></td>
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<tr>
<td>N.A.</td>
<td>Clinical criteria for non-AD + biomarker evidence or neuropathological criteria (requires + both AD biomarkers)‡</td>
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<td><strong>Unlikely AD</strong></td>
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<td>Sudden onset, focal symptoms, early seizures or gait disorders</td>
<td>Evidence of support for alternative diagnosis which rarely overlaps with AD (HD, HIV dementia); possible AD but both biomarkers negative</td>
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Summary

- Dementia diagnosis is better defined in new NIA-AA guideline (behavioral changes considered a domain)
- Specificity? (+/- biomarkers)
- Clinically updated to reflect a better sense of other dementia syndromes and crossover between
- Introduces biomarkers currently of greatest focus to large audience
MCI background

Memory complaint usually corroborated by an informant
Objective memory impairment for age
Essentially preserved general cognitive function
Largely intact functional activities
Not demented

Petersen 99
NIA-AA MCI

- More AD-centric (MCI due to AD)
- Specifies clinically oriented and research oriented
- Diverges slightly from recent recommendation of lexicon of International Working Group for New Research Criteria for the Diagnosis of AD (prodromal AD vs MCI)
NIA-AA MCI

Core Clinical Criteria

- Concern about change (could be identified by physician)
- Mild functional decline (not absence of)
- Episodic memory impairment emphasized
- Longitudinal decline
- Rule out possible non-AD causes
NIA-AA MCI

- **Clinical Research Criteria**
  - Centers on biomarkers
  - Recapitulates AD guidelines
    - Aβ deposition and tau
    - Downstream neuronal injury (also includes tau) - possibly more informative regarding stage or severity
  - Associated biochemical change
    - Oxidative stress, inflammation, synaptic damage
Clinical Core + Biomarkers

- Theoretically provides greater benefit than in the clinical AD stage- Holy Grail of MCI
  - Even more so in non-amnestic presentations
  - Probabilistic framework with varying levels of certainty
    - Highest - + Aβ and biomarker of neuronal injury
    - Intermediate- + Aβ or + neuronal injury marker in the absence (not tested or not available) of the other
    - Uninformative – ambiguous ranges or conflicting results
    - Unlikely to be MCI-AD- negative from both groups +/- presence of other biomarkers supporting alternative diagnosis
MCI due to AD

- MCI- Core clinical criteria
  - Included if clinical situation is appropriate but biomarkers are uninformative

- MCI due to AD- Intermediate likelihood
  - MCI Core Clinical Criteria and + biomarker from amyloid or neuronal injury (with other not available)

- MCI due to AD- High likelihood
  - MCI Core Clinical Criteria and both biomarker groups +

- MCI- Unlikely due to AD*
  - Both biomarker groups (-)
APOE 4?
IMAGING
MRI
Hippocampus

Scheltens, *JNNP 92*
VAD or AD?

PiB amyloid PET

Lee –Neurology- 2011
Susceptibility Weighted Imaging

Cerebral Amyloid Angiopathy

Hypertension

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Tau PET

Compliments of Dr. Julie Price- University of Pittsburgh
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