DSM-5 Renaming Dementia (?)

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Countdown to 2025
Progress on Ending Alzheimer’s Disease
UC Irvine
September 20, 2013
Disclosures

• Pfizer, Inc.: Chair DMC

• Janssen Alzheimer’s Immunotherapy: Chair DMC

• GE Healthcare: Consultant

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  National Institute on Aging:
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Neurocognitive Disorders Work Group

Dilip Jeste (Chair)
Deborah Blacker
Dan Blazer (New Chair)
Mary Ganguli
Igor Grant
Jane Paulsen
Ronald Petersen
Perminder Sachdev
Neurocognitive Disorders

Premises

A. New title
   • Replaces: delirium, dementia, amnestic and geriatric cognitive disorders

B. Cognition
   • Core deficit in cognition
   • Decline from previous level of function
Neurocognitive Disorders

- Delirium
- Major Neurocognitive Disorder (NCD)
- Mild Neurocognitive Disorder (NCD)
Delirium
Delirium

- Disturbance of attention and awareness
- Change over a short period of time
- Includes disturbance in cognition
- Not better explained by preexisting condition
- Caused by physiological consequence of medical condition, substance use, or withdrawal
DSM-IV Definition

• "The essential feature of a delirium is a disturbance in consciousness that is accompanied by a change in cognition that cannot be better accounted for by a preexisting or evolving dementia."
Proposed Changes in DSM-5

Change
A. *Disturbance in level of awareness or arousal* with reduced ability to direct, focus, sustain, and shift attention.

Current
A. *Disturbance of consciousness* (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.
Addition

- Note: The following supportive features are commonly present in delirium but are not key diagnostic features: sleep-wake cycle disturbance, psychomotor disturbance, perceptual disturbances (e.g., hallucinations, illusions), emotional disturbances, delusions, labile affect, and EEG abnormalities (generalized slowing of background activity).
Neurocognitive Disorders
General Approach to NCD’s

• Characterize the patient syndromically
  Mild NCD
  Major NCD

• Determine etiology of syndrome
Major Change

• Now including a pre-dementia condition termed “Mild Neurocognitive Disorder”

• DSM IV characterized mostly conditions at the dementia stage and their subtypes
Neurocognitive Disorders

Major vs Mild

1. Severity
2. Independence
3. Usually a continuum with evolution
   Not always
4. Etiology
### Neurocognitive Disorders

<table>
<thead>
<tr>
<th>Domain</th>
<th>Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex attention</td>
<td>Major: diminished, multiple stimuli</td>
</tr>
<tr>
<td></td>
<td>Mild: takes longer</td>
</tr>
<tr>
<td>Executive abilities</td>
<td>Major: abandon complex activities</td>
</tr>
<tr>
<td></td>
<td>Mild: ↑ effort, multi-tasking</td>
</tr>
<tr>
<td>Learning/memory</td>
<td>Major: repeat self in conversation</td>
</tr>
<tr>
<td></td>
<td>Mild: recent events, occas repeat</td>
</tr>
<tr>
<td>Language</td>
<td>Major: anomia, paraphasias</td>
</tr>
<tr>
<td></td>
<td>Mild: ↓ naming, word finding</td>
</tr>
<tr>
<td>Visuoconstruction</td>
<td>Major: not driving, ↓ navigation</td>
</tr>
<tr>
<td>Visuoperception</td>
<td>Mild: maps, effort</td>
</tr>
<tr>
<td>Social cognition</td>
<td>Major: insensitivity social contexts</td>
</tr>
<tr>
<td></td>
<td>Mild: subtle personality, ↓ empathy</td>
</tr>
</tbody>
</table>
Mild Neurocognitive Disorder (MCI)

1. Cognitive decline
2. Single cognitive domain impaired (usually)
3. Preservation of independence

Major Neurocognitive Disorder (Dementia)

1. Cognitive decline
2. Significant cognitive impairment in one or more often multiple cognitive domains
3. Loss of independence
Major NCD
Dementia

A. Cognitive decline (1 or usually 2 cognitive domains)
   1. Report by patient, informant, clinician and
   2. Deficits on assessment

B. Interfere with independence assistance in IADL’s

C. Not delirium

D. Not primarily attributable to another disorder
Mild NCD
MCI

Rationale
Mild cognitive impairment
Early recognition
Intervention
Clinical trials

Criteria
A. Cognitive decline
   1. Report by patient, informant, clinician
      and
   2. Mild cognitive deficits

B. Not interfere with independence greater effort
C. Not delirium
D. Not primarily attributable to other axis 1 disorder
NCD Etiologies

• Alzheimer’s Disease
• Frontotemporal degen
• Lewy body disorders
• Vascular cognitive imp
• Traumatic brain injury
• Substance/medications

• HIV/AIDS
• Prion disorders
• Parkinson’s disease
• Huntington disease
• Other medical issues
• Multiple causes
Alzheimer’s Disease

General

1. Neurodegenerative disease
2. Gradual onset and decline
3. Typically includes a memory impairment
4. ? role of imaging and biomarkers
Alzheimer’s Disease

Major
1. Meets criteria for Major NCD

Mild
1. Meets criteria for Mild NCD

Probable and Possible AD
Alzheimer’s Disease

Major Probable AD
1. Genetic mutation
2. All 3
   Memory + other domain
   Progressive
   No additional contributions

Mild Probable AD
1. Genetic mutation

Mild Possible AD
1. All 3
   Memory disorder
   Progressive
   No additional contributions
Other Newish Criteria

- Alzheimer’s Disease Spectrum
  NIA-AA

- Prodromal Alzheimer’s Disease
  International Work Group
Hypothetical Model of Dynamic Biomarkers of the Alzheimer’s Pathological Cascade

- Abnormal biomarker magnitude
- Normal biomarker magnitude
- Aβ
- Tau-mediated neuronal injury and dysfunction
- Brain structure
- Memory
- Clinical function

Clinical disease stage:
- Cognitively normal
- MCI
- Dementia

Jack et al: Lancet Neurol, 2010
Alzheimer’s Disease Spectrum

- Preclinical AD
- MCI Due to AD
- Dementia Due to AD
## Dementia Due to AD

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>Biomarker probability of AD etiology</th>
<th>Aβ (PET or CSF)</th>
<th>Neuronal injury (tau, FDG, sMRI)</th>
</tr>
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<tbody>
<tr>
<td>Probable AD dementia</td>
<td>Uninformative/available</td>
<td>Conflicting/indeterminant or unavailable</td>
<td></td>
</tr>
<tr>
<td>Probable AD with evidence of path AD</td>
<td>Intermediate</td>
<td>?</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Highest</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Possible AD dementia atypical with path</td>
<td>High consider</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>secondary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia unlikely AD</td>
<td>Lowest</td>
<td>Negative</td>
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McKhann et al: 2011
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<td></td>
</tr>
<tr>
<td>MCI due to AD – intermediate likelihood</td>
<td>Intermediate Intermediate Untested</td>
<td>Positive Untested Positive</td>
<td></td>
</tr>
<tr>
<td>MCI due to AD – high likelihood</td>
<td>Highest Positive Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCI – unlikely due to AD</td>
<td>Lowest Negative Negative</td>
<td></td>
<td></td>
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Albert et al: 2011
### Preclinical AD

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<th>Aβ (PET or CSF)</th>
<th>Neuronal injury</th>
<th>Clinical</th>
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<tbody>
<tr>
<td>Stage 1</td>
<td>Positive</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Sage 0</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
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Sperling et al: 2011
Prodromal Alzheimer’s Disease

- Episodic memory deficit
  - Supported by biomarkers
  - Essentially, amyloid by imaging or CSF
Case Example
53 y/o woman

- 1½ yr history loss of self-confidence
- Not want to move
- Says “can’t think”
- Forgets rapidly in conversation
- Daughters have noticed x 1 yr
- Decreased reading comprehension
- Family human compass
- Sleep ok
- Concerned but not depressed
53 y/o woman

• Family history negative for dementia
• PMH: Good health, postpartum hemorrhage
• Med: supplements, Zoloft, ASA
53 y/o woman

- **STMS:** 37/38
- **VIQ:** 107, **PIQ:** 97
- **Attention/Executive**
  - Trails A and B: 50\textsuperscript{th} %ile
  - Stroop: 50\textsuperscript{th} %ile
- **Language**
  - Fluency: 90\textsuperscript{th} %ile
  - BNT: 59/60
53 y/o woman

• Visuospatial
  Rey O copy: 50th %ile
  JLO: 50th %ile

• Memory
  Logical Memory: 17/10
  Visual Reproductions: 64/21
  AVLT: 7,6,11,10,8; DR 3
# MCI Due to AD

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<td>Lowest</td>
<td>Negative</td>
<td>Negative</td>
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Albert et al: 2011
2008

5/22/2008 MRI Scan
Hippvol in normal range
(-0.31; greater than -0.7 is normal)

Mayo MCI Subject
2/4/2008 FDG Scan
Parietal temporal hypometabolism
(Global FDG AD score of 1.14 is abnormal)
2/4/2008 PIB Scan

Positive; Ratio 2.5
**MCI Due to AD**

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Albert et al: 2011
DSM-5

• Mild neurocognitive disorder
  Possible AD
Clinical Progression 2 yr later

- Getting lost
- Frequent forgetting
- Not driving
- Despondent
- Needs assistance
55 y/o woman

• STMS: 32/38
• VIQ: 107, PIQ: 97
• **Attention/Executive**
  Trails A and B: 25\textsuperscript{th} %ile
  Stroop: 30\textsuperscript{th} %ile
• **Language**
  Fluency: 60\textsuperscript{th} %ile
  BNT: 50/60
55 y/o woman

• **Visuospatial**
  Rey O copy: 30\textsuperscript{th} %ile
  JLO: 25\textsuperscript{th} %ile

• **Memory**
  Logical Memory: 12/5
  Visual Reproductions: 32/15
  AVLT: 3,4,3,5,4; DR 0
7/1/2010 FDG Scan
Progressive hypometabolism; Ratio 1.08
7/1/2010 PIB Scan
Progressive
Ratio 2.7
## Dementia Due to AD

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McKhann et al: 2011
DSM-5

• Major neurocognitive disorder
  Probable AD
Mild Neurocognitive Disorder (MCI)

1. Cognitive decline
2. Single cognitive domain impaired (usually)
3. Preservation of independence

Major Neurocognitive Disorder (Dementia)

1. Cognitive decline
2. Significant cognitive impairment in one or more often multiple cognitive domains
3. Loss of independence
Cognitive complaint

Not normal for age
Not demented
Cognitive decline
Essentially normal functional activities

MCI

Memory impaired?

Amnestic MCI
Non-amnestic MCI

Amnestic MCI
Single domain
Multiple domain

Non-amnestic MCI
Single domain
Multiple domain

DMS-5

MCI due to AD
- Uncertain
- Intermediate
- High

Prodromal AD

Mild Neurocognitive Disorder

No or conflicting AB and MRI or FDG PET

Plus biomarker for AB or MRI or FDG PET

Plus biomarker for AB and MRI or FDG PET

Plus biomarker for AB
Summary

• DSM-5
  New terminology, but no conceptual deviations
  MCI due to AD and Dementia due to AD can be subsumed
  Adoption of terminology, e.g., Major NCD vs. Dementia to be determined