Mild Cognitive Impairment (MCI) – How do we detect it and does it go on to dementia?

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19th Congress of the Australasian Menopause Society
September 25, 2015
Outline

• Definition(s) of MCI
  • MCI Subtypes

• Epidemiology of MCI
  • Incidence and prevalence
  • Progression to dementia
  • Reversion

• Risk factors for progression

• DSM-V: Mild Neurocognitive Disorder (NCD)
Mild Cognitive Impairment
Cognitive Spectrum

- Cognitive Normal
- MCI
- Dementia
Core Clinic Criteria of MCI

- Self- or informant-reported cognitive complaint
- Objective cognitive impairment
- Preserved independent in functional abilities
- No dementia

Petersen, 2004, 2014
Mild Cognitive Impairment

Cognitive complaint

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

MCI

Memory impaired?

Yes
Amnestic MCI

Memory impairment only?

Yes
Amnestic MCI
Single domain

No
Amnestic MCI
Multiple domain

Non-amnestic MCI

No
Single non-memory cognitive domain impaired?

Yes
Non-amnestic MCI
Single domain

No
Non-amnestic MCI
Multiple domain

Petersen, 2004, 2014
Mild Cognitive Impairment

Clinical classification

<table>
<thead>
<tr>
<th>Single domain</th>
<th>Multiple domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amnestic MCI</td>
<td>AD</td>
</tr>
<tr>
<td>Non-amnestic MCI</td>
<td>AD</td>
</tr>
</tbody>
</table>

Etiology

- Degenerative
  - AD
  - FTD
  - DLB
- Vascular
  - VCI
- Psychiatric
  - Depr
- Med Cond
  - Depr
Introduction to the Recommendations from the National Institute on Aging-Alzheimer’s Association Workgroups on Diagnostic Guidelines for Alzheimer’s Disease

Clifford R. Jack, Jr, Marilyn S. Albert, David S. Knopman, Guy M. McKhann, Reisa A. Sperling, Maria C. Carrillo, Bill Thies, Creighton H. Phelps
Hypothetical Model of Dynamic Biomarkers of the Alzheimer’s Pathological Cascade

- Aβ
- Tau-mediated neuronal injury and dysfunction
- Brain structure
- Memory
- Clinical function

Biomarker magnitude

Clinical disease stage:
- Cognitively normal
- MCI
- Dementia

Jack et al: Lancet Neurol 2010
Biomarkers for AD

• **Early Biomarkers (Amyloid)**
  - Amyloid PET imaging
  - CSF Amyloid

• **Later Biomarkers (Neurodegeneration)**
  - Structural MRI
  - FDG-PET
  - CSF tau
The Diagnosis of Mild Cognitive Impairment Due to Alzheimer’s Disease: Recommendations from the National Institute on Aging-Alzheimer’s Association Workgroups on Diagnostic Guidelines for Alzheimer’s Disease

Marilyn S. Albert, Steven T. DeKosky, Dennis Dickson, Bruno Dubois, Howard H. Feldman, Nick C. Fox, Anthony Gamst, David M. Holtzman, William J. Jagust, Ronald C. Petersen, Peter J. Snyder, Maria C. Carrillo, Bill Thies, Creighton H. Phelps
MCI due to AD

• 2 sets of criteria
  • Core clinical for health care providers
  • Criteria based on biomarkers – used only in the research setting or clinical trials

• Clinic Criteria
  • Essentially the same as the Petersen criteria and previous MCI criteria, with extra focus on memory
## MCI Criteria Incorporating Biomarkers

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>Biomarker probability of AD etiology</th>
<th>( A_\beta ) (PET or CSF)</th>
<th>Neuronal injury (tau, FDG, sMRI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCI</td>
<td>Uninformative</td>
<td>Conflicting/indeterminant</td>
<td>Untested</td>
</tr>
<tr>
<td>MCI due to AD – intermediate likelihood</td>
<td>Intermediate</td>
<td>Positive</td>
<td>Untested</td>
</tr>
<tr>
<td>MCI due to AD – high likelihood</td>
<td>Highest</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>MCI – unlikely due to AD</td>
<td>Lowest</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>
Epidemiology of MCI
Incidences and Prevalence: Any MCI

- Average prevalence ≥ 65 years = 18.5%
- Average incidence ≥ 65 years = 47.9/1000 person-years
  - Both increase with age
  - Men may have a higher prevalence and incidence
- Estimates vary considerably, depending on:
  - Source of participants (epidemiological; clinical)
  - Definition (use of strict cognitive cut-points on 1 or more tests versus more of a clinical judgment)

Petersen, RC et al., 2014
MCI Annual Progression Rates

• Epidemiological studies: 7-9%

• Clinical settings: 10-15%
Stability of MCI diagnosis: Rate of reversion from MCI to normal

- Median 5.1 years of follow-up
- 65% who reverted from MCI to Normal, again developed MCI/dementia
Cumulative Incidence of Dementia by MCI status

Roberts et al., 2014
Risk factors for progression from MCI to dementia

Roberts et al., 2014

<table>
<thead>
<tr>
<th>Predictors</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAQ ≥5</td>
<td>2.86</td>
<td>1.94-4.23</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Apathy</td>
<td>2.02</td>
<td>1.26-3.24</td>
<td>.004</td>
</tr>
<tr>
<td>Depression</td>
<td>1.83</td>
<td>1.21-2.76</td>
<td>.004</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.72</td>
<td>1.12-2.61</td>
<td>.01</td>
</tr>
<tr>
<td>Slow gait</td>
<td>1.57</td>
<td>1.00-2.46</td>
<td>.05</td>
</tr>
<tr>
<td>APOE ε4</td>
<td>1.23</td>
<td>0.81-1.85</td>
<td>.33</td>
</tr>
</tbody>
</table>
Transition to DSM 5 – Neurocognitive Disorder (NCD)
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
Mild Cognitive Impairment

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Not demented
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MCI

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Multiple domain

Non-amnestic MCI

Non-amnestic MCI
Single domain

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Multiple domain

Mild Neurocognitive Disorder

DSM-5

MCI due to AD

- Uncertain
  - No or conflicting $A\beta$ or MRI or FDG PET or tau

- Intermediate
  - Plus biomarker for $A\beta$

- High
  - Plus biomarker for $A\beta$

Prodromal AD

- Plus biomarker for $A\beta$ or tau/$A\beta$

Petersen et al., J Int Med, 2013
Conclusions and Discussion

• MCI is an intermediate phase between cognitively normal and dementia
• Not everyone with MCI develops dementia
• While there is instability, the vast majority of individuals with a diagnosis of MCI in the community go on to develop dementia
• Notice of new criteria for both clinical and research
Thank You!

Questions & Discussion