Interface between Normal Aging and Mild Cognitive Impairment

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Cognitive continuum showing the overlaps

Adapter from Petersen, 2004
Diagnostic criteria for dementia of the Alzheimer’s type

• Development of multiple cognitive deficits manifested by both
  – 1) memory impairment
  – 2) one or more of the following cognitive disturbances: aphasia, apraxia, agnosia, or disturbance in executive functioning

• Cognitive deficits in (1) and (2) each cause significant impairment in social or occupational functioning and represent a decline from a previous level of functioning

• Gradual onset and progressive course

DSM-IV
Diagnostic criteria for MCI*

- Not cognitively normal for age
- Does not meet criteria for a dementia diagnosis
- Evidence of cognitive decline
  - Self and/or informant report a decline
  - and impairment on objective cognitive tasks
  - and/or decline over time on cognitive tasks
- Preserved basic activities of daily living/ minimal impairment in complex activities

*Minor neurocognitive disorder DSM-V
Brain changes characteristic of Alzheimer’s disease
Plaque above and tangles below
2010 Model of dynamic biomarkers of the Alzheimer’s disease pathological cascade

2013 Model of temporal order of Alzheimer’s disease biomarkers

What are age-related changes in cognition?

What is causing these changes?
Cognitive functions that show little change with age

“Hold” tests or “crystallized intelligence”
Information performance at 25$^{th}$ percentile by age

WAIS-IV Scaled score = 8; y = % of total correct
Vocabulary performance at 25\textsuperscript{th} percentile by age

Scaled score = 8; y = % of total correct
Cognitive functions that decline with advanced age

“Fluid intelligence”
Processing speed
Block Design performance at 25\textsuperscript{th} percentile by age

Scaled score = 8; \( y = \% \) of total correct
Matrix Reasoning performance at 25th percentile by age

Scaled score = 8; y = % of total correct
Coding performance at 25\textsuperscript{th} percentile by age

Scaled score = 8; y = % of total correct
Logical Memory II performance at 25th percentile by age

Scaled score = 8; y = % of total correct
Factors affecting individual differences

• Genetics
• Experience
• Cognitive reserve
• Health and brain disease
Genetic influence

• In twin studies of elders, heritability estimated at:
  • .60 for verbal abilities
  • .50 for spatial abilities and speed
  • .40 for memory

  Plomin et al., Behav Genet, 1994, 24, 207-215

• More than 50 genes have been implicated.
  • Payton, Neuropsychol Rev, 2009, 19, 451-477
Experience

• Early childhood experiences
• Education and occupation

• Le Carret et al., Dev Neuropsychol, 2003, 23, 317-337
Cognitive reserve

The ability to perform cognitive tasks effectively despite brain injury or disruption.

May operate through additional synapses or recruitment of redundant or alternative brain networks.

Influenced by genetics and experience
Health

• **Systemic illness**
  - E.g., thyroid, anemia, infections

• **Cerebrovascular risk factors**
  - diabetes, hypertension, hypercholestremia, smoking

• **Drugs and alcohol**

• **Mood**
  Kook et al., J Affect Disord, 2012, Jul 25
Health cont’d

• Exercise
  Sofi et al., J Internal Med, 2010, 269, 107-117

• Nutrition
  Bowman et al., Neurology, 2012, 78, 241-249

• Social activity
  James et al., JINS, 2011, 17, 998-1005
Brain changes with aging

• Structures
  • Brain’s volume at peak in early 20s
  • Atrophy prefrontal > temporal > parietal = occipital
    Raz and Rodrigue, Neurosci Biobeh Rev, 2006, 30, 730-748
  • White matter deterioration

• Distributed networks
  • Alterations in connectivity of distributed neural systems
    Ystad et al., Neuroimage, 2011, 55, 24-31
    Seeley et al., Neuron, 2009, 62, 42-52
Default network, lateral view

Buckner et al., 2008, Ann NY Acad Sci, 1124, 1-38
Default network, medial view

Buckner et al., 2008, Ann NY Acad Sci, 1124, 1-38
Default network. Anterior correlations to posterior functional correlations are markedly reduced in advanced aging.

Y axis is temporal correlation between medial prefrontal cortex and posterior cingulate/retrosplenial cortex.

Black = young adults. Green = older adults.
Andrews-Hanna et al., 2007, Neuron, 56, 2924-935
Cognitive continuum showing the overlaps

Adapter from Petersen, 2004
Logical Memory and Pre-MCI
Howieson et al., JINS 2008
Animal Fluency and Pre-MCI

Howieson et al., JINS 2008
Cognitive impairment in MCI

<table>
<thead>
<tr>
<th>Deficit</th>
<th>%</th>
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<tr>
<td>Memory only</td>
<td>30</td>
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<tr>
<td>Memory and visuospatial</td>
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<td>Memory and executive</td>
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<td>Executive only</td>
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<tr>
<td>Visuospatial and executive</td>
<td>9</td>
</tr>
</tbody>
</table>

“This illustrates that AD need not begin as a memory problem.” Storandt et al, Neurol, 2006, 67, 467-473
Risk Factors for MCI

• Age
• APOE4 allele
• Lower educational level
  » Manly et al, Arch Neurol, 2005, 62, 1739-46
• Midlife elevated serum cholesterol level
• Vascular disease
• Depression
Conclusions about prognosis of MCI

• Prevalence in the general elderly population is 3 – 19%.
• The risk of developing dementia is 11- 33% over two years.
• A sizable proportion (e.g., 44%) of patients with MCI returned to normal a year later.

» Ritchie, Dialogues Clin Neurosci, 2004, 6, 401-08
Conditions affecting prognosis from MCI

- Age
- How long MCI has existed
- Whether amnestic MCI or other subtype of MCI
- APOE allele (2 or 3 vs. 4)
- Vascular risk factors
- Hippocampal atrophy
Problem identifying MCI

- A low score on a test may be normal for that individual: 26% of healthy adults have 1 or 2 scores 1 SD below mean on the WAIS-III/WMS-III battery.
  
  Binder et al., Arch Clin Neuropsychol, 2009

- For some people average scores represent a decline from a previous higher level of functioning.
Recommendations for diagnosis

- Take a careful history including premorbid cognition, lifestyle, and vascular risk factors.
- Get detailed functional information from an informant.
- Assess for depression, medication side-effects, alcohol abuse, etc.
- Use the best age- and education-corrected norms available.
- Try to assess the individual at two time points.
Clinical recommendations

• Elders and MCI patients should keep physically and cognitively active.
• They should reduce vascular risk factors as much as possible.
• MCI patients may benefit cognitive-behavioral treatment to improve daily functioning. More studies are needed.
AD pathological cascade

Anoop et al., Int J Alzheimer Dis. 2010