Mild Cognitive Impairment

De Cock anne-Marie
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Vakgroep ELIZA UA,
Aantal personen met dementie in het Vlaamse Gewest 2015-2060
Dementia is a continuum
Clinical Characterization of MCI

Petersen Criteria:
1. Memory Complaint
2. Normal Activities of Daily Living (ADLs)
3. Normal General Cognitive Function
4. Abnormal Memory for Age
5. Not Demented
   (Petersen et al 1999)
What’s in a NAME 1999-2016

CIND (cognitive impairment no dementia) = most closely related to MCI (1997)

MCI (Petersen - 1999) (NIA-AA criteria 2011)

AAMI / AACD = is normal ageing

→ is identified as state of impairment similar to MCI (1999)

Preclinical AD (2011 NIA-AA criteria): no MCI – biomarkers positive


2011 NIA-AA

- Pre-clinical stages of AD
- MCI due to AD
- AD
NIA-AA
A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease

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Memory clinic
EVALUATION

1. severity

2. follow-up

3. pro active decision making

4. detection of treatable conditions
Diagnosis

A. In office

Interview (ADL, IADL, AADL, Social)

Cognitive screening (MMSE, MOCA, Addenbrooks Revised)

Medical and neurological examination

Psychiatric conditions
TESTING

• MMSE
• Clock drawing test

MOCA
Addenbrooks cognitive evaluation – revised
B. NPT $\Rightarrow$ CDR

CDR code

CDR 0.5 + MMSE > 24 = MCI
CDR 0 30% of them is MCI
Mild Cognitive Impairment

CDR and GDS

Normal  MCI  AD

CDR 0.5

2  3

GDS
C. Neuro imaging
  CT scan
  MRI
  PET scan
CT versus MRI: GCA
Medial temporal lobe atrophy (MTA)

- Reflects pathology
  - Reflects Braak stage in AD

- Correlates with memory
  - Strong relation learning/recall

- Early diagnosis of AD
  - Differentiates Controls-MCI-AD

- Predicts conversion to AD in MCI
  - Low hippocampal volume predicts AD
CT versus MRI: MTA
MRI

WML

Microbleeds
Cortical AChE activity in MCI is associated with progress to dementias. 

Converted to AD [month of detected conversion]

[6] [14] [18] [18]

No conversion to AD within 18 months

"normal like" or "AD like"

Price, 2005; Rowe, 2007; Pike, 2007; Forsberg, 2007; Kemppainen, 2007
MCI imaging

- MRI / CT
- FDG-PET
- Amyloid-PET
- Tau-PET
Diagnosis
Progression Risk MCI to AD

10% per year
Older age.
Fewer years of education.
Multidomain amnestic MCI.
Life-style
  - High fat diet.
  - Excessive alcohol intake
  - Stressful lifestyle
Medical comorbidities:
  - Metabolic syndrome
Quantitative gait analysis

Falls risk

Attention reserves

MCI -5 years before dementia
Pre MCI Motor changes

Gait speed

Finger tapping

Motoric Cognitive Risk Syndrome and the Risk of Dementia

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Background. Despite growing evidence of links between gait and cognition in aging, cognitive risk assessments that incorporate motoric signs have not been examined. We sought to validate a new Motoric Cognitive Risk (MCR) syndrome to identify individuals at high risk of developing dementia.

Methods. We evaluated 997 community residing individuals aged 70 and older participating in the Einstein Aging Study over a median follow-up time of 36.9 months. MCR syndrome was defined as presence of cognitive complaints and slow gait (one standard deviation below age- and sex-specific gait speed means) in nondemented individuals. Cox models were used to evaluate the effect of MCR syndrome on the risk of developing dementia and subtypes.

Results. Fifty-two participants met criteria for MCR syndrome at baseline with a prevalence of 7% (95% CI: 5–9%). Prevalence of MCR increased with age. Participants with MCR were at higher risk of developing dementia (hazard ratio [HR] adjusted for age, sex, and education: 3.27, 95% CI: 1.55–6.90) and vascular dementia (adjusted HR: 12.81, 95% CI: 4.98–32.97). The association of MCR with risk of dementia or vascular dementia remained significant even after accounting for other confounders and diagnostic overlap with "cognitive" mild cognitive impairment syndrome subtypes.

Conclusions. A motor-based MCR syndrome provides a clinical approach to identify individuals at high risk for dementia, especially vascular dementia, to target for further investigations and who may benefit from preventive interventions.

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Participants met all four criteria:

1. **Cognitive complaints** were assessed questionnaire, Study clinicians’ observations during clinical interviews or informant reports.

2. **Slow gait** as gait speed one standard deviation (SD) or more below age- and sex-appropriate mean values established in the same cohort (reference).

3. **Preserved activities of daily living** assessed by a scale developed for assessing function in community-residing older adults (19) as well as study clinicians’ observations.

4. **Absence of dementia** (in study by follow-up mean 36 months).
Pooled Prevalence of MCR

MCR and risk of incidence

- Cognitive impairment
Title: Poor gait performances and prediction of dementia: results from a meta-analysis.

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Review and meta-analysis

<table>
<thead>
<tr>
<th>Dementia</th>
<th>Pooled Hazar ratio</th>
<th>P-Value</th>
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</thead>
<tbody>
<tr>
<td>All dementia’s</td>
<td>1.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vascular Dementia</td>
<td>1.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-Alzheimer dementia</td>
<td>1.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alzheimer dementia</td>
<td>1.03</td>
<td>0.004</td>
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JAMDA, February 2016
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0178566
Not recommended or no standardization for predicting progression in MCI


Magnetic resonance imaging (MRI), with volumetric measurements of the hippocampus at or below the 25th percentile for matched age and sex.

Cerebrospinal fluid biomarkers

Neuropsychological test measures
Pharmalogical Treatment

Acetylcholinesterase Inhibitors:
- favored donepezil at 1 year but not at 3 years follow-up. (a MCI + ApoE4-positive individuals)

Memantine:
- not been reported to benefit patients with MCI.

Piribedil:
- dopamine receptor agonist, having acetylcholine release in the hippocampus and the frontal cortex as a putative mechanism of action. Piribedil improved cognition over 3 months on the primary outcome in placebo-controlled study by Nagraj et al. in National Institute of Mental Health and Neurosciences (NIMHANS).

Nicotine:
- Brain nicotinic receptors are important for cognitive function. Nicotine patches improved attention, but not global functioning over 6 months.

Cyclooxygenase (COX)-2 inhibitors:
- Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce brain neurotoxic inflammatory responses and so was assumed to improve cognition. Rofecoxib increased incident cases of Alzheimer's dementia in the study and has a fair evidence against its use. Trifusal (COX-1 and COX-2 inhibitors) had no effect on cognition but was associated with a reduced risk of conversion to AD.
Pharmacological Treatment

Gingko biloba:

- increasing brain the blood supply, modifying neurotransmitter systems, and reducing oxygen-free radical density. Results +/-

Vitamin B:

- Higher homocysteine plasma concentrations are decreased by B vitamins. Immediate memory - attention and executive functioning +/-

Antioxidants such as vitamin E, vitamin C, and curcumin (from turmeric)

- reduce oxidative stress and ageing, yet work in this field is largely in the incipient stages.
Non-pharmacological Treatment

Treatment comorbidities

- vascular, such as hypertension, diabetes, atrial fibrillation, obesity, vitamin deficiency, hypothyroidism, depression, and sleep disturbances.

Abstention from heavy alcohol, smoking, and other substances of abuse

Establishment of a fixed and disciplined routine.

Diet: A Mediterranean diet + Second dietary curcumin

Socialization with people, being part of a senior citizen's group, etc.

Spiritual activity.

Computer-assisted cognitive training:
- objective and subjective measures of memory, quality of life, and mood

Cognitive stimulation:
- increase cognitive and social functioning in a nonspecific manner. Decreased risk of cognitive decline, amnestic MCI and AD

Family psychological intervention:
- memory improvement up to 4 months later in a trial that was not placebo-controlled.

Inconsistent results of improvement in fluency, memory, and trail.
MCI is not only a precursor for AD
Diagnosis in a rigorous system of evaluation
Predicting progression to AD is possible
Treatment is still lacking – regular follow-up (6-12)
Prevention and detection of treatable conditions