

## Mild cognitive impairment MCI

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## Disclosure

- Dr. Maria V. Ghetu has no conflict of interest, financial agreement, or working affiliation with any group or organization.

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## Objectives

- Recognize MCI, as stage before dementia
- Early detection of different types of dementia in their prodromal stages
- Learn an approach to MCI
- Prevention and screening
- Available treatment

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## Introduction

- MCI is an intermediate stage between cognitive changes of normal aging and dementia
- Cognitive impairment beyond that expected for age and education
- That does not meet the criteria for dementia
- Heterogeneous state in terms of clinical presentation, etiology, prognosis, and prevalence

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## Definition

- Self-reported memory complaint, preferably corroborated by an informant
- Measurable deficit in cognition in at least one domain
- Intact activities of daily living (ADL) with minimal impairment in instrumental functions
- Absence of dementia

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## Activities of daily living (ADLs)

Activities	Independence	Dependence
	Points (1 or 0)	Points (0)
Bathing	<b>(1 point)</b> Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity.	<b>(0 points)</b> Needs help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing.
Dressing	<b>(1 point)</b> Gets clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.	<b>(0 points)</b> Needs help with dressing self or needs to be completely dressed.
Toileting	<b>(1 point)</b> Goes to toilet, gets on and off, arranges clothes, cleans genital area without help.	<b>(0 points)</b> Needs help transferring to the toilet, cleaning self or uses bedpan or commode.
Transferring	<b>(1 point)</b> Moves in and out of bed or chair unassisted. Mechanical transferring aides are acceptable.	<b>(0 points)</b> Needs help in moving from bed to chair or requires a complete transfer.
Continence	<b>(1 point)</b> Exercises complete self control over urination and defecation.	<b>(0 points)</b> Is partially or totally incontinent of bowel or bladder.
Feeding	<b>(1 point)</b> Gets food from plate into mouth without help. Preparation of food may be done by another person.	<b>(0 points)</b> Needs partial or total help with feeding or requires parenteral feeding.
<b>Total points:</b>		
<small>                     6 points: high (patient independent).                      0 points: low (patient very dependent).                      Katz, S., Down, T.D., Cash, H.R., Grost, R.C. Progress in the development of the index of ADL. The Gerontologist 1970; 10:20.                      Copyright © The Gerontological Society of America. Reproduced by permission of the publisher.                 </small>		

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## Single non-memory domain MCI

- Mono-symptomatic impairment of cognitive functions other than memory
- Anomia (word-finding difficulties)
- Impairment in executive functioning
- Visual-spatial deficits
- Apraxia (impaired ability to carry out motor activities despite intact motor function)
- May progress to frontotemporal dementia (FTD), or dementia with Lewy bodies (DLB)

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## Multiple-domain MCI

- Impairment in multiple domains of cognitive and behavioral functioning with and without memory impairment
- Multiple domains are only slightly impaired, 0.5 SD below
- Patients may manifest subtle problems with ADLs
- Often patients progress to AD or vascular dementia (VaD)

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## DSM-IV Criteria for Dementia Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

1. Memory impairment
2. At least one of the following
  - Aphasia (language disturbance)
  - Apraxia (impaired ability to carry out motor activities despite intact motor function)
  - Agnosia (failure to recognize or identify objects despite intact sensory function)
  - Disturbance in executive functioning (ability to plan, organize and execute normal activities)
3. Disturbance in 1 and 2 significantly interferes with work, social activities or relationships
4. Disturbance does not occur exclusively during delirium

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## The new DSM 5

- Recognizes "dementia" as an acceptable alternative for the newly preferred and more scientific term "neurocognitive disorder"
- Recognizes specific etiologic subtypes of neurocognitive disorder such as AD, PD, HIV infection, DLB, and VaD
- Each subgroup can be further divided into *mild* or *major* degrees of cognitive impairment on the basis of cognitive decline
- In addition there is a subspecifier "with" or "without behavioral disturbances"

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## Types of Dementia

- **AD:** amyloid plaques and neurofibrillary tangles(tau protein) in parietal, temporal, and parieto-occipital cortex
- **VaD:** focal neurological signs or evidence of cerebrovascular pathology on neuroimaging
- **DLB: LB** ( alpha-synuclein protein) subcortical and cortical (frontotemporal) and amyloid plaques
- **FTD:** varying degrees of preferential atrophy of frontal and temporal lobe

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## Epidemiology

- About 15% of those over 70 have MCI and three to four times more likely to develop AD
- Severe cognitive impairment in the form of dementia declined in elderly population in US in recent years, more marked in men, decline of VaD from overall decline in strokes
- Prevalence estimates of MCI range from 16-20% for majority of reviewed studies

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## Underlying cause

- Neurodegenerative
- Vascular
- Persistent depression
- Severe head trauma
- For either subtype may be more than one underlying cause

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## Risk factors for MCI

- Age over 75 years old
- Fewer years of education
- Presence of APOE epsilon 4 gene allele
- Hypertension
- Obesity
- Diabetes mellitus
- Low level of physical, social and mental activity
- History of depression

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## Conversion to Dementia

- Reported as 10%-20% annually based on cohort study
- Mean annual conversion rate is 4.2% in studies with  $\geq$  5-year follow-up based on systematic review
- Amnesic MCI has been linked to AD
- Nonamnesic MCI may progress to other types such as FTD or DLB
- 20% of the patients with MCI remain stable or reverse to baseline

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## Pathology

- One study examined the extent of intermediate levels of AD pathology, cerebral infarcts and LBD, in a total of 180 Catholic clergy who died at a mean age of 76 years
- 37 subjects had MCI, 83 had dementia, and 60 did not have cognitive impairment
- MCI group: majority 49.2 % had an intermediate level of AD pathology compared with the other groups. Cerebral infarctions were present in 35.2%, and 15.6% had LBD

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## Pathogenesis

- Hippocampal atrophy
- Mesial temporal lobe atrophy begins as part of normal brain aging and may precede development of neuropsychological deficits
- Rate of hippocampal atrophy is associated with conversion of amnesic MCI to dementia
- Patients with MCI and hippocampal atrophy can compensate for early functional deficits by activating alternative cortical circuits to achieve correct execution of cognitive tasks

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## Symptoms

- Forgetfulness, self reported or by caregiver
- Common neuropsychiatric symptoms
  - depression
  - anxiety
  - irritability
  - apathy
  - agitation

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## Symptoms

- **Normal aging** - misplace car key, loose car in the parking garage
  - can't remember the name of a former co-worker when met unexpectedly at the grocery store
- **Red flags** - start forgetting things that typically can remember (doctor appointments, weekly game, important occasions)
  - a pattern develops

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## Differential Diagnosis

- Depression also called Pseudodementia
- Adverse effects of medication: analgesics, anticholinergics, sedatives
- Alcohol overuse
- Sleep disturbances: OSA (nocturnal hypoxemia)
- Vitamin B12 deficiency
- Hypothyroidism
- Neurological disease: brain tumor, Parkinson's disease, multiple sclerosis, epilepsy

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## Evaluation of patients with cognitive problems

- First rule out treatable conditions
- Establish the severity of impairments as baseline for follow-up
- Interview with patient/spouse/family on h/o cognitive/behavioral changes and use of meds
- PMH: CVA, Head Trauma, Alcohol abuse, Parkinson's
- Depression presents as "masked depression", somatic complaints rather than admitting

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## Testing overview

- Quality Standards Subcommittee of AAN : provides practice parameters/guidelines for MCI
- Recommends: NST and screening of patients with suspected cognitive impairment (CI)
- **Neuropsychological testing(NST)**: extensive evaluations of multiple domains: orientation, attention, executive function, verbal and spatial memory
- Provides measure of CI, detects depression and used in connection with clinical judgment
- Useful instruments when administered to high risk patients for memory impairment

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## Other rating scales

- **General cognitive instruments** like MMSE: modest accuracy, best value for ruling out dementia, should be used in combination with other methods
- **Brief cognitive assessments**:
  - Mini- Cog: similar S/S with MMSE for detection of dementia
  - CDT: quick, correlates well with MMSE, not sensitive for identifying very mild dementia
- **Informant-based questionnaire** of cognitive decline may provide useful information

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## Laboratory testing

- TSH, B12 level
- CBC, Electrolytes, Glucose
- Renal and liver function tests
- Red blood cell folate (if ethanol dependence)
- RPR (if clinical suspicion of neurosyphilis)

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## Gene mutations

- Autosomal dominant forms of Alzheimer disease with cognitive changes presenting before age 65 years may have mutations involving
  - amyloid beta precursor protein
  - presenilin 1
  - presenilin 2
- Late onset cognitive changes associated with Alzheimer disease may be seen with 1 or 2 copies of e4 alleles in apolipoprotein E gene

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## Neuroimaging studies

- Structural brain imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) may show presence of extensive cerebrovascular disease
- Head CT or MRI may exclude: brain tumor, SDH, NPH

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## CSF biomarkers

- Maybe helpful on identifying risk of developing AD in patients with MCI
- Risk associated with lower CSF beta-amyloid levels (median 356 vs. 579 ng/L) higher phosphorylated-tau (P-tau) levels (median 81 vs. 53 ng/L) higher total tau protein (T-tau) levels (median 582 vs. 294 ng/L)
- Combination of : CSF T-tau values above 320 ng/L , P-tau values above 52 ng/L, positive CSF beta-amyloid (values below 482 ng/L)

Prospective cohort study of 750 patients with MCI, 529 with Alzheimer disease, and 304 controls were followed for  $\geq 2$  years

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## Prevention

- Involves diet, exercise and mental activity
- A study published in 2004 in JAMA: Mediterranean diet combined with nonsmoking, moderate alcohol consumption, and at least 30 minutes of exercise daily reduces mortality rates
- Cognitive decline can be delayed or prevented in all age groups by physical and mental exercise
- Exercise: brisk walking, bicycling, swimming, housework, gardening
- Leisure activities like: reading, playing board games, playing musical instruments and dancing

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## Treatment

- No treatments clearly found to be effective
- Acetylcholinesterase inhibitors
- Vascular risk factor modification
- Ginkgo biloba and Vitamins

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## Acetylcholinesterase inhibitors

- Might decrease conversion to dementia at 2 years compared with placebo based on a Cochrane review
- Associated with increased adverse effects including diarrhea, nausea, vomiting, muscle spasms or leg cramps, insomnia, headache, abnormal dreams, and syncope or dizziness
- Not routinely recommended

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## Acetylcholinesterase inhibitors

- Donepezil may delay onset of AD in patients with amnesic MCI
- During the first year of 3 year study, the rate of progression from MCI to AD was much lower in Donepezil group but no difference seen by the end of the study
- In patient with troublesome memory difficulties a trial of Donepezil may be considered but patient and family should be informed of the potential risk

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## Vascular risk factors modification

- Patients with MCI and AD have a higher prevalence of atherosclerosis risk factors
- Atherosclerosis risk factors should be aggressively treated
- Statin use reduced risk for dementia or cognitive impairment
- Hypertension treatment reduces incidence of dementia
- Higher postprandial plasma glucose excursions associated with declines of cognitive performance

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## Hypertension Treatment in Elderly

- Has a greater absolute decrease in stroke and reduction in dementia
- Perindopril Protection Against Recurrent Stroke Study (PROGRESS), perindopril plus indapamide reduced stroke-related dementia by 34% and cognitive decline by 45%
- In the Rotterdam Study, antihypertensive drugs decreased VaD by 70%

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## Other

- Ginkgo biloba extract does not decrease incidence of dementia or progression to Alzheimer disease in patients with MCI
- B12, B6 and Folate treatment lowered homocysteine levels and was not associated with improved cognition
- Combination therapy with vitamins B6, B12, and folic acid may slow rate of brain atrophy in older adults with MCI

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## Screening patients for dementia

- American Academy of Neurology -Early detection of dementia
- Petersen RC and al- published an evidence-based review on MCI
- Practice Recommendation: Brief cognitive assessments instruments (CDT, 3-item recall ) may be considered when screening patients for dementia
- EBM screening recommendations for dementia, from AAFP and USPSTF: Cannot recommend for or against screening

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## Screening tool

Patient name: \_\_\_\_\_  
 MR # \_\_\_\_\_  
 Date of birth: \_\_\_\_\_  
 Date of exam: \_\_\_\_\_

**Screening for Cognitive Impairment (> 55 y.o.)**

Maximum score	Score	Task										
3	( )	<b>Registration</b> Name 3 common objects (orange, chair, dime) Take one second to say each. Then ask the patient to repeat all 3 after you have said them. Give one point for each correct answer. Count trials and record.										
4	( )	<b>Clock Drawing Task</b> In the space on the back of the page, please draw the face of the clock and put the numbers in the correct positions. Then draw the hands at ten minutes after eleven. <table border="0" style="width: 100%;"> <tr><td>[ Does not successfully accomplish any of the tasks</td><td>0</td></tr> <tr><td>Successfully draws a closed circle</td><td>1</td></tr> <tr><td>Successfully places numbers in correct positions</td><td>1</td></tr> <tr><td>Successfully includes all 12 correct numbers</td><td>1</td></tr> <tr><td>Successfully places clock hands at 10 minutes after eleven</td><td>1</td></tr> </table>	[ Does not successfully accomplish any of the tasks	0	Successfully draws a closed circle	1	Successfully places numbers in correct positions	1	Successfully includes all 12 correct numbers	1	Successfully places clock hands at 10 minutes after eleven	1
[ Does not successfully accomplish any of the tasks	0											
Successfully draws a closed circle	1											
Successfully places numbers in correct positions	1											
Successfully includes all 12 correct numbers	1											
Successfully places clock hands at 10 minutes after eleven	1											
3	( )	<b>Lexical Fluency</b> May not use plurals and proper nouns. In one minute please name words that begin with letter S. <table border="0" style="width: 100%;"> <tr><td>[ More than 11 words</td><td>3</td></tr> <tr><td>Six to 11 words</td><td>2</td></tr> <tr><td>Three to six words</td><td>1</td></tr> <tr><td>Less than 3 words</td><td>0</td></tr> </table>	[ More than 11 words	3	Six to 11 words	2	Three to six words	1	Less than 3 words	0		
[ More than 11 words	3											
Six to 11 words	2											
Three to six words	1											
Less than 3 words	0											
3	( )	<b>Recall</b> Ask for three objects named above. Give one point for each correct answer.										

Total score: \_\_\_\_\_ Date: \_\_\_\_\_  
 Signature: \_\_\_\_\_

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## Summary

- MCI intermediate stage between cognitive changes of normal aging and dementia
- PCP should be familiar with the concept of MCI
- Patients with MCI should be closely monitored and evaluated for treatable causes
- Patients with MCI and clinical or radiological evidence of cerebrovascular pathology should be screened and treated for vascular risk factors
- Acetylcholinesterase inhibitors are not routinely recommended, a trial of donepezil may be considered for symptomatic benefit
- Recreational activities, cognitive stimulation, and physical activity should be promoted.

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