



## Review

## Diagnosing early cognitive decline—When, how and for whom?

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## ABSTRACT

Mild cognitive impairment (MCI) is a term used to describe cognitive impairment in one or more cognitive domains that is greater than any expected age-related changes, but not of the magnitude to warrant a diagnosis of dementia. This review considers how early cognitive decline is diagnosed, focusing on the use of neuropsychological tests and neuroimaging, as well as the differential diagnosis. Potential treatments, including secondary prevention, post-diagnostic support and self-help are discussed. Finally, medico-legal matters such as driving, lasting power of attorney and employment are outlined.

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## 1. Introduction

Mild cognitive impairment (MCI) describes cognitive impairment in one or more cognitive domains that is greater than any expected age related changes, but not of the magnitude and functional impact to warrant a diagnosis of dementia. Depending on the criteria used, the prevalence of MCI in the elderly (aged 75 and older) is found to be between 3 and 20% [1]. The conversion rate of those with MCI to dementia is similarly hard to estimate, but may be between 23 and 47% over 2.6 years [1].

By the time dementia is diagnosed, substantial, irreversible neurological damage has occurred. Current therapies aim to slow further neurodegeneration. Developing a treatment for MCI, or identifying those who are likely to progress to dementia and starting treatment early, could confer huge health benefits for the population and is the focus of development of novel treatments. There is some evidence that secular changes, possible due to change in lifestyle or prophylaxis of cardio-vascular disease has already had an impact on incidence of dementia [2].

This review considers how early cognitive decline is diagnosed, ramifications of the diagnosis and potential treatments.

## 2. Methods

We searched PubMed until October 2016, using the search terms [Mild cognitive impairment or MCI] and [diagnosis or neuropsychology or neuroimaging]; [Mild cognitive impairment or MCI] and [treatment or memantine or donepezil or cholinesterase inhibitor]; dementia and employment. We identified additional studies by hand-searching reference lists.

## 3. Who should be referred and when?

NICE advises that a referral to memory clinic should be considered for all people who show signs of mild cognitive impairment [3]. Memory clinics are usually within secondary care, although increasingly GPs are taking an active role in the assessment and diagnostic process.

## 4. Diagnosis

### 4.1. Concept and diagnostic criteria

The main aim when assessing patients presenting with early cognitive decline is to distinguish MCI from normal ageing and dementia and then, if possible, to identify the subgroup of patients with MCI, who will progress to dementia.

Differentiating MCI from cognitive ageing is challenging because health and pathology overlap. There is a significant heterogeneity in physical, as well as cognitive ageing, with people experiencing more or less severe trajectories of decline as they get older. It is increasingly understood that ageing per se does not cause decline and the observed changes are a result of cumulative pathology. The relationship between pathology and clinical symptoms, however, is not straightforward; the balance between factors conferring risk (age, lifestyle, vascular risk factors) and resilience (education, pre-morbid IQ) determines whether and how soon cognitive deficits develop in the presence of pathology.

More recently, the concept of 'pre-MCI' or 'subjective cognitive decline (SCD)' has been proposed; it is defined as a stage at which

individuals perceive subjective changes in their cognitive abilities, but perform within normal limits on cognitive tests [4]. SCD has been associated with an increased risk of AD biomarker abnormalities [4–6] and dementia [7,8]. Further research is required to investigate the heterogeneity in ageing and to confirm the validity of the 'SCD' construct.

The concept of MCI has evolved over the years. The original Mayo Clinic criteria for a diagnosis of MCI include self- or informant-reported memory complaints and objective memory impairment with essentially preserved general cognitive functioning [9]. For the NIA-AA revised criteria, decline in memory is not mandatory for the diagnosis; impairment in executive function, attention, visuospatial skills, or language, with or without memory impairment also warrants a diagnosis of MCI [10]. The key criteria that distinguish MCI from dementia are preservation of independence in functional abilities, and lack of significant impairment in social or occupational functioning [10]. The US-American DSM-5 refers to this intermediate stage as 'mild neurocognitive disorder', but the criteria used to define it are essentially the same. The main difference between MCI and mild neurocognitive disorder is that the research that led to the construct of MCI primarily involved elderly subjects, while mild neurocognitive disorder includes acquired cognitive disorders at all ages [11].

### 4.2. Assessment

All patients with suspected MCI should undergo a comprehensive assessment, including history, cognitive, mental state, physical and neurological examination, medication review and laboratory testing [3]. Comprehensive assessment is required to identify potentially reversible forms of MCI due to other conditions (depression, B12 deficiency, medication effects). Although reversible causes have decreased over the last years, they remain an important cause of cognitive impairment and represent about 9% of all dementia causes [12]. As dementia, MCI can be due to one or more aetiologies, with Alzheimer pathology, vascular disease and Lewy body pathology being the three most common.

#### 4.2.1. Cognitive function

The first step in the assessment of cognitive function is obtaining a history of cognitive changes over time, confirmed by a reliable informant, if available. Onset, nature, and time-course of cognitive symptoms should be explored. The history provides information that can help to infer the likely primary aetiology. A chief complaint of progressive memory decline is suggestive of Alzheimer's type pathology, multiple vascular risk factors point towards vascular contribution, while fluctuating course, perceptual abnormalities, motor symptoms and REM-sleep behaviour disorder are associated with Lewy body pathology.

Objective evidence for impairment from neuropsychological tests is then required to confirm the diagnosis. Scores on cognitive tests for individuals with MCI are typically 1–1.5 standard deviation below the mean for their age and education, although these ranges are guidelines and not cut-off scores [13].

The neuropsychological test used should assess all cognitive domains, including executive function, visuospatial skills, attention, language, and memory. A systematic review of 26 studies of screening tools for MCI demonstrated that all four comprehensive screening tests (ACE-R, CAMCOG, MoCA, CERAD) and only three (DemTect, M@T, ABCS) of the eleven non-comprehensive screening tests had sensitivities over 80% for detecting MCI among healthy

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