

Diagnosing mild cognitive impairment can prove challenging

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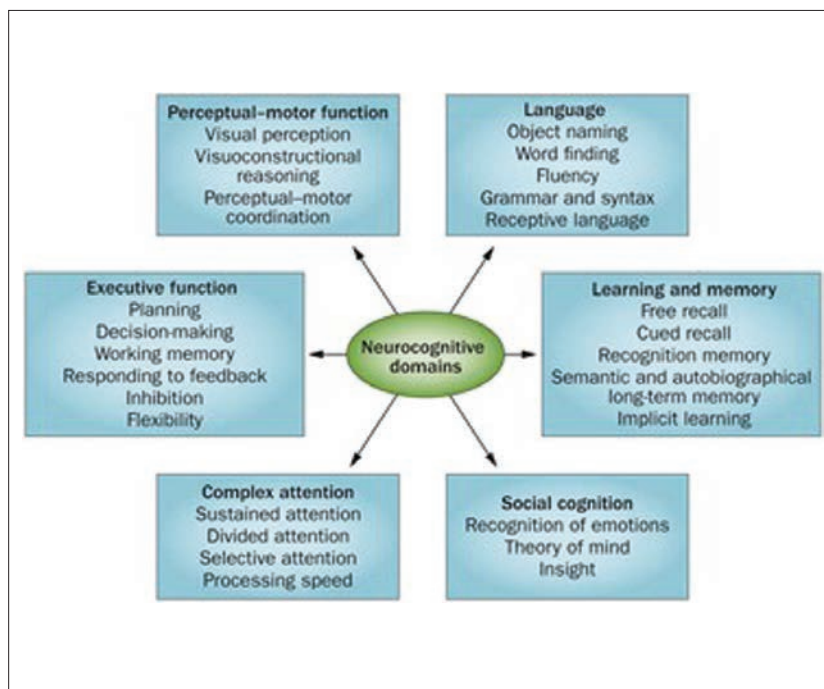
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FIGURE 1

The six cognitive domains in the DSM-5¹¹



How do patients present in primary care?

What are the subtypes of cognitive impairment?

Which patients should be referred?

Sachdev PS, Blacker D, Blazer DG et al. *Nature Rev Neurol* 2014;10(11):634-42



MILD COGNITIVE IMPAIRMENT (MCI) IS A HETEROGENEOUS CLINICAL SYNDROME

describing evidence of cognitive decline greater than expected for an individual's age or educational level but not to a degree that significantly impacts on activities of daily living.¹

Around 6% of those over the age of 60 are thought to have MCI. However, there can be a significant range in incidence and prevalence rates with some studies reporting MCI in up to 20% of over 65s due to variation in diagnostic criteria and assessment tools used.^{2,3}

As dementia research has advanced, particularly in the area of biomarker discovery and functional neuroimaging, conditions such as Alzheimer's disease are now felt to have a long preclinical phase of several years to decades with MCI considered by some to be on the continuum to disease.^{4,5} However, in support of the argument against the continuum theory a proportion of those individuals with MCI will remain stable with little further cognitive decline and never meet the clinical threshold for a dementia diagnosis and some may find that their cognitive function improves.⁶

Approximately 5-15% of individuals

with MCI develop dementia each year and around 50% remain stable after five years of follow-up.⁷

A challenge for clinicians is being able to distinguish between normal cognition, cognitive decline normal for ageing, subjective cognitive decline, temporary changes to cognition as seen in delirium, cognitive decline in MCI and possible dementia as their prognosis and treatments differ, see table 1, p12.

As individuals get older there is an age associated, non-pathological decline in cognitive functioning termed normal cognitive ageing.⁸ In contrast, dementia syndromes caused by conditions such as Alzheimer's disease, vascular dementia, Lewy body dementia, frontotemporal dementia and Parkinson's disease are a pathological, progressive, neurodegenerative process and not a normal process of ageing.⁹ This results in a large spectrum of symptoms between these two clinical domains, where MCI is often diagnosed when other conditions are excluded.

Further challenges in the assessment of individuals with MCI and the dementia spectrum are the slow, insidious onset of symptoms in most cases, often going undiagnosed for some time or reported first by the individual's family or carers.¹⁰

COGNITIVE DOMAINS AND MCI SUBTYPES

Individuals presenting with MCI may report problems with short-term memory or recall (categorised as amnesic MCI) but there may be deficits apparent in other (non-amnesic MCI) or multiple cognitive domains. There have been a range of attempts to reach a consensus on MCI diagnosis both in clinical practice and research.⁷

Figure 1, above, describes the six cognitive domains recorded in the DSM-5.¹¹ The flowchart, see figure 2, p12, can be used to aid recognition of the MCI subtypes.¹² It is important not only to ask individuals about problems pertaining to their memory but also to address these other domains as well.

RISK FACTORS

In keeping with the 'syndrome' definition of MCI, the underlying causes and risk factors vary significantly and are not yet fully understood. Complex and overlapping comorbidities, including increased frailty in older age, can make assessment of cognitive impairment or decline in activities of daily living a challenge.

As described above, in a proportion of individuals presenting with MCI their

symptoms could represent an emerging dementia process and so the risk factors associated with dementia are also linked to MCI risk. Increasing age, strong family history, the APOE e4 gene and cardiovascular risk factors are the

strongest risk factors. The SPRINT trial found that intensive BP treatment in hypertensive adults aged 50 years and over significantly reduced the risk of incident MCI over five years of follow-up.¹³

Cognitive impairment could also be secondary to a range of medical or psychological conditions and MCI can be misdiagnosed in these cases if a careful history and assessment are not completed.

Table 1

Different types of cognitive impairment

Normal cognition	No concerns about cognitive function reported or observed
Normal cognitive ageing	Age associated, non-pathological cognitive decline
Subjective cognitive decline	Self-reported concerns about memory or cognition that would not currently meet MCI or dementia diagnostic threshold
Reversible or transient cognitive decline	Cognitive decline secondary to medical or psychological conditions
Mild cognitive impairment	Cognitive decline greater than expected for age or educational level but not impacting on daily functioning
Dementia	Pathological, progressive, neurodegenerative process not a normal feature of ageing resulting in cognitive and functional decline

MEDICAL CAUSES

Delirium describes an acute, fluctuating disturbance in attention and awareness which may feature additional disturbance in cognition. Causes of delirium can be multifactorial with older age, infection, hospitalisation especially following hip fracture or requiring ICU admission all shown to be risk factors.

Symptoms can take several weeks to resolve fully even after the offending insult has been addressed and should be considered in any new presentation of cognitive impairment after recent illness.

Repeated delirious episodes increase the risk of developing dementia and episodes of delirium can increase the risk of future delirious episodes inferring a cognitive vulnerability in these patients.¹⁴

In addition to delirium, other causes of potentially reversible cognitive impairment include:¹⁵

● Metabolic conditions:

Hypo/hyperthyroidism, hypo/hyperparathyroidism, hypercalcaemia, Cushing's disease, Addison's disease, pituitary insufficiency, hypoglycaemia, vitamin deficiencies (B₁, B₆, B₁₂ and folate), chronic liver failure, chronic respiratory failure or sleep apnoea, chronic renal failure or Wilson's disease

● Neuroinflammation/infection:

meningitis, encephalitis, neurosyphilis, Lyme disease, sarcoidosis or vasculitis

● Neurosurgical conditions:

subdural haematoma, normal pressure hydrocephalus, intracranial tumours or abscesses

● Other:

medication side effects, particularly those with strong anticholinergic activity, alcohol misuse, drugs or toxins and epilepsy

PSYCHOLOGICAL CAUSES

Depression, anxiety, loneliness, social isolation and/or prolonged grief reaction can all impact on cognitive functioning with attention often being the most common domain affected.

ASSESSMENT AND INVESTIGATION

History

A thorough history and assessment can help differentiate between MCI and other potential causes of cognitive impairment. There should be particular focus on the onset and progression of symptoms, with acute or fluctuating courses indicating potentially reversible causes.

Association with onset of symptoms and any precipitating causes should be made such as cerebrovascular events, other recent physical illness, medication change or stressful life events.

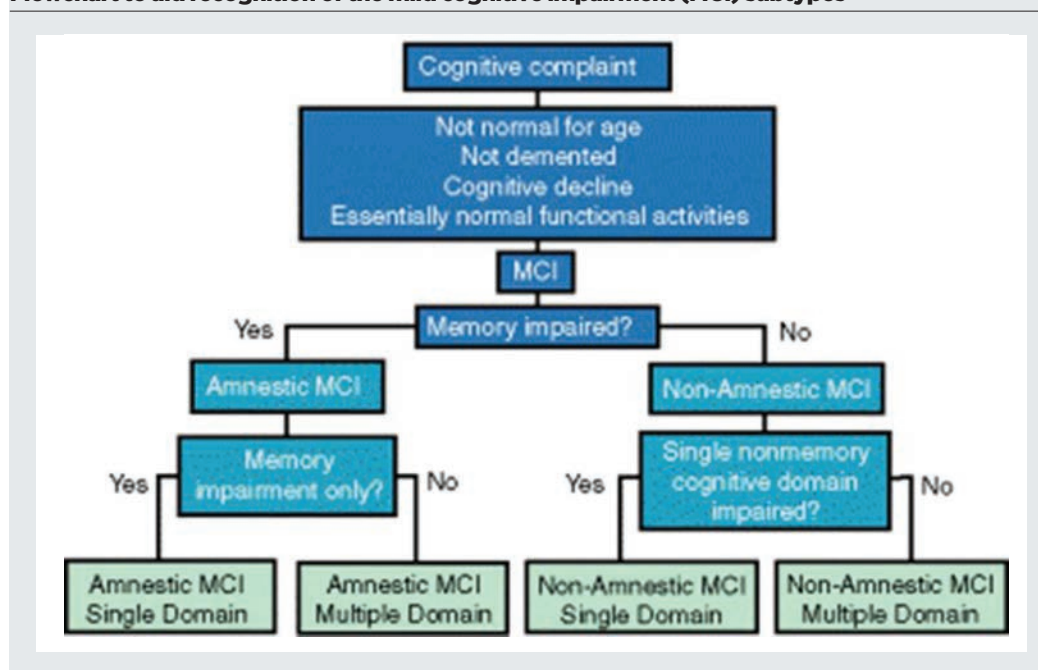
Past medical history can identify cardiovascular risk and/or reversible causes. Family history of cognitive impairment or dementia and social history including level of educational attainment or previous occupation, smoking status, alcohol intake and level of social support or requirement for carers should be recorded.

A collateral history is important to corroborate the patient's account and is useful to determine level of premorbid function or any associated behavioural change. Determining if there is any risk to the individual as a result of the cognitive impairment is important, e.g. driving, medication errors, level of social support, any episodes of wandering or problems in the kitchen such as leaving the oven on.

During interaction with the patient

Figure 2

Flowchart to aid recognition of the mild cognitive impairment (MCI) subtypes¹²



key points

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Mild cognitive impairment (MCI) is a heterogeneous

clinical syndrome defined as evidence of cognitive decline which is greater than expected for an individual's age and educational level but which does not significantly impact on activities of daily living. Around 6% of those over the age of 60 are thought to have MCI.

Alzheimer's disease is now thought to have a long

preclinical phase which lasts for several years to decades, and some consider MCI to be an intermediate stage along a continuum from normal cognition to dementia. However, a proportion of those with MCI will remain stable with little further cognitive decline or find that their cognitive function improves. Only 5-15% of individuals with MCI develop dementia each year and around 50% remain stable after five years of follow-up. Risk factors associated with dementia are also linked to MCI risk, and the strongest of them are increasing age, family history, the APOE e4 gene and cardiovascular risk factors.

The challenge for clinicians is to distinguish between

normal cognition, cognitive decline normal for ageing, subjective cognitive decline, delirium, MCI and dementia. The history should focus on the onset and progression of symptoms. An acute or fluctuating course suggests delirium or another potentially reversible cause. It is important to identify any recent physical illnesses, medication changes or stressful life events. Risk factors for MCI and dementia should be recorded together with the level of social support or requirement for carers. It is also important to determine if there is any risk to the individual as a result of their cognitive impairment.

To meet the diagnostic criteria for MCI there must be

evidence of cognitive decline but maintained activities of daily living and so an assessment of both is required. In the primary care setting cognitive screening tools such as the GPCOG are widely used but it is important to be aware that a normal score does not rule out cognitive impairment or dementia. A full physical examination (including neurological examination) and screening blood tests are required to identify any potentially reversible causes.

No medications are approved for the treatment of MCI.

Where there is concern about future dementia risk or diagnostic uncertainty it may be useful to make a referral to a specialist memory clinic. If MCI is confirmed patients should be offered six monthly or annual reviews for cognitive monitoring and assertive management of risk factors. A multidomain approach targeting cardiovascular risk factors, diet, exercise and cognitive training has been shown to have a small benefit on cognition.

Table 2

Routine blood tests typically performed in primary care to screen for reversible causes of cognitive impairment

Blood tests	Conditions
Full blood count, ESR, CRP	Anaemia, vasculitis
Renal function, thyroid function, liver function, lipids, bone profile, iron studies, B ₁₂ , folate, fasting glucose or HbA _{1c}	Metabolic conditions

there may be clues to cognitive function on simple observation. Obvious dressing errors, stains on clothing, change in mobility, level of alertness or engagement, any obvious mood disorders, level of orientation, verbal fluency or problems with comprehension as well as any sensory impairment.

Assessment

To meet the diagnostic criteria there must be evidence of cognitive decline but maintained functioning in activities of daily living and so an assessment of both is required. Cognitive testing can cause some distress to patients so consider asking relatives or carers to sit outside and ensure the room is free from distractions and any sensory impairment has been addressed.

In the primary care setting cognitive screening tools such as the GPCOG,¹⁶ are widely used as they are brief and have a similar sensitivity to detecting dementia as the mini-mental state examination (MMSE).¹⁷ A score less than 5 on the patient section or less than 3 on the informant questionnaire of the GPCOG indicates cognitive impairment but a normal score does not rule out cognitive impairment or dementia.¹⁸

Additional cognitive assessment tools such as the Addenbrooke's Cognitive Examination Revised (ACE-R) are useful to differentiate deficits in the different cognitive domains, particularly in non-amnesic MCI presentations.¹⁹

Functional assessment could include the basic activities of daily living (BADL) or instrumental activities of daily living (IADL) questionnaires.^{20,21}

A full physical examination including neurological examination is required to help rule out potentially reversible causes as described above.

Additional investigations

Blood tests should be completed as part of initial investigations to help rule out potential reversible causes, see table 2, above.

Depending on availability and access

to services, neuroimaging is also indicated, most commonly a CT brain scan mainly to rule out major structural abnormalities or vascular events.

MANAGEMENT

There is currently no UK national guidance for MCI. There are also no medications approved for the treatment of MCI. Drugs used in the treatment of Alzheimer's disease have been investigated but have not demonstrated any improvement in cognitive function in MCI.²²

As the causes are multiple and include a range of medical and lifestyle factors the best evidence appears to be for a multidomain approach.

The FINGER trial was a double blind randomised controlled trial in community settings in Finland. It investigated the effects of a multidomain approach targeting cardiovascular risk factors, diet, exercise and cognitive training in older people at increased risk of dementia.²³

Inclusion criteria were CAIDE (Cardiovascular Risk Factors, Ageing and Incidence of Dementia) dementia risk score of at least 6 points and cognition at mean level or slightly lower than expected for age. A total of 1,260 participants aged 60-77 years were randomised to the intervention group (n = 631) or control group (n = 629).

In the intervention group cognitive benefits, quality of life and physical function were better maintained over the two-year follow-up period although the effect size was small. The study has now been expanded to other countries with longer follow-up planned.

REFERRAL AND FOLLOW-UP

Where there is concern about future dementia risk or diagnostic uncertainty it may be useful to make a referral to a specialist memory clinic which may be run by neurology, geriatric or psychiatry of old age specialist teams. These teams may have access to additional structural or functional neuroimaging »

such as fluorodeoxyglucose positron emission computed tomography (FDG-PET) or blood or CSF based biomarkers in accordance with NICE early dementia recommendations. The use of these investigations tends to be assessed on an individual basis where diagnosis is uncertain and Alzheimer's disease suspected.^{7,24}

If MCI is diagnosed some memory clinics will discharge the patient back to primary care or offer a six month or annual review to monitor cognition with assertive management of risk factors, as mentioned above.

Programmes provided by organisations such as Age UK, see Useful information box below, can offer some practical tips to help individuals overcome some of the challenges their cognitive impairment creates, e.g. by the use of adaptive technology.

Specialist community nurses, social workers or occupational health practitioners may also provide additional support but access to these services and referral criteria can vary significantly.

Competing interests

Professor Peter Passmore has received honoraria and travel grants from Pfizer, Eisai, Shire, Johnson & Johnson and Nutricia. The other authors have no competing interests.

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Useful information

For patients
Age UK
www.ageuk.org.uk

We welcome your feedback

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