

Forgetfulness, stress or mild dementia?

Cognitive assessment of older patients

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Cognitive complaints are common among older people and have many causes, including the normal changes of ageing. A detailed history and cognitive screening are essential for diagnosis, and screening for medical and psychiatric conditions may identify a treatable cause. All older patients presenting with forgetfulness may benefit from neuroprotective advice. Specialist referral should be considered in complex cases or when dementia is suspected.

Memory or cognitive impairment is common among older patients in general practice. The presentation may be direct or covert, such as:

- an older patient complains of difficulty remembering names, finding words or misplacing things
- a family member worries that their loved one seems confused or struggles to do previously routine tasks such as cooking or paying bills
- a patient with a chronic illness who is well known to the practice appears less 'on the ball' than usual, or their previously stable disease becomes difficult to control or deteriorates unexpectedly
- a patient who is usually regular in attending the practice misses appointments
- a patient presents for review after an unexpected car accident while driving. Although memory or cognitive

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impairment can herald a diagnosis of early or mild dementia, it may be a presentation of a psychiatric condition such as depression or anxiety or a part of normal ageing. This article aims to provide guidance for GPs to aid confident assessment of patients with potential cognitive impairment.

Terminology

Cognitive difficulties

When patients complain of memory problems, they could be referring to difficulties in a number of possible cognitive domains (Table 1). Although learning and memory



KEY POINTS

- Concerns about memory are common in older patients.
- Cognitive changes are normal for almost all people as they age, and assessment should focus on differentiating the normal changes of ageing from abnormal cognitive functioning.
- Primary cognitive problems should be differentiated from secondary disorders, such as those caused by a medication, medical condition or psychiatric problem.
- Assessment and follow up should include use of a cognitive screening tool such as the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) or General Practitioner Assessment of Cognition (GPCOG).
- The management of mild cognitive impairment includes good medical care and general neuroprotective advice, which is relevant to all older patients presenting with memory concerns.

possible causes, with Alzheimer's disease being the most common in older people. It is generally of gradual onset with a chronic course, although there are exceptions. Dementia must be distinguished from delirium (acute confusional state), which by definition is of acute or recent onset and associated with loss of awareness of surroundings, a global disturbance in cognition, changes in perception and the sleep-wake cycle, and other features.

Mild cognitive impairment

As dementia develops gradually, individuals go through an intermediate stage, generally referred to as mild cognitive impairment (MCI) or mild neurocognitive disorder. This stage involves both subjective and objective evidence of modest cognitive decline but not to a degree that compromises independent functioning. Higher-level function is affected, for which the individual uses compensation strategies.¹

Although MCI is often termed 'pre-dementia', there is evidence that a significant proportion of patients diagnosed with MCI will not progress or may even revert and no longer meet the diagnostic criteria on follow up. The prevalence of MCI in adults aged 65 years and older is 10 to 20%, and the estimated annual conversion rate to dementia, in particular Alzheimer's disease, is

is often the most salient of these domains, the problems could also be in:

- attention (ability to sustain or shift focus)
- language (naming, producing words, comprehension, grammar or syntax)
- perceptual and motor skills (construction, visual perception)
- executive function (planning, reasoning, decision making, mental flexibility)
- social cognition (reading others' emotions and intentions, regulating behaviour).

It is thus often more appropriate to refer to cognitive rather than memory complaints or deficits.

Dementia

Dementia, now also referred to as 'major neurocognitive disorder' in the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, is defined by the presence of substantial cognitive decline from a previous level of functioning to the degree that the individual's ability to live independently is compromised owing to the cognitive deficits. Dementia is a syndrome with many

TABLE 1. COGNITIVE DOMAINS AND EXAMPLES OF SKILLS AND ASSESSMENT QUESTIONS

Domain	Examples of skills	Warning signs and questions
Learning and memory	Short-term recall Semantic and autobiographical Long-term memory Implicit learning	Have you noticed you have been talking to someone and soon after forget the conversation? Have you had difficulty remembering the names of people you have just met? Have you had trouble keeping track of dates and appointments? Have you had any difficulty remembering events from your past? Have you had any difficulty doing activities previously thought of as automatic, like driving or typing? [To informant] Has he or she been repeating him or herself lately?
Language	Object naming Word finding Receptive language	Have you noticed any word-finding difficulties? [To informant] Has he or she had more difficulty understanding you lately?
Executive function	Planning Decision making Working memory Flexibility	Have you had more difficulty managing your finances lately? [To informant] Have you noticed difficulties with his or her capacity to plan activities or make decisions?
Perceptual-motor function	Visual perception Perceptual-motor co-ordination	Have you had trouble using day-to-day objects, such as the phone or cutlery? Have there been new driving difficulties, such as difficulty staying in the lane?
Complex attention	Sustained attention Selective attention	Are you having difficulty following what's going on around you? [To informant] Have you noticed that he or she is more easily distracted?
Social cognition	Recognition of emotions Appropriateness of behaviour to social norms	[To informant] Has he or she been behaving inappropriately in social situations? Is he or she able to recognise social cues? Is he or she able to motivate him or herself?

reportedly 10 to 15% in clinic patients and 6 to 10% in epidemiological studies.^{2,3}

Stress, depression and anxiety

Stress is the body's response to environmental demands or threats, either physical or psychological. Whereas some stress is normative, stress can become pathological if it is chronic or overwhelming in relation to the person's coping abilities. This can lead to psychiatric conditions such as depression or anxiety, which can have direct effects on cognition, including inattention, slowed processing and short-term memory impairment.

Anxiety, depression or a combination of the two may also be primary psychiatric conditions, exacerbated by a neurocognitive disorder, or may be related to associated physical disorders. In some instances, depression or anxiety may occur in the prodromal phase of a neurocognitive disorder. It is therefore important to screen patients for symptoms of anxiety and depression

as part of the differential diagnosis, and to treat these conditions appropriately.

Cognitive changes of normal ageing

Finally, it must be recognised that normal ageing is associated with some cognitive change, with few people experiencing no cognitive decline. The primary decline is in processing speed, such that with age individuals become slower in reacting to stimuli and performing cognitive tasks. This has effects on the ability to remember information, resulting in 'on the tip of the tongue' experiences, where words or names are occasionally forgotten but come to mind later or with a prompt. There can be a slow recall of stored knowledge, although the detail is essentially retained. Memory recall may sometimes be short on detail.

Normal memory changes vary between individuals, but the capacity for immediate recall and long-term memory does not tend to change. The capacity to understand instructions or follow stories on television

or in newspapers or books is also usually preserved. These changes do not herald dementia. Differences between forgetfulness associated with healthy brain ageing, stress or depression, MCI and dementia are summarised in Box 1.

History taking

Distinguishing between forgetfulness related to depression/anxiety, MCI or mild dementia can be a challenge, and therefore any concern about a decline in cognition requires careful evaluation. Although the history should be taken from the patient where possible, it is imperative that information is also obtained from a close family member or friend who knows the patient well. Subtle changes may otherwise be missed. Sometimes the physician may note telltale signs of cognitive impairment, such as the patient having difficulty following instructions, unexplained missed appointments, lost prescriptions or poor control of diabetes, hypertension or other chronic conditions.

Key points to obtain from the history include:

- details of the memory complaint, such as
 - onset (When was it first noticed? Was the onset abrupt or insidious?)
 - course (Has it been stable, deteriorating or improving? Is it worse at a certain time of the day? Is there ‘sun-downing’?)
 - specific examples of the complaint, where possible
- cognitive concerns other than memory, such as in language, executive function or social cognition, and personality changes (see Table 1 for examples of questions)
- functional capacity, including
 - basic activities of daily living (ADLs) such as washing, dressing and feeding
 - instrumental ADLs such as shopping, managing finances, telephone use, transport use, keeping appointments and managing medications
 - particular enquiry into whether a person is still driving and whether they have been involved in any driving accidents or near-misses
 - performance on tools such as the Functional Activities Questionnaire, which may be helpful when functional status is unclear from the history⁴
- substance use history, being sure not to overlook alcohol use
- medication review, as several medication classes can contribute to cognitive impairment, including prescription and over-the-counter medications. In particular, it is worth screening for the use of benzodiazepines, anticholinergics, opiates and antiepileptics
- family history of dementia.

Psychiatric and medical evaluation

Medical and psychiatric histories are necessary to assess for risk factors for

cognitive impairment and to clarify the differential diagnosis.⁵ It is important to ask about:

- symptoms of depression – low mood, tearfulness, lack of pleasure in normally enjoyable activities (anhedonia), loss of appetite, sleep disturbance, feelings of guilt and suicidality
- symptoms of anxiety – feeling worried, tense or ‘on edge’ most of the time, initial insomnia, episodes of panic, flashbacks to or nightmares of previous trauma
- cardiovascular risk factors – a history of cardiovascular or cerebrovascular disease, hypercholesterolaemia, hypertension, diabetes, smoking, obesity or atrial fibrillation (these are associated with an increased risk of cognitive impairment), hypotension or hypoglycaemia (which may cause cognitive impairment)
- sensory impairments, which may negatively affect an individual’s capacity to function independently
- history of severe head injury resulting in a loss of consciousness
- cognitive reserve factors, including years of education, engagement in complex mental activities, social activity and physical exercise, all of which are thought to correlate with a reduced risk of MCI.

A targeted neurological examination should be completed to assess for reversible causes. In particular, this should include assessment for:

- any focal neurological deficits (suggesting stroke)
- extraocular movements
- abnormal gait or other movements (suggesting Parkinson’s disease, a Parkinson’s plus syndrome or dementia with Lewy bodies)
- peripheral neuropathy (such as in vitamin B₁₂ deficiency).

Neurological signs and their possible aetiology in patients with cognitive impairment are listed in Table 2.⁶

1. FEATURES OF CONDITIONS ASSOCIATED WITH MEMORY IMPAIRMENT

Normal ageing

- Memory deficits are usually subtle (e.g. misplacing items, forgetting names)
- Items recalled at a later time (e.g. ‘tip of tongue phenomenon’)
- No evidence of progressive worsening
- Function is preserved

Pathological stress or depression

- Presence of recent major stressful events or chronic stress for the individual such as bereavement, relationship problems, financial hardship, health issues
- History of depression or other psychiatric problem
- Symptoms of depression or anxiety are present such as low mood, lacking interest in usual activities, suicidal thinking

Mild cognitive impairment

- Memory (or other cognitive) concern, usually not noticed by others but noticed by the individual and/or those close to them
- Objective memory (or other cognitive) impairment suggestive of modest decline
- Intact instrumental activities of daily living
- Not better explained by another cause (e.g. depression, anxiety)

Dementia (major neurocognitive disorder)

- Substantial cognitive decline from a previous level of performance, both subjectively and on the basis of objective testing
- Impairment interferes with independent living
- Cognitive deficits are not better explained by another mental disorder (such as depression) or delirium

Cognitive screening

Several screening tools are available for the rapid assessment of cognitive function in the clinical setting. Probably the most widely known, well-validated tool is the Mini-Mental State Examination (MMSE).⁷

TABLE 2. NEUROLOGICAL SIGNS AND THEIR POTENTIAL AETIOLOGY IN PATIENTS WITH DEMENTIA*

Neurological sign	Possible aetiology
Abnormal eye movements	PSP, Wernicke's disease, corticobasal degeneration, mitochondrial disorders, raised intracranial pressure, Huntington's disease, CJD
Alien hand	Corticobasal degeneration
Anosmia	Traumatic brain injury, subfrontal meningioma, Alzheimer's disease, Parkinson's disease, Huntington's disease
Ataxia	Normal pressure hydrocephalus, CJD, paraneoplastic disease, cerebellar ataxia, leukodystrophies, Wernicke's disease
Bulbar features	Frontal dementia with motor neuron disease
Cortical blindness	Vascular dementia
Early onset incontinence	Normal pressure hydrocephalus, tumour, PSP
Extrapyramidal signs	Dementia with Lewy bodies, Parkinson's disease, PSP, vascular dementia, frontotemporal degeneration, CJD, Huntington's disease, Wilson's disease, Niemann-Pick disease, mitochondrial disorders
Fasciculations	Frontotemporal degeneration with motor neuron disease
Grimacing facial expression	Wilson's disease
Involuntary movements	Huntington's disease, CJD, Wilson's disease, corticobasal degeneration, SLE, Whipple's disease
Myoclonus	CJD, post-anoxia, Alzheimer's disease, myoclonic epilepsies, dementia with Lewy bodies, corticobasal degeneration, SSPE, Hashimoto's disease
Papilloedema	Tumour, subdural haematoma, hydrocephalus
Peripheral neuropathy	Vitamin B ₁₂ deficiency, paraneoplastic disorders, neuroacanthocytosis, lead poisoning
Pyramidal signs	Vascular dementia, motor neuron disease, CJD, vitamin B ₁₂ deficiency, multiple sclerosis, multisystem atrophy, Alzheimer's disease, frontotemporal degeneration, hydrocephalus, mitochondrial disorders, adrenoleukodystrophy
Seizures	Vasculitis, vascular dementia, neoplasm, limbic encephalitis, AIDS dementia complex, neurosyphilis, SSPE, Alzheimer's disease

Abbreviations: CJD = Creutzfeldt-Jakob disease; PSP = progressive supranuclear palsy; SLE = systemic lupus erythematosus; SSPE = subacute sclerosing panencephalitis.

* Adapted from: Cooper and Greene. *J Neurol Neurosurg Psychiatry* 2005; 76 Suppl 5: v15-v24.⁶

Although the MMSE does not predict who will develop dementia among those with MCI, a systematic review of more than 10,000 participants has shown that it has high sensitivity (0.81; 95% CI, 0.78 to 0.84) and specificity (0.89; 95% CI, 0.87 to 0.91) for the diagnosis of dementia.^{8,9}

The limitations of the MMSE include the impact of practice effects, limited scope for short-term memory testing and failure to test frontal lobe function. The Montreal Cognitive Assessment (MoCA) has an additional component to test frontal lobe function and has comparable performance

to the MMSE for the detection of MCI.⁹

The General Practitioner Assessment of Cognition (GPCOG) was designed specifically for use by GPs and consists of a short patient interview (less than four minutes) and an optional informant interview (two minutes).¹⁰ It has been translated into multiple languages, has a negative predictive validity similar to that of the MMSE and is freely available online from the NHMRC Dementia Collaborative Research Centre (www.gpcog.com.au).

Several other screening tools are available but may be less useful to GPs because of cost and time prohibitions. A comprehensive summary and comparison of screening tools is available from the Dementia Knowledge Translation Hub (www.dementiakt.com.au/doms/domains/cognition).

Importantly, all cognitive screening tests need to be interpreted in the clinical context. For example, patients who are depressed may, in addition to having difficulty with short-term recall, appear tired and flat in affect and have difficulty sustaining effort during testing and a 10 generalised slow processing speed. These symptoms and signs are less likely in patients with MCI or dementia. Moreover, screening tools lack sensitivity in patients with MCI, especially those with high premorbid cognitive function. Consequently, persistent concerns of a patient or informant should not be dismissed, even if the patient scores above the cut-off for cognitive impairment on screening tests.

Although a cross-sectional cognitive assessment is of benefit, repeat testing after 12 months is often helpful to provide the longitudinal follow-up frequently needed to clarify the diagnosis.

Laboratory investigations

Laboratory testing should be completed to exclude reversible causes of cognitive impairment. Basic screening should include:

- full blood count
- biochemistry, including renal and liver function tests, measurement of electrolytes (including calcium,

TABLE 3. COMMON CAUSES OF DEMENTIA AND MCI IN THE ELDERLY AND RELATIVE FREQUENCIES

Cause	Relative frequency*
Alzheimer's disease	50%
Vascular dementia	10 to 15%
Mixed Alzheimer's and vascular	15 to 20%
Dementia with Lewy bodies	4 to 8%
Frontotemporal dementias (Pick's or non-Pick's)	<5%
Others <ul style="list-style-type: none"> • Subcortical dementias <ul style="list-style-type: none"> – progressive supranuclear palsy – Huntington's disease – Parkinson's disease • Alcohol • Normal pressure hydrocephalus • Trauma, anoxia, infections • Prion disease 	<10%

Abbreviation: MCI = mild cognitive impairment.
* Commonly accepted relative frequencies.

- magnesium and phosphate), fasting blood glucose and lipid profile
- thyroid function tests (TSH level)
 - serum vitamin B₁₂ and folate levels.

Current Australian clinical practice guidelines on dementia do not advocate routine serological screening for syphilis or HIV, unless the history suggests the patient is at risk.¹¹ Other investigations may be necessary if abnormal neurological signs are present.

Imaging

The past decade has seen neuroimaging take on a broader role in patients with dementia syndromes, moving from an emphasis on ruling out reversible and treatable causes of dementia to inclusion of diagnostic subtyping of neurodegenerative diseases. Recent studies have found differing patterns of morphological, physiological and pathological change in

the various dementia syndromes.¹²

Broadly, neuroimaging can be classified as structural, functional or molecular, with the latter two modalities available predominantly in tertiary and academic settings.¹¹ Structural imaging encompasses CT and MRI. MRI is specifically preferred in the first-line assessment of younger patients aged under 65 years, who are more likely than older people to have atypical and reversible causes of dementia.¹³ MRI, with its superior anatomical resolution, can assess for volumetric loss including hippocampal atrophy, which is an early sign of Alzheimer's disease. It can also detect white matter and other changes suggesting small vessel disease. However, MRI requires specialist referral. CT is therefore more easily available and remains a way to rule out underlying pathology causing secondary dementia, including stroke, subdural haematomas, hydrocephalus and space-occupying lesions.

The common causes of dementia and MCI and their relative frequencies are listed in Table 3. As dementia and MCI differ only in the level of impairment, their causes are the same.

Specialist referral

Any patient presenting with focal neurological signs, including signs of a movement disorder, should be referred to a neurologist.

If there is concern about dementia then it is recommended that the patient be referred for specialist assessment. This may be to a geriatrician, psychogeriatrician or neurologist who specialises in memory disorders, or a memory clinic if available. The specialist may perform a brief cognitive assessment or refer the patient for a detailed neuropsychological assessment if the pattern of cognitive impairment seems atypical, for clarification of dementia subtypes or because of patient preference.

Psychiatric and medical conditions may skew the results of neuropsychological assessment and should be treated if possible before the referral is organised, as described below. A psychiatric or psychogeriatric referral should be considered for patients

with atypical mental health presentations or significant psychiatric histories.

Management

Typically, patients and their families are anxious about a possible diagnosis of dementia, so assessment should be completed promptly and the diagnosis communicated sensitively and with adequate consultation time allocated. MCI, with its diagnostic instability, should be communicated as an abnormal condition with an uncertain course. Providing written materials and arranging follow up are particularly important to ensure the patient and their family understand the diagnosis and to assess for the psychosocial impact of the diagnosis.

Management includes general neuroprotective advice, treatment optimisation for comorbid conditions, rationalisation of medications with known cognitive impairment profiles and consideration of pharmacological treatments such as acetylcholinesterase inhibitors or memantine. Recommended websites and resources are listed in Box 2.

Neuroprotective and other advice

All patients should receive general neuroprotective advice. This includes advice about management of vascular risk factors, including blood pressure, diabetes, hypercholesterolaemia and weight. Blood pressure control may reduce dementia risk independent of stroke prevention.¹⁴

Advice and support should be provided for smoking cessation. Exercise should be encouraged, both aerobic exercise and resistance training. Moderation of alcohol intake is to be emphasised. Intellectual stimulation (especially with new, unfamiliar and somewhat difficult activities) and social contact are to be encouraged.¹⁵ There is some evidence that the Mediterranean diet may reduce the risk of MCI converting to dementia.⁵

Discussion of wills and power of attorney is relevant for all older patients irrespective of the diagnosis.

Safe driving should be addressed. Dementia is a reportable medical condition

to licensing authorities. When dementia is diagnosed then the patient needs to notify the licensing authority of this. Driving problems should be sought in the history. If difficulty with driving is suspected or unclear then a driving assessment with an occupational therapist should be recommended and the licensing authority notified.

Support organisations such as Alzheimer's Australia (www.fightdementia.org.au) can be invaluable sources of information and support for patients with concerns about cognition or actual cognitive decline.

Optimising treatment of comorbid conditions

In addition to the above advice, patients with a diagnosis of MCI or mild dementia with comorbid medical conditions should have their treatments optimised, aiming to address any reversible causes of dementia. Obstructive sleep apnoea and atrial fibrillation should be treated.¹⁶

Medications should be rationalised, with particular attention to reducing or ceasing medications that are known to cause cognitive impairment. These include (but are not limited to) opioids, benzodiazepines, anticonvulsants, antihistamines, tricyclic antidepressants, anticholinergics, corticosteroids and beta-blockers.

Pharmacological treatments

There are currently no evidence-based recommendations on medications to treat MCI.¹⁷ If dementia is suspected then specialist referral is recommended, as described above, for confirmation of the diagnosis. If Alzheimer's disease is confirmed then PBS-covered pharmacological treatment can be considered (e.g. acetylcholinesterase inhibitors such as donepezil, galantamine or rivastigmine, or the N-methyl-D-aspartate receptor antagonist memantine).¹¹

Patients with simple anxiety or depression are treated with standard therapies. A psychiatric or psychogeriatric referral should be considered for:

- patients who do not respond to first- or second-line treatment
- patients with atypical mental

2. RECOMMENDED WEBSITES AND RESOURCES ON DEMENTIA

DementiaKT (Knowledge Translation)
(www.dementiakt.com.au/doms)

- Developed by the Dementia Collaborative Research Centres in partnership with Dementia Training Australia
- Provides access to screening tools, guidelines and brochures on living with dementia, care planning and prevention

Alzheimer's Australia
(www.fightdementia.org.au)

- Has extensive written educational resources and access to support for clinicians, patients and carers

General Practitioner Assessment of Cognition (GPCOG)
(www.gpcog.com.au)

- Supported by the Dementia Collaborative Research Centres, UNSW Australia and NSW Department of Health
- Provides access to the online version of the GPCOG and support for GPs in screening for cognitive impairment

health presentations

- patients with significant psychiatric histories, including complicated depression and/or anxiety or comorbid severe mental illnesses such as schizophrenia and bipolar affective disorder.

Follow up

If the diagnosis remains unclear after a detailed assessment then provide general advice as described above and watchfully wait. All patients should have a cognitive review with a screening instrument every 12 months, or sooner if deterioration is detected by the patient or their family.

Risk factors for progression of MCI to dementia include older age, less education, stroke, diabetes and hypertension. Patients who are younger, more educated with higher baseline cognitive function and a nonamnestic domain of cognitive impairment are more likely to revert from MCI to normal cognition. Even after 10 years, between 40 and 70% of patients with MCI may not have developed dementia.^{17,18}

Conclusion

Memory or cognitive complaints are common in older patients, although the cause of this presentation can be manifold. A detailed history from the patient and a carer can elucidate the particular nature of the cognitive problems and their functional impact. Screening for medical and psychiatric conditions may identify treatable causes. Cognitive assessment is essential, and screening tools are available that can be used to objectively track cognition over time.

Specialist referral should be considered when patients have complex medical or psychiatric histories or new neurological

signs, or dementia is suspected. There are no medications indicated to treat mild cognitive impairment, but neuroprotective advice is appropriate for all ageing patients. All patients should be followed up and rescreened within 12 months, as often dementia is diagnosed over an extended period of surveillance. **MT**

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A list of references is included in the website version of this article (www.medicinetoday.com.au).

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