Having a senior moment?

Differentiating normal age-related memory loss from early onset dementia

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Key concepts

- Normal age-related memory loss affects everybody
- Assessing memory loss can be complex
- A simple place to start is to rule out other causes, especially depression and look for red flags
- Differentiate normal age-related cognitive decline from early stage dementia
- Consider performing a memory test
- Make a plan for follow-up, investigations and referral

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The aging brain

As we age, brain volume shrinks, neurons are lost at a greater rate than they are regenerated, synapses deteriorate and neurotransmitters become less efficient at carrying information.[1, 2] This process begins when we are in our 20s and starts to accelerate at around age 50, when changes in cognitive function may become noticeable.[1]

A person in their 50s may take longer to recall names and words, learn new tasks or multi-task and attention to detail declines. In their 60s, these changes become more perceptible. It becomes harder to concentrate and to tune out distractions, new memories are more difficult to form and it takes longer to recall information.[1]

The rate at which the brain ages is dependent on many factors such as genetics, hormones, neurotransmitters (e.g. dopamine, serotonin), co-morbidities, experiences and environmental factors.

Types of memory

Different parts of the memory are affected in different ways during the aging process. The terms, short-term and long-term memory, are still used but it is helpful to consider memory functioning in more detail:[2, 3]

Episodic memory is information that is stored with mental tags about when, where and how it was picked up e.g. your first day of school, what you ate for dinner last night. Memories may be stored from minutes to years. The ability to learn new information and recall recently learned memory declines from middle age. Remote memories are more resistant to loss.

Semantic memory is the memory of meanings (factual and conceptual knowledge) e.g. knowing that Wellington is the capital of New Zealand or why a fork is different from a knife. The volume of this memory increases gradually from middle age to the young elderly but declines in very elderly people.

Procedural memory is the "how to" knowledge of skills and procedures, and can be explicit (purposeful, conscious) e.g. learning to ride a bike, or implicit (automatic, unconscious) e.g. knowing the sequence of keys on a computer keyboard. This memory is usually retained into late life.

Working memory is information remembered over a brief period of time (seconds to minutes) before it is dismissed or transferred to a longer-term memory. It can be phonological e.g. name of a person you just met, keeping a phone number in your head as you dial it, or spatial e.g. mentally following a route or rotating an object in your head. With aging, working memory span often becomes shorter, making it more difficult to retain a memory for long enough to use it.

Is this memory loss normal?

A 65 year old male presents complaining of increased forgetfulness and problems with his memory. He is worried that he is developing dementia. What would you do?

History, observation and examination will generally guide the clinician as to when a formal cognitive assessment is required (if at all). Assessing memory loss may in some circumstances be straight forward and require simple reassurance but in other circumstances may be complex and take several consultations.

The following framework may be helpful to structure your approach:

1. Rule out other causes; consider depression, red flags (see page 38)
2. Differentiate normal age-related cognitive decline from early stage dementia
3. Consider performing a memory test
4. Make a plan; follow-up, investigations, referral?

1. Rule out other causes for memory loss

Are there any potentially reversible factors in this case which may explain the memory loss:

- Is the patient taking any medications that cause cognitive impairment?
- Does the patient have a history of drug or alcohol misuse?
- Are there any signs or symptoms of infection?
- Is there evidence of recent head trauma?

Consider depression

Depression is a common cause of memory impairment and often co-exists with dementia in elderly people.[4] Memory may appear selective or patchy rather than generally impaired and symptoms usually have a duration of weeks or months rather than a gradual decline over years.[4] A screening tool such as the Geriatric Depression Scale may be used.

See BPJ 11 (February 2008) "Depression in elderly people".

Are there any red flags?

Referral for more extensive investigation is required for memory loss in the presence of the following factors:[4]

Patient:

- Age less than 60 years

History:

- Rapid (i.e. over one to two months) decline in cognition or function
- Unexplained neurological symptoms (e.g. new onset severe headache, seizures)
- Use of anticoagulants or history of bleeding disorder
- History of cancer
- Family history of neurodegenerative disease

Examination:

- Any new localising sign (e.g. positive glabellar tap, grasp reflex)
- Unusual or atypical cognitive symptoms or presentation
- Gait disturbance

Causes of memory loss[4]

Medical conditions associated with memory loss include:

- Mental illness e.g. depression
- Cerebrovascular disease
- Neurodegenerative disease e.g. Alzheimer's disease, Parkinson's disease, Creutzfeldt-Jakob disease
- Medications (e.g. tricyclic antidepressants, cytotoxics)
- Substance misuse/dependence (e.g. alcohol, benzodiazepines, opiates)
- Brain tumour and infections
- Head injury
- Epilepsy
- Chronic pain, anxiety, stress
- Sleep disorders
- Thyroid disease
- Malnutrition, vitamin deficiencies

2. Differentiate normal age-related cognitive decline from early stage dementia

After ruling out any other explanations for the memory loss, now consider whether this is normal age-related memory decline or early symptoms of dementia.

Normal age-related memory decline is characterised by:

- Subjective memory concern
- Mild episodic memory impairment
- Preserved procedural and semantic memory
- Possible mild non-memory cognitive dysfunction (e.g. attention)
- No functional impairment or behavioural abnormalities[6]

The main distinction between memory loss due to aging and memory loss due to dementia is that problems in age-related memory loss do not affect daily functioning or the ability to live independently.

Mild cognitive impairment is a "grey area" between normal age-related memory loss and dementia, and is defined as objectively impaired neuropsychological test performance but intact activities of daily living.[6]

- Most people are able to maintain their cognitive ability at a functioning level throughout their life.
- Approximately 20% of people aged over 65 years have mild cognitive impairment.[7]
- For some people, mild cognitive impairment is a precursor to dementia. A recent meta-analysis reported that the annual conversion rate from mild cognitive impairment to dementia is approximately 5–10%. Many people with mild cognitive impairment however did not progress to dementia even with ten years follow up.[8]
- Between 3–11% of people aged over 65 years and around 33% of people aged over 85 years have dementia.[7]

Table 1 shows the general distinctions between types of memory impairment.

Table 1: Characteristics of memory impairment (adapted from Neurological Foundation of New Zealand).[9]

Normal age-related "forgetfulness"	Mild cognitive impairment	Dementia
Sometimes misplaces keys, spectacles, or other items	Frequently misplaces items	Forgets what an item is used for or puts it in an inappropriate place
Momentarily forgets an acquaintance's name	Frequently forgets people's names and is slow to recall them	May not remember knowing a person
Occasionally has to "search" for a word	Finding words becomes more difficult	Begins to lose language skills. May withdraw from social interaction
Occasionally forgets to run an errand	Begins to forget events or newly learned information	Loses sense of time. Doesn't know what day it is
May forget an event from the distant past	May forget more recent events or newly learned information	Working memory is seriously impaired. Has difficulty learning or remembering new information
When driving may momentarily forget where to turn. Quickly orients self	May temporarily become lost more often. May have trouble understanding and following a map	Becomes easily disoriented or lost in familiar places, sometimes for hours
Jokes about memory loss	Worries about memory loss. Family and friends notice the lapses	May have little or no awareness of cognitive problems

Is this just memory loss or are there other signs of cognitive impairment?

If the memory loss is accompanied by other signs of cognitive impairment, this may be suggestive of dementia. Signs and symptoms include:

- Aphasia (impairment in producing and understanding speech)
- Apraxia (difficulty in performing motor tasks)
- Agnosia (inability to recognise familiar people, places and objects)
- Disturbance in executive function (difficulty sequencing, organising, abstracting, planning)
- Change in behaviour/mood (i.e. agitation, apathy, anxiety, disinhibition)
- Physical signs including gait disturbance, extra pyramidal symptoms, focal or lateralising neurological signs

Ask the patient if they have any trouble with managing money, using the telephone, using transportation or remembering to take medications. In dementia the earliest changes are seen in the ability to do these tasks.[5] The patient may not be aware of some of these changes, so asking permission to speak to someone who knows them well, may be necessary.

3. Consider performing a memory test

A diagnosis of mild cognitive impairment or dementia is predominantly made from the clinical history provided by the patient and an informant. Memory tests can be used to help confirm and quantify cognitive impairments.

A diagnosis of cognitive impairment can have a significant impact on self-esteem, independence, relationships, employment and plans for the future. Assessing cognitive decline with a memory test is only appropriate if the benefit of early detection of dementia is greater than the harm it may cause.

Early diagnosis allows people to make arrangements such as appointing Enduring Powers of Attorney, updating wills, moving homes and visiting family overseas. It also can provide an explanation for changes that have been occurring in the person for a long time (sometimes years) before they come to see the doctor. There is no cure for dementia but there are treatments that can alter the course of the illness.

Conversation with the patient during the consultation so far may have given clues as to whether a memory test is warranted – how did they answer questions? Did they hesitate to find words or recall facts or sequence of events? Were there any anomalies in their use of language? Is their reported cognitive impairment beyond what could be classified as normal age-related "forgetfulness"?

Which memory test?

A full battery of cognitive tests is usually not appropriate in a primary care setting. A brief, standardised cognitive screening tool may be used.[5]

The Mini Mental Status Examination (MMSE) is the most commonly used memory screening tool. Like many memory tests it is associated with age, educational, language and cultural bias. Some practitioners may be reluctant to use it as it takes ten minutes or more to administer.[10]

The Mini Assessment of Cognition (Mini-COG) and General Practitioner Assessment of Cognition (GPCOG) have an administration time of five minutes or less, a misclassification rate less than or equal to the MMSE (15%), high sensitivity and specificity (≥ 80%) and have been validated in studies relevant to general practice (large sample size, clinical diagnosis used as reference standard).[10] The Six Item Cognitive Impairment Test (6CIT) is also recommended.[7]

The Mini-COG is a good brief initial test that gives a result of "probably demented" or "probably not demented". GPCOG and 6CIT have the advantage of a scoring system so that severity can be monitored over time. However the GPCOG can involve an informant interview which may not be practical at the time of the appointment. See page 43 for tests.

4. Make a plan

Consider findings from the patient history and examination, observations and results of the memory test (if performed). Remember that it is possible for a person to score quite well on a memory test and still have significant cognitive impairment. Conversely a person who functions well can score badly on a cognitive test, e.g., if they are anxious or have mild dysphasia.

At this stage the patient may be classified into one of three alternatives:

a) Suspicion of dementia, for which further assessment and referral is appropriate

b) Suspicion of mild cognitive impairment, for which lifestyle advice and follow-up is appropriate

c) No signs of cognitive impairment, for which lifestyle advice and reassurance is appropriate

Follow-up mild cognitive impairment

In memory loss with no other domains of cognition involved and preservation of function:[4]

- Follow up carefully every three to six months to watch for deterioration
- Perform serial observations with mental state testing (e.g. GPCOG, 6CIT, MMSE) to confirm progression

Ask the patient to recruit a close family member to help them objectively observe any worsening cognitive impairment or impact on activities of daily living.

Consider laboratory investigation

Investigations help to rule out potentially reversible factors such as medical conditions.

If mild cognitive impairment has been identified, general investigation includes CBC, CRP, TSH, vitamin B12, folate, serum electrolytes, calcium and glucose. In some cases referral for a CT/MRI brain scan may be considered. White matter changes are associated with worsening cognitive function.[4, 7]

How to keep your brain healthy

Lifestyle interventions to reduce cardiovascular risk such as regular exercise, eating a balanced diet, low to moderate alcohol intake and being a non-smoker also seem to protect against age-related cognitive decline. A healthy lifestyle, both mental and physical, is the best preventative defence.[2]

Hypertension, stroke and small vessel disease, diabetes, hyperlipidaemia, obesity and hyperhomocysteinaemia have all been associated with an increased risk of age-related cognitive decline.[2]

Exercise

An increased level of fitness is associated with improved memory and learning and a reduction in age-related cognitive decline.[2, 13]

Alcohol

Consumption of small quantities of alcohol (one standard unit of alcohol a day) on a regular basis is thought to stimulate the hippocampus, therefore counteracting cognitive decline. This follows a U or J shaped curve where teetotal or heavy drinkers are disadvantaged.[2]

Diet

A healthy, balanced diet rich in antioxidants (e.g. blueberries, strawberries, cocoa, tea) and omega-3 (e.g. oily fish) may help to slow age-related cognitive decline.[6, 14] It is preferable (and safer) to use naturally occurring sources of antioxidants and omega-3 oils than supplement forms.

Supplements

Gingko biloba is a commonly used supplement for memory loss. In an analysis of 36 trials, it was concluded that gingko biloba appears to be safe with no excess side effects, however there is no consistent or reliable evidence

that it has any clinically significant benefit for people with dementia or cognitive impairment.[15]

Antioxidant supplements such as vitamin A, vitamin E and beta-carotene show no significant improvement in longevity, in fact they may actually increase mortality.[16]

Also see BPJ 14 "Antioxidants and aging".

Pharmacological treatments

There is no pharmacological treatment for delaying age-related cognitive decline or improving mild cognitive impairment.

Cholinesterase inhibitors such as donepezil, galantamine and rivastigmine are often used to temporarily stop or slow cognitive and functional decline in people with Alzheimer-type dementia and dementia associated with Parkinson's disease. Clinical trials show mixed evidence of their effectiveness. These medications are not subsidised.

There is no quality clinical evidence to support the use of oestrogen or hormone replacement therapy to prevent or treat cognitive decline. Some studies report evidence of increased mortality with these treatments.

Brain exercises

A higher level of education or occupational attainment is considered to be a protective factor against age-related cognitive decline.[2] However it is never too late to start exercising the brain. There is growing evidence that participating in activities such as reading, puzzles, computer activities and crafts reduces the risk of age-related cognitive decline.[17] Social interaction is beneficial too. In a study involving almost 1000 elderly people, it was discovered that those who participated less frequently in social activity, had a more rapid rate of decline in cognitive function.[18]

In addition to exercising the brain, there are several strategies that can be adopted to help memory recall:[1]

- Place commonly lost items in the same spot every time
- Write things down e.g. make a "to do" list
- Say words out loud e.g. "I have turned off the iron", repeat a persons name after being introduced
- Use memory aids e.g. notepad, diary, wristwatch alarm, voice recorder
- Group items using mnemonics e.g. alphabetise a list, create an acronym or acrostic (using the first letter of each item to form a sentence), use rhymes or create a story to connect the information
- Concentrate and relax when trying to remember
- Sleep on it – research has shown that the brain continues to solve a problem while we sleep

Best practice tip: Encourage elderly patients to take up dancing! This combines physical activity, brain exercise (counting rhythms, learning steps etc) and social interaction. Some patients may prefer to join a walking or exercise group.

Driving safety

If a patient has cognitive impairment that is worsening over time, this is likely to have implications on driving safety. Relatives may sometimes raise concerns. Relinquishing a driver's licence is often a very sensitive issue. A patient with worsening cognitive impairment could be gradually prepared for this (unless they are clearly unsafe) by suggesting that they might require periodic on-road driving assessment or need to restrict their driving to familiar routes and only during daylight.[19]

Note that a medical practitioner has a legal obligation to advise the Land Transport Safety Authority if a patient poses a danger to public safety by continuing to drive when advised not to.

Cognitive screening tools

Copies of the cognitive screening tools mentioned in this article can be accessed on the following websites:

GPCOG www.patient.co.uk/doctor/General-Practitioner-Assessment-of-Cognition-(GPCOG)-Score.htm
Mini-Cog www.hospitalmedicine.org/geriresource/toolbox/pdfs/clock_drawing_test.pdf
6CIT www.patient.co.uk/showdoc/40026041/
MMSE www.nzgg.org.nz/guidelines/0103/Appendix___MMSE___Mini_Mental_State_Examination.pdf

Mini-Cog[11]

1. Ask the patient to repeat three unrelated words e.g. hat, apple, table

   If necessary the clinician may repeat the words up to six times for the patient to learn them

2. Ask the patient to draw a clock, put in all the numbers and set the hands at ten past eleven.

   A normal clock includes: clock circle, numbers in correct order, numbers in correct spaces on clock, two hands of clock, correct time.

3. Ask the patient to recall the three words from question 1.

Score: 3 words recalled + normal clock	probably not demented
Score: 1–2 words recalled + normal clock	probably not demented
Score: 0–2 words recalled + abnormal clock	probably demented

GPCOG Patient examination (Brodaty et al)[12]

Unless specified, each question should be only asked once

Recall

1. Give the patient a name and address and ask them to repeat it and remember it as you will ask them to recall it again *e.g. John Brown, 42 West Street, Kensington. (Allow a maximum of four attempts to repeat the address).*

Time orientation

2. What is the date? *1 point. Exact only*

Clock drawing (visuospatial functioning) Use a page with printed circle

3. Please mark in all the numbers to indicate the hours of a clock. *1 point. Correct spacing required.*
4. Please mark in hands to show 10 minutes past 11 o'clock. *1 point*

Information

5. Ask the patient to tell you something that happened in the news recently (in the past week) *1 point*

Recall

6. Ask the patient to recall the name and address from Question 1. *1 point for each of: John, Brown, 42, West Street, Kensington*

Score = 9	no cognitive impairment, interview not necessary
Score = 5–8	proceed to informant interview
Score = 0–4	cognitive impairment, interview not necessary

GPCOG Informant interview

Ask the informant: Compared to a few years ago:

1. Does the patient have more trouble remembering things that have happened recently?
2. Does he or she have more trouble recalling conversations a few days later?
3. When speaking, does the patient have more difficulty in finding the right word or tend to use the wrong words more often?
4. Is the patient less able to manage money and financial affairs (e.g. paying bills, budgeting)?
5. Is the patient less able to manage his or her medication independently?
6. Does the patient need more assistance with transport (either private or public)?

Score one point for each "no" answer

Score = 4–6	no cognitive impairment
Score = 0–3	cognitive impairment detected

References

1. Neurological Foundation of New Zealand. How our brain ages. Neurological News Headlines;78. Available from: www.neurological.org.nz/html/article.php?documentCode=7064 (Accessed July 2009).
2. Peters R. Ageing and the brain. Postgrad Med J 2006;82(964):84-8.
3. Budson A, Price B. Memory dysfunction. N Engl J Med 2005;352(7):692-9.
4. Towards Optimized Practice (TOP). Cognitive impairment: is this dementia? Alberta Clinical Practice Guidelines. Alberta, Canada, 2009. Available from: www.topalbertadoctors.org (Accessed July 2009).
5. Karlawish J, Clark C. Diagnostic evaluation of elderly patients with mild memory problems. Ann Intern Med 2003;138:411-9.
6. Ellison J. A 60-year-old woman with mild memory impairment. JAMA 2008;300(13):1566-74.
7. Woodford H, George J. Cognitive assessment in the elderly: a review of clinical methods. Q J Med 2007 2007;100:469-84.
8. Mitchell A, Shiri-Feshki M. Rate of progression of mild cognitive impairment to dementia - meta analysis of 41 robust inception cohort studies. Acta Psychiatr Scand 2009;119(4):252-65.
9. Neurological Foundation of New Zealand. Memory loss stages. Neurological News Headlines;78. Available from: www.neurological.org.nz/html/article.php?documentCode=10667 (Accessed July 2009).
10. Brodaty H, Low L, Gibson L, Burns K. What is the best dementia screening instrument for general practitioners to use? Am J Geriatr Psychiatry 2006;14(5):391-400.
11. Borson S, Scanlan J, Brush M, et al. The Mini-Cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. Int J Geriatr Psychiatry 2000;15:548-61.
12. Brodaty H, Pond D, Kemp N, et al. The GPCOG: A new screening test for dementia designed for general practice. J Am Geriatr Soc 2002;50:530-4.
13. van Praag H. Exercise and the brain: something to chew on. Trends Neurosci 2009;32(5):283-90.
14. Coultrap S, Bickford P, Browning M. Blueberry-enriched diet ameliorates age-related declines in NMDA receptor-dependent LTP. Age 2008;30(4):263-72.
15. Birks J, Grimley Evans J. Gingko biloba for cognitive impairment and dementia. Cochrane Database Syst Rev 2009;1:CD003120.
16. Bjelakovic G, Nikolova D, Gluud L, et al. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. Cochrane Database Syst Rev 2008;2:CD007176.
17. Cassels C. Intellectually Stimulating Activities Linked to Decreased MCI Risk Medscape Medical News: American Academy of Neurology 61st Annual Meeting, 2009.
18. Buchman A, Boyle P, Wilson R, et al. Association between late-life social activity and motor decline in older adults. Arch Intern Med 2009;169(12):1139-46.
19. Pond D, Brodaty H. Diagnosis and management of dementia in general practice. Aust Fam Phys 2004;33(10):789-3.