

Subjective memory problems

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The National Dementia Strategy for England, published in 2009,¹ urges general practitioners to become skilled at recognising dementia at an early stage and to promptly refer those at risk to specialist memory services. The implementation of the strategy includes a public awareness campaign to reduce the stigma of dementia and encourage people to approach their GP if they have concerns about their memory. Subjective memory loss, which is seen as the cardinal symptom of dementia by the public, is likely to be the main problem reported by those who consult their doctor. However, the findings of the Kungsholmen cohort study, which included 1435 people aged 75-95 years without dementia, suggest that only 18% of future cases of dementia will be identified in the preclinical phase by investigating those who screen positive for memory problems.²

What evidence is available to guide GPs in management and referral decisions for patients with subjective memory loss? This clinical review is based on the findings of five systematic reviews, three of which³⁻⁵ investigated the association between subjective memory problems and concurrent objective memory impairment (mild cognitive impairment, dementia, or objective impairment meeting neither clinical diagnosis criteria) or the risk for subsequent memory impairment or dementia. These three reviews included 21, 26, and 10 studies, respectively. The other two reviews investigated patients' quality of life associated with subjective memory problems (five stud-

SUMMARY POINTS

Subjective memory problems are much more common in later life than the objective problems that suggest minor cognitive impairment or dementia

Subjective memory problems are not simply a characteristic of the "worried well" and should be taken seriously

Depression is associated with subjective memory problems, as are older age, female sex, and low educational attainment

Depression is itself a risk factor for dementia, making the diagnostic task even more difficult

Subjective memory problems are a poor predictor of dementia syndrome (loss of memory and one other aspect of cognition sufficient to cause impairment)

When deciding whether to refer to specialist services, practitioners need to rely on rules of thumb to evaluate the extent and possible significance of symptoms or subjective memory loss

SOURCES AND SELECTION CRITERIA

We did a systematic review of published work in three databases—Embase, Medline, and PsycINFO—using 17 search categories that cover the breadth of patient demographics and health thought to have a possible association with memory problems. We searched for reviews of studies in human beings that were published in the English language between January 1989 and May 2009. We excluded cognitive science studies, studies in animals, studies of people with learning difficulties or HIV infection, trials of interventions, correspondence, and commentaries.

ies)⁶ and methods used to ascertain subjective memory impairment (44 studies).⁷ In addition to exploring factors associated with subjective memory symptoms, we describe tools and "rules of thumb" that could assist GPs in managing patients who report such problems.

How common are subjective memory problems in older people?

The prevalence of memory problems in people aged 65 and older ranges from 25% to 50%³ dependent on the method of measuring or eliciting symptoms and on the characteristics of study populations.⁷ The prevalence of subjective memory problems increases with age,⁸ from 43% in people aged 65-74 to as high as 88% in those older than 85. In a postal survey of nearly 2000 Dutch people aged 25 to 85, 52% of those aged 70 to 85 reported forgetfulness and 23% of this age group reported impairment in everyday living because of memory problems.⁹ In a recent systematic review a pooled analysis from eight community studies of people aged 50 and over found the prevalence of dementia to be 8.8%, whereas in a pooled analysis from seven community studies 16.8% of people aged 60 and older had mild cognitive impairment.⁵ Because a large proportion of patients with mild cognitive impairment later develop dementia, such impairment is assumed to be the prodrome of dementia syndrome (loss of memory and one other aspect of cognition sufficient to cause impairment).¹⁰

Are subjective memory problems associated with concurrent objective memory impairment?

In the most recent review, eight studies with a pooled population of 9148⁵ reported the rate of subjective memory problems in patients with dementia, seven reported the rate in those with mild cognitive impairment, and of these four compared the rates in dementia and mild cog-

Box 1 | Types of memory and other cognitive impairments to consider

- Episodic memory—memory of specific past events that involved the person; forgetting a wedding anniversary is qualitatively different from forgetting that you are married.
- Semantic memory—the store of facts and general knowledge (for example, knowing the answer to the question “who is the monarch?” in the abbreviated mental test score)
- Implicit memory—the non-conscious part of memory that uses past experience to shape current behaviour. Inhibitions may be lost and much offence caused by someone whose manners and social behaviour had been impeccable
- Executive functioning—the forms of thinking necessary for goal directed behaviour. Anticipation of and adaptability to new situations are reduced when executive function is impaired, and thinking becomes concrete rather than conceptual and abstract. For example, driving on an unfamiliar route becomes problematic, and proverbs lose their meaning

Box 2 | Simplified version of global assessment of early dementia, based on clinical dementia rating scale²⁰

- The patient is impaired by their loss of memory for recent events (for example, they may forget that they have already collected their repeat prescription and argue with the receptionist about it)
- Some variable disorientation occurs in time and place, but not in relation to people (the individual gets lost easily or turns up for an appointment days late or early)
- Some difficulty with complex problems (such as understanding what a letter or official form is telling them or requiring them to do)
- Engagement in some social activities, but not independently (the individual may appear normal because they retain the ability to conduct “small talk,” but they cannot sustain a serious conversation)
- More difficult tasks and hobbies are abandoned (bills go unpaid, the garden is neglected)
- Some prompting is needed for personal care (clothes are not washed or baths are missed)

nitive impairment head to head. Subjective memory problems were reported by 43% of those with known dementia and 38% of those with known mild cognitive impairment. Across the spectrum of cognitive impairment (mild cognitive impairment or dementia) 40% of patients had subjective memory problems compared with 17% in healthy adult controls.⁵ In this review the pooled sensitivity of subjective memory problems for prediction of dementia was 43% and the specificity was 86%. For mild cognitive impairment, the pooled sensitivity was 37% and specificity was 87%. In cross sectional community studies people with subjective memory problems only had 20-30% probability of concurrently having either dementia or mild cognitive impairment.⁵

Even with direct questioning, 60% of those with dementia and 62% of those with mild cognitive impairment do not report simple memory problems,⁵ suggesting that loss of awareness of change occurs early in cognitive impairment. If general practitioners asked directly about problems with memory the majority of the patient group they were trying to identify would deny any difficulty, whereas 17% of healthy adults would answer positively.⁵

Are subjective memory problems a symptom of depression?

Cross sectional studies do not show a consistent association between subjective memory problems and current objective memory impairment⁴ until adjustment is made for depression.³ Depression may mimic dementia, as memory loss is reported in both conditions, and there is a view that subjective memory problems are the chief complaint in older adults with depression.¹¹ Although

loss of awareness is a feature of dementia, awareness of memory loss is increased in patients with dysthymia and anxiety, but it is not in those with major depression.¹² Some epidemiological evidence from longitudinal studies suggests that depression increases the likelihood of developing dementia syndrome independently¹³ and synergistically with diabetes, itself a risk factor for dementia syndrome (fully adjusted hazard ratio 2.69, 95% confidence interval 1.77 to 4.07).¹⁴ In depressed patients with and without mild cognitive impairment, however, findings on increased risk of incident mild cognitive impairment or its progression to dementia are conflicting.¹⁵ The study design, the sample population, the length of follow-up, and methodological differences may affect the detection of an association between baseline depression and subsequent development of mild cognitive impairment or dementia. Depressive symptoms may be an early manifestation of, rather than a risk factor for dementia, and in some subsets of elderly patients late life depression, mild cognitive impairment, and dementia might represent a clinical continuum.¹⁵

Are subjective memory problems a risk factor for developing dementia?

Most longitudinal studies have shown that patients with subjective memory problems have an increased risk of future cognitive decline or dementia. The risk of developing dementia if subjective memory problems are present varies, and studies use different methods to ascertain subjective and objective impairment. For example, in the Adult Changes of Thought study of 1883 people aged 65 and older, a subset with normal cognition at baseline but high levels of subjective memory problems were nearly three times more likely to develop dementia than their asymptomatic peers (odds ratio 2.7, 95% CI 1.45 to 4.98).¹⁶

Baseline cognitive impairment may be an important factor for progression to dementia in patients with subjective memory problems.⁴ In a study of 364 community dwelling older people without dementia,¹⁷ those who reported subjective memory problems at follow-up and not at baseline were nearly five times more likely to have significant cognitive impairment than those without subjective memory problems at follow-up (odds ratio 4.5, 95% CI 1.3 to 15.4). However, not all longitudinal studies support the view that subjective memory problems are associated with an increased risk of developing dementia. The Maastricht Aging Study, which involved 557 participants aged 55 to 85 years, showed that although being forgetful might indicate slower general information processing and delayed recall at baseline, it did not predict cognitive change over six years.¹⁸

Do subjective memory symptoms indicate other problems?

Older age, female sex, and low education level are more commonly associated with subjective memory problems in cross sectional community studies.³ In studies where participants were volunteers or had referred themselves to memory clinics, those with subjective memory problems tended to be younger and their symptoms correlated with depression rather than objective memory problems

on cognitive tests.³ Subjective memory problems were strongly associated with depression, neurotic personality trait, or both, even when there was no association with objective cognitive performance, in 26 studies in one review.⁴

All five studies included in a systematic review reported an association between subjective memory problems and poorer quality of life.⁶ The Maastricht Aging Study also reported such an association that persisted over a period of nine years.¹⁹ These findings suggest that even if subjective memory problems are not a direct risk factor for dementia, they are not simply a characteristic of the “worried well” and should be taken seriously.

How should general practitioners approach patients with concerns about their memory?

History and examination

As asking non-specific questions about subjective memory loss is not helpful, practitioners need other tools to assess concerns about forgetfulness. Box 1 lists the types of cognitive loss to consider in a patient with subjective memory loss. This list is not exhaustive but may help practitioners to assess the extent of change in cognitive function.

The categories in the global assessment of early dementia take the clinical inquiry away from memory into function and behaviour, changes that may overshadow memory loss (box 2).²⁰

Box 3 lists the “questions for informants” from the GPCog (GP assessment of cognition) test,²¹ a brief assessment tool designed for general practice that includes the clock drawing test and a checklist for informants that may provide information on some of the forms of memory shown in box 1.

Box 3 | Questions for informants from the GPCog test²¹

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

Box 4 | MIMIC—a mnemonic proposed for characterisation of patients with memory problems

- Memory loss—what type? (box 1)
- Informant history—use GPCog checklist (box 3) or global assessment of early dementia (box 2)
- Mood—depressed mood, now or in the past; PHQ-9 (patient health questionnaire) score
- Individual—age, sex, education, other long term psychological problems (anxiety, personality type)
- Cognitive function test results—from, for example, the mini-mental state examination, the six item cognitive impairment test (6CIT), or the GPCog score

QUESTIONS FOR FURTHER RESEARCH

- What symptoms predict the onset of dementia syndrome, and how important is memory loss as a herald symptom? The clinical problem of distinguishing those patients with subjective memory concerns who will develop dementia syndrome is made worse by the wide variation in the definition and measurement of subjective memory problems.⁷
- What is included under the heading of subjective memory impairment and how is it assessed? As most research has been conducted with selected populations, community based longitudinal studies are needed to explore the context in which memory problems are ascertained. We may suspect that an individual with a cognitively demanding lifestyle is more likely to notice memory loss than someone in a less demanding environment, but we do not yet know this. Longer follow-up studies will allow the risk of conversion to dementia to be estimated more reliably and also to measure help seeking behaviour and service use in those reporting memory problems.
- How exactly is depression associated with dementia? If depression is a risk factor for dementia then treatment for depression may affect the incidence of dementia syndrome. If, on the other hand, depression is one part of a continuum towards dementia then treatment would be for symptom relief alone.

ADDITIONAL EDUCATIONAL RESOURCES FOR PATIENTS

- *Worried About Your Memory?* (www.alzheimers.org.uk/memoryworry)—Information, including a factsheet and booklet, from the Alzheimer’s Society
- *Memory Loss and Dementia* (www.patient.co.uk/health/Memory-Loss-and-Dementia.htm)—Memory loss, age associated memory impairment, and dementia are discussed on the Patient UK website

Use of a brief cognitive function test, as recommended in the dementia clinical guidelines of the National Institute for Health and Clinical Excellence and Social Care Institute for Excellence, may reveal cognitive losses.²² As the guideline points out, however, the tests do not perform well enough to always detect mild cognitive impairment. One new instrument, the memory alteration test (M@T), distinguished between subjective memory impairment, mild cognitive impairment, and Alzheimer’s disease in a Spanish study, but further evaluation is needed.²³

Referral

Publicity campaigns suggesting that memory loss is a sign of dementia may result in increasing pressure from patients for referral to specialist services. In the absence of simple, well validated reliable tests for mild objective cognitive impairment²² GPs need to rely on “rules of thumb” to guide referral.²⁴ When referring patients with subjective memory loss it is helpful to note possible causes of impaired memory and to identify potential associated factors. In box 4 we suggest a list of important factors to remember for patients concerned about forgetfulness; the acronym “MIMIC” captures the themes that arise from the synthesis of published reviews and from our workshops with general practitioners, in which we discussed the complexities of early diagnosis of dementia.²⁵ This is not a validated tool, but we suggest that it may help

GPs to characterise forgetful patients when considering or making a referral.

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ANSWERS TO ENDGAMES, p 717. For long answers go to the Education channel on bmj.com

PICTURE QUIZ

A woman with fatigue, dyspnoea, and orthopnoea

- 1 The diagnosis is pericardial effusion with features of tamponade.
- 2 Echocardiography should be the next investigation.
- 3 The most likely underlying cause is hypothyroidism.
- 4 Diastolic hypertension, sinus bradycardia, narrow pulse pressure, and coronary artery disease can also occur in hypothyroidism.
- 5 If tamponade is confirmed, emergency pericardiocentesis should be performed. In the absence of tamponade, the underlying hypothyroidism should be corrected.

STATISTICAL QUESTION

Variables and parameters

Answer *b* is correct; answers *a*, *c*, and *d* are false.

CASE REPORT

Life threatening lactic acidosis

- 1 In the differential diagnosis of severe lactic acidosis, poor tissue perfusion and oxygenation are the main considerations, and these occur in septic shock, acute heart failure, unrecognised bowel ischaemia, and acute liver failure. Some drugs can also cause life threatening lactic acidosis, especially metformin and nucleoside reverse transcriptase inhibitors.
- 2 The most likely diagnosis is incidental metformin associated lactic acidosis. This was caused by diarrhoea induced dehydration associated with drug induced acute kidney injury, which resulted in acute renal failure and accumulation of the metformin.
- 3 Incidental metformin associated lactic acidosis is a life threatening toxicological emergency. It carries a poor prognosis, with mortality approaching 50%.
- 4 Successful treatment of metformin associated lactic acidosis depends on early admission to the intensive care department to ensure supportive care (haemodynamic and ventilatory support) coupled with prompt renal replacement therapy.