

# Clinical review

## What we need to know about age related memory loss

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Memory changes cause concern to many patients as they grow older. Gary Small provides reassurance and gives a strategy for assessing age related memory loss and protecting brain health

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As doctors and scientists have focused more attention on Alzheimer's disease and related dementias, patients are expressing greater concern about their common, age related memory changes. When results of new research on early detection and prevention reach a wider audience, our patients often come to the office with questions about what they can do to preserve their memory abilities as they age. Many of today's doctors trained during a time when minimal information was provided on these topics during their medical training. This paper will provide a practical strategy for assessing age related memory loss and will discuss interventions that may or may not protect brain health.

### Sources and selection criteria

The viewpoints presented were based on my clinical experience and a databased literature review. I selected articles with Medline searches using key words relevant to the theme of this review, emphasising peer reviewed journals and data from controlled clinical trials or methodologically sound epidemiological studies when available.

### Definitions

With age comes the increasing likelihood of developing memory loss. The mildest form, age associated memory impairment, is characterised by self perception of memory loss and a standardised memory test score showing a decline in objective memory performance compared with younger adults.<sup>1</sup> About 40% of people aged 65 or older have age associated memory impairment—in the United States, about 16 million people. Only about 1% of them will progress to dementia each year.

Mild cognitive impairment represents a more severe form of memory loss and is often defined by important memory deficits without functional impairments. Although patients with mild cognitive impairment are able to continue to live independently, they show objective memory impairments similar to those seen in people with very mild Alzheimer's disease.<sup>2</sup> About 10% of people aged 65 years or older have mild cognitive impairment, and nearly 15% of them develop Alzheimer's disease each year. Studies of drugs to treat mild cognitive impairment in order to

### Summary points

Patients with mild memory loss are common in clinical practice; if their symptoms warrant a diagnosis of dementia, treatment with cholinesterase inhibitor drugs is needed

Doctors need to be cautious about unproved treatments for slowing brain ageing because of potential side effects

Lifestyle choices may protect people with mild forms of age related memory loss from future decline: essentially, what is healthy for the body is healthy for the brain

The risks of these interventions are minimal and are not likely to outweigh the many benefits

delay the onset of Alzheimer's disease are currently in progress.

As people live longer, the risk for developing Alzheimer's disease increases dramatically. Although it is the most common cause of late life dementia, other causes, particularly vascular disease, contribute to the occurrence of dementia, often defined as impairment in several cognitive domains including memory to the extent that it interferes with daily life.<sup>3</sup>

### Assessment

Because age related memory change may signal treatable medical conditions, it is important to take any complaint seriously. Risk factors that should trigger a memory screen include age older than 65 years, illnesses that increase the possibility of a diagnosis of dementia (diabetes, Parkinson's disease, stroke disease, etc), or a family history of dementia. A simple screening question asking about the patient's memory ability is often informative.

The first assessment step is to determine if the patient falls into one of the three main categories of memory loss: age associated memory impairment,

**Box 1: Word list task<sup>6</sup>**

Ask the patient to study the following words for up to one minute:

Dirt  
Gallery  
Lemon  
Vest  
Ambassador  
Snake  
Lump  
Mantle  
Elbow  
Kettle

When the minute is up, reset the timer for a 20 minute break. After the 20 minutes, ask the patient to write down as many of the words as possible. Recalling fewer than five words could indicate a problem with delayed recall

mild cognitive impairment, or dementia. It is helpful to obtain a standardised score of cognitive ability using rating scales like the mini-mental state examination, which consists of 30 items that rate memory, orientation, attention, calculation, language, and visual skills.<sup>4</sup> The test takes only about 10 minutes, but is limited because it will not detect subtle memory losses, particularly in college graduates. More detailed memory assessments, known as neuropsychological tests, will provide a better idea about subtle memory deficits. In the memory clinic at University of California, Los Angeles, doctors ask patients to perform a task involving delayed recall (for example, giving the patient a list of words (box 1) and testing them 20 minutes later) to identify subtle memory loss in educated people. Such tests have been standardised and can provide a preliminary diagnosis of mild cognitive impairment. In the United States, positron emission tomography is sometimes used to help in the diagnosis of dementia because it has high diagnostic accuracy and sensitivity for detecting Alzheimer's disease early in its course.<sup>5</sup>

The evaluation of memory loss (box 2) should include review of the onset and course of symptoms, a physical examination, and laboratory assessment to rule out treatable medical conditions that could affect memory. An inventory of the patient's drugs will help sort out possible drug toxicity as a cause of memory loss. Screening for depression can often be done through a standardised questionnaire while the patient is in the waiting room. Laboratory assessments should at least include some blood tests to screen out thyroid disease, vitamin B-12 deficiency, anaemia, liver disease, and various metabolic disturbances, which could possibly cause memory change.

**Treatment options**

If the memory loss is severe enough to warrant a diagnosis of dementia, then cholinesterase inhibitor therapy would be indicated.<sup>3</sup> In the United States, many physicians also recommend vitamin E because of findings that high doses (2000 units daily) delay functional decline in patients compared with placebo treatment.<sup>3</sup> For milder forms of memory loss, drug treatments have not been approved.

Not everyone is destined to develop Alzheimer's disease, and genetic predisposition explains only some of the risk for the disease. Thus, lifestyle choices may be important in disease risk and prevention.<sup>7</sup> Recent findings about possible non-genetic factors contributing to brain health suggest several practical strategies that may decelerate brain ageing and delay onset of dementia (but see box 3). For my patients with age associated memory impairment and related conditions, I briefly review these possible strategies and discuss the potential benefits and risks of each.

**Risk factors and protective factors for brain ageing**

Research during the last decade found a major genetic risk for Alzheimer's disease, the apolipoprotein E-4 allele.<sup>3</sup> This allele has a dose related effect on increasing risk and lowering the age of onset of Alzheimer's disease. A test of the apolipoprotein E genotype, either alone or in combination with other tests, is not considered a useful predictor of future cognitive decline in people without dementia.<sup>8</sup>

Studies of monozygotic twins show concordance rates of approximately 50% for Alzheimer's disease, indicating that non-genetic factors contribute to development of the disease. While severe head trauma and lower educational achievement seem to increase the risk for Alzheimer's disease, other factors may be protective. Unproved but possible protective factors include use of non-steroidal anti-inflammatory drugs, postmenopausal oestrogen in women, anti-oxidant vitamins, and cholesterol-lowering statin drugs; low fat diet; and aerobic conditioning.<sup>6</sup>

**Strategies for maintaining brain health****Stress reduction**

Chronic stress may be detrimental to brain health and memory performance. Animal studies show that

**Box 2: Assessing age related memory loss**

- Screen patients with such risk factors as older age, concerns about memory loss, or family history of dementia
- Get a history about the nature of the memory symptoms, their onset, and their course
- Take a medication inventory
- Use a standard memory assessment tool
- Screen for depression
- Obtain laboratory tests to rule out medical conditions that can affect memory ability

**Box 3: Some treatments under investigation but not proved to prevent Alzheimer's disease**

- Ginkgo biloba
- Cholinesterase inhibitor drugs
- Anti-inflammatory drugs
- DHEA (dehydroepiandrosterone)
- Oestrogen
- Testosterone



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prolonged exposure to stress hormones has an adverse effect on the hippocampus, a brain region involved in memory and learning.<sup>9</sup> Human investigations indicate that several days of exposure to high levels of the stress hormone cortisol can impair memory.<sup>10</sup> Chronic stress can contribute to depression and anxiety disorders, which often interfere with normal memory processing, particularly as people age. Taken together, these findings suggest that minimising stress may have a beneficial impact on brain health.

#### Physical activity

When laboratory animals exercise regularly they develop new neurones in the hippocampus compared with inactive animals.<sup>11</sup> The physical exercise may increase cerebral blood flow, which in turn promotes nerve cell growth. Studies of people who have been physically active between the ages of 20 and 60 show that they have a lower risk for Alzheimer's disease later in life.<sup>12</sup> A recent study of healthy adults between ages 60 and 75 found that mental tasks involved in executive control—monitoring, scheduling, planning, inhibition, and memory—improved in a group taking aerobic exercise but not in a control group.<sup>13</sup>

#### Healthy diet

People with excess body fat have a greater risk for such illnesses as diabetes and hypertension. These obesity related conditions increase the risk for cerebrovascular disease, which often leads to memory decline and dementia. Epidemiological studies show that lower fat diets in young and middle aged adults may reduce the risk for Alzheimer's disease decades later. Some fats, however, may benefit brain health. A recent investigation found that a Mediterranean diet high in olive oil is protective against age related cognitive decline.<sup>14</sup>

Antioxidant vitamins may also protect the brain. In people with mild memory complaints, vitamins E and C may protect brain health, but at what dose is not known.<sup>15</sup>

Nutritional scientists have developed methods to determine the degree of antioxidant potency of various foods, and such antioxidant effects may protect brain health as we age. Fruits such as blueberries, strawberries, and tomatoes, as well as vegetables such as broccoli, have relatively high antioxidant capacity.<sup>16</sup>

A diet rich in carbohydrates with high glycaemic indices (pretzels, French fries, etc) can increase the risk for diabetes, which can lead to stroke disease and vascular dementia,<sup>17</sup> but dietary changes can reverse such effects. A recent study found that the combination of weight loss, eating a healthy diet, and exercising regularly can reduce the risk for developing type 2 diabetes by more than 50%.<sup>18</sup>

#### Mental activity

The risk of developing Alzheimer's disease is lower in people who have been intellectually active than in those who have not.<sup>12</sup> Studies also indicate that higher mental function in one's 20s predicts better cognitive function late in life. People who spend time reading and who have mentally stimulating jobs or educational experiences maintain their memories better and longer as they age. Other studies have shown that college graduates have a lower risk of eventually developing Alzheimer's disease than people with less educational achievement.<sup>19</sup>

Animal studies have shown that enriched environments lead to more neurones in hippocampal memory centres.<sup>20</sup> Additional research supports the idea that continual, life long mental stimulation is healthy for human brains as well. People with advanced education and professional accomplishments tend to have greater density of neuronal connections in brain areas involved in complex reasoning.<sup>19</sup>

These discoveries point to the conclusion that mental stimulation, or exerting our brains in various ways intellectually, may not only improve memory performance but may stave off future cognitive decline.

#### Other lifestyle choices

People with a history of head trauma with loss of consciousness for an hour or more have double the risk for

#### Box 4: Strategies that may protect brain health<sup>6</sup>

- Stress reduction—prepare ahead, balance work and leisure, set realistic expectations, and take relaxation breaks at regular intervals
- Mental activity—do crosswords, puzzles, read, or challenge yourself intellectually
- Healthy brain diet—drink six glasses of water each day, eat low fat foods and plenty of fruits and vegetables, avoid fried foods, and take the antioxidant vitamins E and C
- Regular physical exercise, including an adequate aerobic workout
- Sports and activities with low risk for head trauma
- Avoidance of tobacco and excessive use of alcohol
- Activities that have personal meaning

### Additional educational resources

Gary Small's book, *The Memory Bible: An Innovative Strategy for Keeping the Brain Young* (London: Penguin, 2002), updates readers on the latest research and practical approaches to age related memory loss. This book could be recommended to patients with mild memory complaints and their families

John Rowe and Robert Kahn summarise the MacArthur findings in their book, *Successful Aging* (New York: Pantheon, 1998) and show that several lifestyle choices determine physical and mental health as we age

Arthur Kramer and colleagues describe how physical conditioning influences cognitive vitality in "Exercise, aging and cognition: healthy body, healthy mind?" in Fisk AD, Rogers W, eds. *Human Factors Interventions for the Health Care of Older Adults*. (Hillsdale, NJ: Erlbaum, 2001)

A balanced review of complementary medicines can be found in Spencer JW, Jacobbs JJ, eds. *Complementary/Alternative Medicine: An Evidence-Based Approach*. (St Louis: Mosby-Year Book, 1999)

### Websites

The Natural Pharmacist ([www.tnp.com](http://www.tnp.com)) provides a database of information on nutritional products

Websites with exercises to stimulate mental activity: AgeNet.Inc (<http://agenet.agenet.com>; search for Aerobics of the Mind), Brainbashers ([www.brainbashers.com](http://www.brainbashers.com)), The Ultimate Puzzle Site ([www.dse.nl/puzzle/index\\_us.html](http://www.dse.nl/puzzle/index_us.html)), and The Grey Labyrinth ([www.greylabyrinth.com](http://www.greylabyrinth.com))

Alzheimer's Society ([www.alzheimers.org.uk](http://www.alzheimers.org.uk))—UK's leading care and research charity for people with all forms of dementia and their carers

British Geriatrics Society ([www.bgs.org.uk](http://www.bgs.org.uk))—the national professional organisation that works to restore an ill and disabled person to a level of maximum ability and wherever possible return the person to an independent life at home

Association of British Neurologists ([www.theabn.org](http://www.theabn.org))—the national professional organisation that supports research, education, and clinical care

Royal College of Psychiatrists ([www.rcpsych.ac.uk](http://www.rcpsych.ac.uk))—the national professional organisation that provides public information about mental health and illness

developing Alzheimer's disease later in life.<sup>21</sup> A study comparing amateur soccer players in their mid-20s and swimmers and runners (who were less likely to incur head injuries) of the same age found that over 30% of the soccer players had memory impairments, compared with less than 10% of the swimmers and runners.<sup>22</sup> Avoiding head trauma seems to be an important strategy to keeping the brain healthy throughout life.

Smoking is another risk for memory loss as we age. One study found that smokers had double the risk of getting Alzheimer's disease of people who never smoked.<sup>23</sup> However, when people quit smoking, at whatever age, they are able to reduce their risk.

An eight year long epidemiological investigation found that mild to moderate alcohol consumption—defined as one to four drinks each day—actually lowered a person's risk for developing severe memory loss compared with non-drinkers or heavy drinkers.<sup>24</sup> Similar studies of moderate wine drinkers indicate lower risks for Alzheimer's disease compared with

heavy drinkers and non-drinkers. Exactly how alcohol might protect the brain or heart is not fully known, but it may involve an antiplatelet effect that lowers the blood's tendency to clot and cause tissue damage.

The MacArthur study of successful ageing also found that staying in close contact with people and remaining involved in meaningful activities predicted successful ageing.<sup>25</sup> Because a large component of the study's definition for successful ageing was cognitive success, such activities will likely promote brain health as well.

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