



## **Establishing the cause of memory loss in older people**

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# Establishing the cause of memory loss in older people

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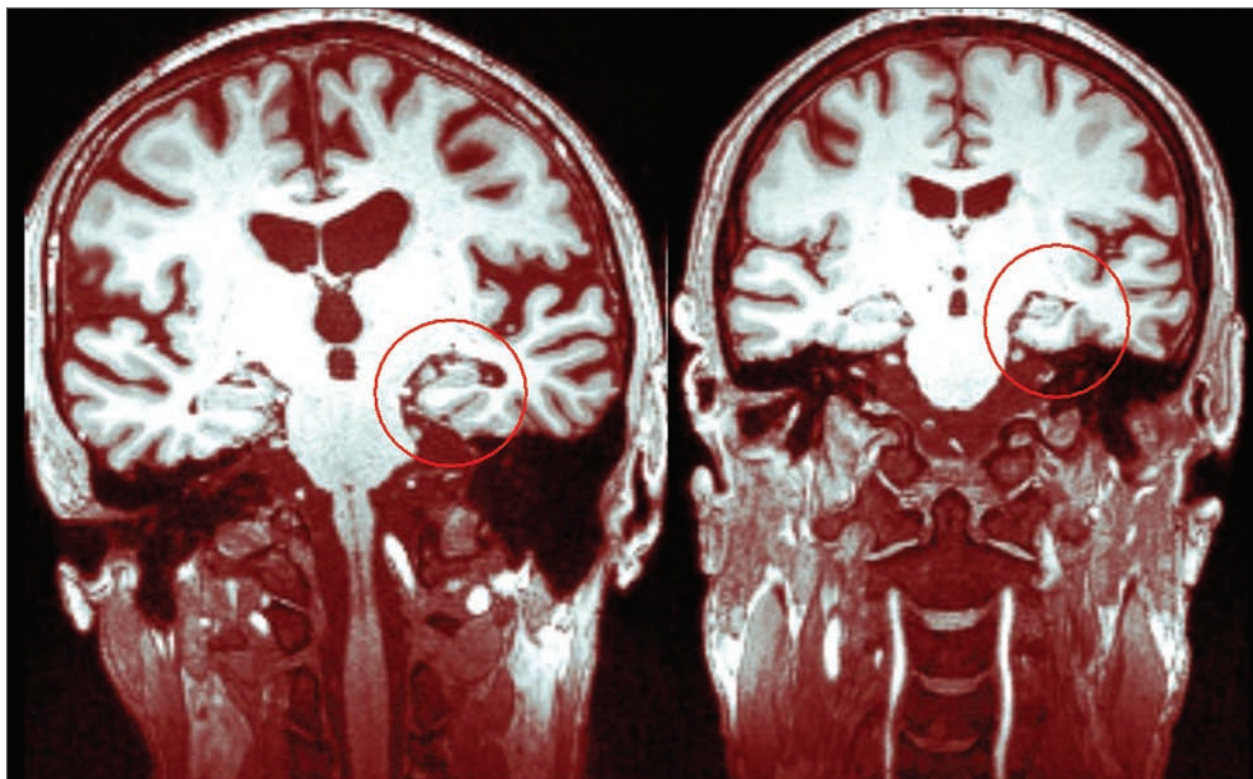
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## FIGURE 1

Hippocampal atrophy is associated with degree of memory impairment and risk of conversion from mild cognitive impairment to Alzheimer's disease

**What** are the main causes of memory loss?



### THE INCREASING NUMBER OF PEOPLE SURVIVING INTO OLDER AGE HAS RESULTED IN

a rise in patients with age-related memory impairment.

Common causes of memory loss in older people are mild cognitive impairment (MCI), the various types of dementia, and psychiatric illness, mainly depression.<sup>1–3</sup>

The prevalence of MCI is estimated to be 3–30% of those above 65, while about 20% will experience symptoms of depression.<sup>4,5</sup> Approximately 36 million people worldwide suffer from dementia, 850,000 in the UK.<sup>6</sup>

Around 10% of patients with MCI progress to dementia each year.<sup>7,8</sup> The most common type is Alzheimer's disease (AD), accounting for 60–80% of

**How** should patients be investigated?

all cases. Other common types of dementia are vascular, frontotemporal (FTD), Lewy body (DLB), Parkinson's and mixed type dementia, where features of different dementias are present.<sup>9,10</sup>

**'Around 10% of patients with mild cognitive impairment progress to dementia each year'**

**Which** patients should be referred?

Older people with depression usually present with low mood and the biological symptoms of depression, such as sleep disturbance and loss of appetite.<sup>1</sup> However, a substantial proportion will experience, and complain of, memory loss and cognitive impairment.<sup>11</sup> Nearly 50% of older people with symptoms of depression will experience symptoms of cognitive impairment that can persist.<sup>12</sup> Executive function, episodic (e.g. word list) memory and processing speed are the most commonly affected cognitive domains. Pseudodementia can be difficult to differentiate from an underlying diagnosis of dementia.<sup>11</sup>

There are of course other causes of memory impairment, such as delirium, often iatrogenic associated with

operations and medication, or rare conditions such as space-occupying lesions, normal pressure hydrocephalus, intracranial infections, endocrine disorders, prion diseases, dementia in progressive supranuclear palsy, and dementia in Huntington disease. These conditions are beyond the scope of this article.

## ‘Nearly 50% of older people with symptoms of depression will experience symptoms of cognitive impairment’

### UNDERLYING MECHANISMS

The pathophysiology of cognitive impairment and dementia is distinct in each of the different disorders, yet they all result in a common progressive neurodegenerative process involving synaptic loss, neuronal cell death, neurotransmitter deficits, loss of connectivity between brain regions and brain shrinkage.<sup>13,14</sup>

There is evidence suggesting that dementia pathology is established before the onset of any symptoms, and therefore MCI can be considered as a prodementia stage.<sup>15,16</sup>

### Alzheimer’s disease

The hallmarks of AD are the deposition of extracellular amyloid plaques and intracellular neurofibrillary tangles. The spread of AD plaques and tangles into different brain regions correlates with localising symptoms.<sup>17</sup>

Early-onset AD is caused by mutations of genes involved in amyloid processing, the late-onset form is attributed to ageing and the interaction between genetic predisposition and environmental factors, such as diet, smoking, alcohol, education and little physical exercise.<sup>18,19</sup> Moreover, hypertension, obesity, hyperlipidaemia, diabetes mellitus and vascular disease have also been linked with increased risk of late-onset AD.<sup>18,19</sup>

### Vascular dementia

Vascular dementia is heterogeneous and frequently comorbid with AD,

stroke and vascular disease. It is sub-classified as multifocal/diffuse or focal based on the number and distribution of infarcts or haemorrhagic lesions observed in the brain.<sup>20</sup>

### Other dementias

FTD consists of a group of disorders involving predominant degeneration of the frontal and temporal lobes through neuronal loss and gliosis. FTD is attributed to the presence of genetic mutations encoding several proteins, such as tau or progranulin.<sup>21</sup>

DLB and dementia in Parkinson’s disease share similar clinical-pathological features and are associated with the spreading of Lewy bodies (neuronal  $\alpha$ -synuclein aggregates) throughout the brain.<sup>22</sup>

### Depression

The exact mechanisms underlying cognitive dysfunction in depression are poorly understood.

Neuroendocrine changes, and HPA axis dysregulation observed in depression, as well as comorbidity with vascular disease have been implicated in the cognitive deficits associated with depression.<sup>1,23</sup>

## EXAMINATION AND INVESTIGATION

### Medical history

A detailed history is required from both the patient and an informant, usually a relative. This should include enquiry about the:

- Mode of onset
- Course of progression
- Pattern of cognitive impairment
- Presence of other symptoms such as behavioural disturbance, hallucinations and delusions

A full medical and psychiatric history should be elicited, plus any relevant family history. An alcohol and drug history may inform the diagnosis. Information about social circumstances will be vital to guide future management. Of vital importance is a thorough analysis of current medications. Not only may this give clues as to possible aetiology, it will inform decisions about potential pharmacological treatments.

### Mental state examination

Particular attention should be paid to any signs of neglect, state of dress (which may indicate dyspraxia), agitation or poor attention. Dysphasia may be present. Difficulty in naming objects is often present (semantic memory deficit). Evasive or

circumstantial responses may indicate an attempt to minimise and conceal impairments.

Mood symptoms (including suicidal ideation) may be primary or comorbid. Abnormal thoughts and perceptions should be probed for, as psychotic symptoms are common. Finally, insight into symptoms, prognosis, and concordance with treatment should be explored.

### Cognitive examination

Cognitive testing can be perceived as humiliating and should be approached sensitively. NICE guidance<sup>24</sup> suggests examination of: attention, concentration, short- and long-term memory, praxis, language and executive function.

A standardised instrument should be used. Primary care options include: the General Practitioner Assessment of Cognition (GPCOG; [www.gpcog.com.au/info.php](http://www.gpcog.com.au/info.php))<sup>25</sup> (taking < 6 minutes) or the Abbreviated Mental Test Score (5 minutes).<sup>26</sup>

The 6-Item cognitive impairment test (< 5 minutes)<sup>27</sup> is well validated in hospital settings. Screening tools used in memory clinics include the Addenbrooke’s Cognitive Examination (ACE), Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE). The MMSE is reliable in detecting dementia in those with suspected cognitive impairment.<sup>28</sup>

## ‘A full medical and psychiatric history should be elicited, plus any relevant family history’

When interpreting results of such instruments, care should be taken to contextualise them with respect to education level, prior functioning, language, sensory impairments, psychiatric and physical health. Detailed neuropsychological testing may be appropriate for mild cases or in distinguishing subtle specific deficits.

### Physical examination

It is essential to screen for coexisting medical conditions that are common in older people and for potential causes of dementia.

Physical examination should cover

## Box 1

### Routine blood tests in the assessment of memory loss

- Routine haematology (full blood count)
- Biochemistry (including electrolytes, calcium, glucose, renal and liver function)
- Thyroid function tests
- Serum vitamin B12 and folate

neurological and cardiovascular systems.

The former should include: observation of gait; inspection for tremor; examination for rigidity, bradykinesia, frontal release signs, and upper motor neurone lesions. Pulse and blood pressure should be checked.

## ‘Of vital importance is a thorough analysis of current medications’

### Blood tests

Blood from patients presenting with memory problems should be routinely sent for the tests listed in box 1, above. HIV and syphilis serology should only be requested if there is a specific indication.

Examination of urine, chest X-ray and echocardiography may be necessary if the clinical picture deems these investigations appropriate. Current evidence does not support the routine use of electroencephalopathy or cerebrospinal fluid examination in the diagnosis of dementia. However, if sporadic Creutzfeldt-Jakob disease is suspected then a lumbar puncture may be appropriate.

### Brain imaging

Structural brain imaging can improve diagnostic accuracy, exclude other pathologies and act as a prognostic marker of dementia progression. The overlap in structural changes between the dementias makes imaging alone insufficient for diagnostic purposes.

The most robust finding in AD is regional atrophy of the medial temporal lobe (MTL).<sup>29</sup> The degree of MTL atrophy correlates with neuropathological disease progression and clinical deficit, see figure 1, p15.<sup>30</sup> However, it increases with age and is common in other dementia subtypes.<sup>31</sup> It may be a useful prognostic marker as it is thought to start four years before symptoms first appear.<sup>32</sup>

In vascular dementia, findings include large infarcts or small vessel disease consisting of cerebral atrophy, white matter lesions, or microbleeds (thought to represent haemosiderin deposits in the brain).<sup>33</sup> The pattern of atrophy in FTD, is more focused on frontal and temporal lobes than in AD.<sup>34</sup> Single photon emission computed tomography (SPECT) can be helpful in the differential diagnosis of dementias, see box 2, below.

### TREATING RISK FACTORS

Currently, NICE guidelines<sup>24</sup> do not recommend a population screening approach aimed at early diagnosis and prevention, but emphasise identification and treatment of modifiable risk factors, such as smoking, high blood pressure, hyperlipidaemia, alcohol, and obesity.

Genetic counselling is recommended for patients likely to have a genetic cause for their dementia, such as autosomal dominant AD, FTD, Huntington disease or CADASIL.<sup>35</sup>

## ‘Cognitive testing can be perceived as humiliating and should be approached sensitively’

Statins,<sup>36-39</sup> NSAIDs,<sup>40</sup> vitamin E,<sup>41-43</sup> and hormone replacement therapy<sup>44,45</sup> have been proposed as agents able to prevent or slow the onset of dementia, as their anti-inflammatory, anti-platelet and antioxidant effects may be neuroprotective. Unfortunately, efforts to identify clear therapeutic effects have failed so far.

Among non-pharmacological interventions, physical exercise before the onset of MCI (45-59 years) appears to be a predictor of healthier cognitive ageing and less dementia at follow-up.<sup>46</sup> Unfortunately, the beneficial cognitive effects of physical exercise are debatable once dementia or MCI have been diagnosed.<sup>47,48</sup> Even if its beneficial effects are not entirely clear, exercise improves cardiovascular function, maintains a healthy BMI and enhances older patients' ability to cope with activities of daily living.

Secondary prevention focuses on tackling smoking and alcohol intake, diabetes, obesity, high blood pressure and hyperlipidaemia. Interventions are obviously relevant in vascular dementia, but can also reduce comorbidities such as infections, diabetic emergencies, cardiovascular and cerebrovascular accidents leading to poor health and hospitalisation. »

## Box 2

### NICE recommendations on imaging in dementia assessment

- Structural imaging to exclude other pathologies and help establish subtype diagnosis. MRI preferable (early diagnosis and subcortical vascular changes) but CT can be used
- HMPAO SPECT should be used to help differentiate between Alzheimer's disease, vascular dementia and frontotemporal dementia if the diagnosis is in doubt
- FP-CIT SPECT should be used to help establish the diagnosis of Lewy body dementia if the diagnosis is in doubt

## ‘Physical examination should cover neurological and cardiovascular systems’

### key points

#### SELECTED BY

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**Approximately 10% of patients with mild cognitive impairment progress to dementia each year.** The most common type is Alzheimer's disease (AD), accounting for 60–80% of all cases. Other common types of dementia are vascular, frontotemporal (FTD), Lewy body (DLB), Parkinson's and mixed type dementia, where features of different dementias are present. There is evidence to suggest that dementia pathology is established before the onset of symptoms, and therefore mild cognitive impairment can be considered as a pre-dementia stage.

**Early-onset AD is caused by mutations of genes** involved in amyloid processing, the late-onset form is attributed to ageing and the interaction between genetic predisposition and environmental factors, such as diet, smoking, alcohol, education and little physical exercise.

**NICE guidance suggests examination of: attention, concentration, short- and long-term memory, praxis, language and executive function.** Particular attention should be paid to any signs of neglect, state of dress, agitation or poor attention. Dysphasia and difficulty in naming objects is often present. Mood symptoms (including suicidal ideation) may be primary or comorbid. Abnormal thoughts and perceptions should be probed for, as psychotic symptoms are common.

**Primary care options for cognitive testing include the** General Practitioner Assessment of Cognition (GPCOG) or the Abbreviated Mental Test Score. Physical examination should include observation of gait, inspection for tremor; examination for rigidity, bradykinesia, frontal release signs, upper motor neurone lesions, pulse and blood pressure.

**Structural brain imaging can improve diagnostic accuracy, exclude other pathologies and act as a prognostic marker of dementia progression** but the overlap in structural changes between the dementias makes imaging alone insufficient for diagnostic purposes.

**NICE guidelines recommend referral to a memory clinic** for patients with mild cognitive impairment, those at high risk of dementia, such as patients with learning disabilities, Parkinson's disease, or patients who have had several strokes. Secondary prevention focuses on targeting smoking and alcohol intake, diabetes, obesity, high blood pressure and hyperlipidaemia.

**Pharmacological management of cognitive and behavioural symptoms** in mild to moderate AD and DLB include acetylcholinesterase inhibitors: donepezil, rivastigmine, and galantamine. Antipsychotic drugs and benzodiazepines can be used to manage agitation, aggression or violence, after obvious causes have been excluded and if behavioural interventions prove ineffective, but they should be given at the lowest therapeutic dose, and the patient should be monitored for dystonia and extrapyramidal side effects.

## 'Structural brain imaging can improve diagnostic accuracy, exclude other pathologies...

### REFERRAL

NICE guidelines recommend referral to a memory clinic for patients with MCI, those at high risk of dementia, such as patients with learning disabilities, Parkinson's disease, or patients who have had several strokes. Memory clinics organise further investigations, such as neuroimaging and may provide follow-up. Patients with dementia should be managed in the community, if at all possible. Patients may require referral to psychiatric services, if they are severely disturbed and agitated or have complex psychiatric problems.

### MANAGEMENT OPTIONS

Non-pharmacological interventions encompass reality orientation, reminiscence, behavioural and validation therapy, but also alternative therapies such as aromatherapy, music and art therapies. Their aim is to prevent agitation and distress, preserve patients' independence, and prevent institutionalisation arising from aggressive behaviour or accidents.<sup>49</sup>

Pharmacological management of cognitive and behavioural symptoms in mild to moderate AD and DLB include acetylcholinesterase inhibitors: donepezil, rivastigmine, and galantamine which increase the availability of acetylcholine. Their main side effects are a consequence of their action on the parasympathetic system: bradycardia, bronchoconstriction, diarrhoea, and hypersecretion.

Patients who are intolerant to acetylcholinesterase inhibitors or have severe AD may be prescribed memantine (an NMDA receptor antagonist). Memantine is not effective in mild AD.<sup>50</sup>

Antipsychotic drugs and benzodiazepines can be used to manage agitation, aggression or violence after obvious causes (e.g. pain) have been excluded and if

behavioural interventions prove ineffective, but they should be given at the lowest therapeutic dose, and the patient should be monitored for dystonia and extrapyramidal side effects.

Potential complications, such as cerebrovascular accidents following antipsychotic use and disinhibition and muscle relaxation with benzodiazepines, and sedation and falls for both, should be weighed against potential benefits. Behavioural problems are often temporary, so that frequent review of sedating medication is indicated.

## ... and act as a prognostic marker of dementia progression'

With growing numbers of older cognitively impaired patients in the community, GPs will become increasingly adept at diagnosing and managing these patients, preserving their quality of life for as long as possible.

### REFERENCES

- 1 Allan CE, Valkanova V, Ebmeier KP. Depression in older people is underdiagnosed. *Practitioner* 2014;258 (1771):19–22
- 2 Callahan CM, Hendrie HC, Tierney WM. Documentation and evaluation of cognitive impairment in elderly primary care patients. *Ann Intern Med* 1995;122(6):422–9
- 3 Ebmeier KP. Normal cognitive decline or dementia? *Practitioner* 2010;254(1725):23–7
- 4 Luppa M, Sikorski C, Luck T et al. Age- and gender-specific prevalence of depression in latest-life – systematic review and meta-analysis. *J Affect Disord* 2012;136(3):212–21
- 5 Ward A, Arrighi HM, Michels S, Cedarbaum JM. Mild cognitive impairment: disparity of incidence and prevalence estimates. *Alzheimers Dement* 2012;8(1):14–21
- 6 Prince M, Bryce R, Albanese E et al. The global prevalence of dementia: a systematic review and meta-analysis. *Alzheimers Dement* 2013;9(1):63–75 e2
- 7 Petersen RC, Smith GE, Waring SC et al. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol* 1999;56(3):303–8
- 8 Bruscoli M, Lovestone S. Is MCI really just early dementia? A systematic review of conversion studies. *Int Psychogeriatr* 2004;16(2):129–40
- 9 Fratiglioni L, Launer LJ, Andersen K et al. Incidence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. *Neurology* 2000;54(11 Suppl 5):S10–5
- 10 Lobo A, Launer LJ, Fratiglioni L et al. Prevalence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. *Neurology* 2000;54(11 Suppl 5):S4–9
- 11 Herrmann LL, Goodwin GM, Ebmeier KP. The cognitive neuropsychology of depression in the elderly. *Psychol Med* 2007;37(12):1693–702
- 12 Kohler S, Thomas AJ, Barnett NA, O'Brien JT. The pattern and course of cognitive impairment in late-life depression. *Psychol Med* 2010;40(4):591–602
- 13 Huang Y, Mucke L. Alzheimer mechanisms and therapeutic strategies. *Cell* 2012;148(6):1204–22
- 14 Valkanova V, Ebmeier KP. Neuroimaging in dementia. *Maturitas* 2014;79(2):202–8
- 15 Jack CR Jr, Knopman DS, Jagust WJ et al. Hypothetical

- model of dynamic biomarkers of the Alzheimer's pathological cascade. *Lancet Neurol* 2010;9(1):119-28
- 16 Negash S, Bennett DA, Wilson RS et al. Cognition and neuropathology in aging: multidimensional perspectives from the Rush Religious Orders Study and Rush Memory And Aging Project. *Curr Alzheimer Res* 2011;8(4):336-40
- 17 Nelson PT, Alafuzoff I, Bigio EH et al. Correlation of Alzheimer disease neuropathologic changes with cognitive status: a review of the literature. *J Neuropathol Exp Neurol* 2012;71(5):362-81
- 18 Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol* 2011;10(9):819-28
- 19 Reitz C, Brayne C, Mayeux R. Epidemiology of Alzheimer disease. *Nat Rev Neurol* 2011;7(3):137-52
- 20 Igoumenou A, Ebmeier KP. Diagnosing and managing vascular dementia. *Practitioner* 2012;256(1747):13-16
- 21 van Swieten JC. Genetic basis of frontotemporal dementia. *Lancet Neurol* 2007;6(10):840-1
- 22 Rolinski M, Ebmeier KP. Tackling dementia in patients with Parkinson's disease. *Practitioner* 2011;255(1736):15-17
- 23 Butters MA, Young JB, Lopez O et al. Pathways linking late-life depression to persistent cognitive impairment and dementia. *Dialogues Clin Neurosci* 2008;10(3):345-57
- 24 National Institute for Clinical Excellence. CG42. Dementia: Supporting people with dementia and their carers in health and social care. NICE. London. 2006
- 25 Brodaty H, Pond D, Kemp NM et al. The GPCOG: a new screening test for dementia designed for general practice. *J Am Geriatr Soc* 2002;50(3):530-4
- 26 Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. *Age Ageing* 2012;41 Suppl 3:iii35-40
- 27 Brooke P, Bullock R. Validation of a 6 item cognitive impairment test with a view to primary care usage. *Int J Geriatr Psychiatry* 1999;14(11):936-40
- 28 Petersen RC, Stevens JC, Ganguli M et al. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2001;56(9):1133-42
- 29 Scheltens P, Leys D, Barkhof F et al. Atrophy of medial temporal lobes on MRI in "probable" Alzheimer's disease and normal ageing: diagnostic value and neuropsychological correlates. *J Neurol Neurosurg Psychiatry* 1992;55(10):967-72
- 30 Morra JH, Tu Z, Apostolova LG et al. Automated 3D mapping of hippocampal atrophy and its clinical correlates in 400 subjects with Alzheimer's disease, mild cognitive impairment, and elderly controls. *Hum Brain Mapp* 2009;30(9):2766-88
- 31 Barber R, Scheltens P, Gholkar A et al. White matter lesions on magnetic resonance imaging in dementia with Lewy bodies, Alzheimer's disease, vascular dementia, and normal aging. *J Neurol Neurosurg Psychiatry* 1999;67(1):66-72
- 32 Tondelli M, Wilcock GK, Nichelli P et al. Structural MRI changes detectable up to ten years before clinical Alzheimer's disease. *Neurobiol Aging* 2012;33(4):825 e25-36
- 33 Roob G, Schmidt R, Kapeller P et al. MRI evidence of past cerebral microbleeds in a healthy elderly population. *Neurology* 1999;52(5):991-4
- 34 Whitwell JL. Voxel-based morphometry: an automated technique for assessing structural changes in the brain. *J Neurosci* 2009;29(31):9661-4
- 35 Addressing global dementia. *Lancet* 2014;383(9936):2185
- 36 Chataway J, Schuerer N, Alsanousi A et al. Effect of high-dose simvastatin on brain atrophy and disability in secondary progressive multiple sclerosis (MS-STAT): a randomised, placebo-controlled, phase 2 trial. *Lancet* 2014;383(9936):2213-21
- 37 Ma M, Uekawa K, Hasegawa Y et al. Pretreatment with rosuvastatin protects against focal cerebral ischemia/reperfusion injury in rats through attenuation of oxidative stress and inflammation. *Brain Res* 2013;1519:87-94
- 38 Moon GJ, Kim SJ, Cho YH et al. Antioxidant effects of statins in patients with atherosclerotic cerebrovascular disease. *J Clin Neurol* 2014;10(2):140-7
- 39 Vaughan CJ, Delanty N. Neuroprotective properties of statins in cerebral ischemia and stroke. *Stroke* 1999;30(9):1969-73
- 40 Wang J, Tan L, Wang HF et al. Anti-inflammatory drugs and risk of Alzheimer's Disease: An updated systematic review and meta-analysis. *J Alzheimers Dis* 2014. Sep 16. [Epub ahead of print] DOI:10.3233/JAD-141506
- 41 Morris MC, Evans DA, Tangney CC et al. Relation of the tocopherol forms to incident Alzheimer disease and to cognitive change. *Am J Clin Nutr* 2005;81(2):508-14
- 42 Brewer GJ. Why vitamin E therapy fails for treatment of Alzheimer's disease. *J Alzheimers Dis* 2010;19(1):27-30
- 43 Farina N, Isaac MG, Clark AR et al. Vitamin E for Alzheimer's dementia and mild cognitive impairment. *Cochrane Database Syst Rev* 2012;11:CD002854
- 44 Barron AM, Pike CJ. Sex hormones, aging, and Alzheimer's disease. *Front Biosci (Elite Ed)* 2012;4:976-97
- 45 Spence RD, Hamby ME, Umeda E et al. Neuroprotection mediated through estrogen receptor-alpha in astrocytes. *Proc Natl Acad Sci USA* 2011;108(21):8867-72
- 46 Elwood P, Galante J, Pickering J et al. Healthy lifestyles reduce the incidence of chronic diseases and dementia: evidence from the Caerphilly cohort study. *PLoS One* 2013;8(12):e81877
- 47 Gates N, Fiatarone Singh MA, Sachdev PS, Valenzuela M. The effect of exercise training on cognitive function in older adults with mild cognitive impairment: a meta-analysis of randomized controlled trials. *Am J Geriatr Psychiatry* 2013;21(11):1086-97
- 48 Forbes D, Thiessen EJ, Blake CM et al. Exercise programs for people with dementia. *Cochrane Database Syst Rev* 2013;12:CD006489.
- 49 Douglas S, James I, Ballard C. Non-pharmacological interventions in dementia. *Advances in Psychiatric Treatment* 2004;10:171-7
- 50 Schneider LS, Dagerman KS, Higgins JP, McShane R. Lack of evidence for the efficacy of memantine in mild Alzheimer disease. *Arch Neurol* 2011;68(8):991-8.

## Useful information

### Age UK

[www.ageuk.org.uk](http://www.ageuk.org.uk)

### Alzheimer's Association

[www.alz.org/uk/dementia-alzheimers-uk.asp](http://www.alz.org/uk/dementia-alzheimers-uk.asp)

### Alzheimer's Research UK

[www.alzheimersresearchuk.org](http://www.alzheimersresearchuk.org)

### Alzheimer Scotland

[www.alzscot.org](http://www.alzscot.org)

### Alzheimer's Society

[www.alzheimers.org.uk](http://www.alzheimers.org.uk)

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