

Early diagnosis beneficial in Alzheimer's disease

Allan CL, Behrman S, Ebmeier KP. Early diagnosis beneficial in Alzheimer's disease.

Practitioner 2013;257 (1757):15-18

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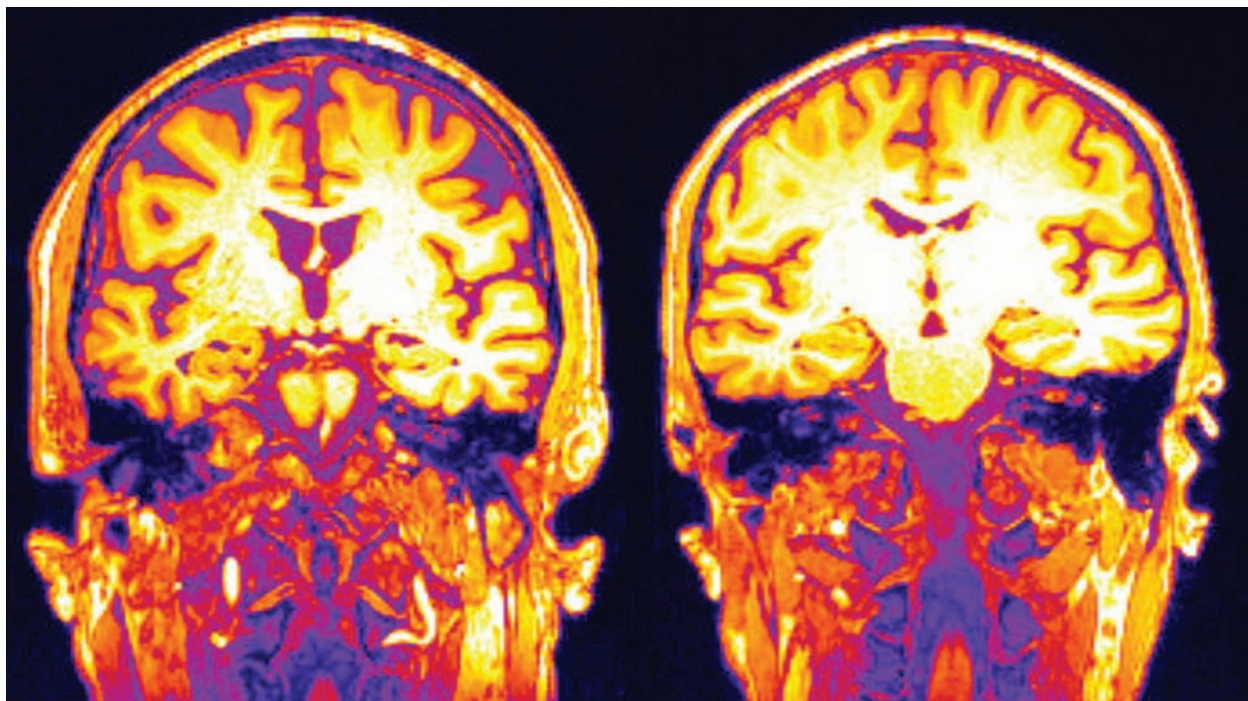
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FIGURE 1

Hippocampal atrophy as organic correlate of amnesia (Scheltens scale 2, left and 0, right). The Scheltens scale²⁶ is a visual estimation of medial temporal lobe size as a correlate of hippocampal atrophy (normal = 0, severe atrophy = 4), which can be used in conjunction with a clinical assessment to give weight to a diagnosis of Alzheimer's disease



How should diagnosis be confirmed?



THE NUMBER OF PEOPLE AGED OVER 65 IS PREDICTED TO DOUBLE BETWEEN 2008 AND 2051,¹ AND WITH THIS

population change the presentation of memory loss will become increasingly common in primary care.

DIAGNOSIS

A diagnosis of Alzheimer's disease requires clinical and pathological evidence.² In clinical practice, GPs should consider a diagnosis of dementia when a patient presents with functional impairment (e.g. needing a greater level of help with activities of daily living, struggling to manage own finances and bills) in addition to at least two changes in cognitive function e.g. short-term memory, language, reasoning, spatial orientation, or personality change. The patient, friends, family or professional carers should have noticed these changes

How should patients be assessed?

for at least six months.

Patients should be referred to a memory clinic to make a formal diagnosis of probable or possible Alzheimer's disease and to exclude other types of dementia including vascular, Lewy body and frontotemporal dementia. When the history, neuro-imaging and cognitive scores are taken into consideration, a clinical diagnosis of Alzheimer's disease can be made with high sensitivity and specificity, see box 1, p16,^{2,3} however, post-mortem confirmation of the clinical diagnosis remains the gold standard.⁴

Early diagnosis should be communicated in a careful and considerate manner, ideally within specialist memory services where treatment, information, care and support are available. The National Dementia Strategy⁵ highlights the benefits of early diagnosis, in particular

What are the evidence-based treatments?

the advantage of improved access to treatment and information for patients and their carers, see box 2, p16. Although early diagnosis is beneficial for the majority of patients, participating in a programme of early diagnosis and treatment must be voluntary, and may not be appropriate for all.

ASSESSMENT

Key to assessment is a careful history of cognitive and functional changes, medical conditions and past psychiatric history. Enquiring about social circumstances is important, as this will have a significant impact on future care. An objective cognitive assessment is important, and in primary care screening tools such as the General Practitioner Assessment of Cognition (www.gpcog.com.au) provide a useful adjunct to justify referral to specialist services.

More thorough measures of



SYMPOSIUM CARE OF THE ELDERLY

ALZHEIMER'S DISEASE

cognition can be performed relatively quickly. The Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE) can both be used to assess cognition, although the MoCA is superior as a global assessment tool, particularly in determining the earlier stages of cognitive decline.⁶ The accuracy of both scales is increased if used in conjunction with a measure of functional deterioration, such as the

Bristol Activities of Daily Living Scale (BADLS).

Patients should have a physical examination and a dementia screen to exclude treatable causes of cognitive impairment, see box 3, below. Structural brain imaging is needed to assist with diagnosis, but more importantly to exclude differential diagnoses including tumours and hydrocephalus. A CT brain scan is used most frequently, but if available,

an MRI scan provides greater anatomical detail, and can be used to support a positive diagnosis of Alzheimer's disease, see figure 1, p15.

Box 1

Clinical diagnosis of Alzheimer's disease (adapted from McKhann et al 2011²)

Possible Alzheimer's disease	Probable Alzheimer's disease
Atypical course, e.g. sudden onset	Insidious onset
Insufficient historical detail or objective cognitive documentation of decline	Clear-cut history of worsening of cognition
	Initial prominent deficits (>1) are for: ● learning and recall of information ● word finding ● object or face recognition ● reasoning, judgment, problem solving
Aetiologically mixed presentation with some evidence of: ● concomitant cerebrovascular disease ● dementia with Lewy bodies ● relevant active comorbidity or medication	No evidence of: ● substantial cerebrovascular disease ● dementia with Lewy bodies ● behavioural variant frontotemporal dementia ● semantic variant primary progressive aphasia or nonfluent/agrammatic variant primary progressive aphasia ● active comorbidity or medication
Increased level of certainty, but alternative aetiology possible, with: ● evidence of a causative genetic mutation (in APP, PSEN1, or PSEN2) ● positive evidence of beta-amyloid (PET or CSF) ● evidence of neuronal injury (CSF tau, FDG-PET, structural MRI)	Increased level of certainty with: ● formally documented decline

Box 2

Benefits of early diagnosis (adapted from Banerjee and Owens, 2009⁵)

- Enables early, planned intervention
- Allows patients and carers to access good quality information
- Enables access to peer support
- Reduces crisis situations
- Delays planned admission to care homes (and helps prevent unplanned admissions)
- May improve quality of life for patients and carers

Box 3

Investigation of suspected dementia⁷

- Blood tests: routine haematology, electrolytes, calcium, glucose, renal function, liver function, thyroid function, vitamin B₁₂ and folate levels
- Mid-stream urine sample, if delirium is suspected
- Chest X-ray and ECG, if clinically indicated
- If there are specific risk factors, consider syphilis serology and an HIV test
- Ideally MRI, or if not available CT, scan of the brain
- SPECT (HMPAO and DaTSCANTM) if diagnosis is not clear

REFERRAL

Referral should be for two purposes: to clarify diagnosis and to initiate treatment. A central triage service should be commissioned which involves specialties with relevant expertise, such as psychiatry, neurology and geriatric medicine. This central service can direct referrals through the most appropriate pathway depending on the nature of a patient's presentation, and local availability of imaging and treatments.

Specialist treatments are currently available for Alzheimer's disease, such as acetylcholinesterase inhibitors and memantine. The management and prophylaxis of cerebrovascular disease is well within the purview of general practice; behavioural and family intervention, community care, safeguarding, and the organisation of care packages may require the involvement of the psychiatric team.

'An MRI scan can be used to support a positive diagnosis of Alzheimer's disease'

TREATMENT

Possible treatment targets are the maintenance of cognitive and functional abilities, management of behavioural and psychological symptoms, and treatment of comorbid affective disorders. Additionally, all carers should receive a specific assessment of their own needs.⁷

Acetylcholinesterase inhibitors and memantine (an NMDA receptor antagonist) both slow the progression of cognitive decline and extend independence in activities of daily living.^{8,9,10,11}

NICE recommends donepezil, rivastigmine or galantamine for mild to moderate Alzheimer's disease, and memantine for severe Alzheimer's disease (or those with moderate disease who are intolerant of acetylcholinesterase inhibitors).¹²

key points

SELECTED BY

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GPs should consider a diagnosis of dementia when

a patient presents with functional impairment in addition to at least two changes in cognitive function e.g. short-term memory, language, reasoning, spatial orientation, or personality change. The patient, friends, family or professional carers should have noticed these changes for at least six months. Patients should be referred to a memory clinic to make a formal diagnosis of probable or possible Alzheimer's disease and to exclude other types of dementia.

Key to assessment is a careful history of cognitive and functional changes, medical conditions and past psychiatric history. An objective cognitive assessment is important, and in primary care screening tools such as the General Practitioner Assessment of Cognition provide a useful adjunct to justify referral to specialist services. Patients should have a physical examination and a dementia screen to exclude treatable causes of cognitive impairment.

Treatment targets are the maintenance of cognitive

and functional abilities, management of behavioural and psychological symptoms of dementia (BPSD), and treatment of comorbid affective disorders. Additionally, all carers should receive a specific assessment of their own needs. Acetylcholinesterase inhibitors and memantine both slow the progression of cognitive decline and extend independence in activities of daily living. NICE recommends donepezil, rivastigmine or galantamine for mild to moderate Alzheimer's disease, and memantine for severe Alzheimer's disease.

With the exception of comorbid affective disorders,

the primary management strategies recommended for BPSD are behavioural, environmental or psychosocial. It is important to make a thorough physical assessment of any patient with dementia presenting with behavioural disturbance, and to search for triggers and maintaining factors. Pharmacological interventions for BPSD have become a source of contention, with the recognition that antipsychotic drugs may not be quite so clinically effective as once believed and can significantly increase the risk of cerebrovascular events and death.

Primary care is optimally placed to screen for

cognitive impairments, to provide essential longitudinal information that will make a diagnosis of dementia safer. Primary care also has a crucial role in primary and, particularly secondary, prevention programmes to tackle excessive weight, lack of activity, smoking, and other lifestyle risk factors for dementia, including Alzheimer's disease, as well as the treatment of medical conditions which increase dementia risk.

These should be commenced soon after diagnosis, following a discussion with the patient, and their family or carers.

Other proposed interventions, such as vitamin E, nimodipine, folic acid and ginkgo biloba are ineffective or have adverse effects which outweigh any potential benefit.¹³

Psychosocial interventions for Alzheimer's disease lack a robust evidence base. NICE recommends cognitive stimulation, which involves activities with some degree of cognitive processing, often in a social context, for those with mild to moderate Alzheimer's disease.^{7,14} There is insufficient evidence to recommend more structured, individually tailored therapies such as cognitive training or cognitive rehabilitation.¹³

Behavioural and psychological symptoms of dementia (BPSD) cover a variety of symptoms, and therefore require diverse management strategies. With the exception of comorbid affective disorders, the primary management strategies recommended for BPSD are behavioural, environmental or psychosocial.⁷

Evidence from case series and small non-randomised trials supports the use of: aromatherapy, multisensory stimulation, animal-assisted therapy, massage, and therapeutic use of music and/or dancing.

It is important to make a thorough physical assessment of any patient with dementia presenting with behavioural disturbance, and to search for triggers and maintaining factors. A study of patients with dementia in nursing homes found a significant reduction in agitation in the group started on analgesia, suggesting that some patients may be agitated in response to physical pain.¹⁵

Pharmacological interventions for BPSD have become a source of contention, with the recognition that antipsychotic drugs, which are prescribed for agitation and psychosis in dementia without strong cost-benefit evidence,¹⁶ may not be quite so clinically effective as once believed.¹⁷ Furthermore, they can significantly increase the risk of cerebrovascular events and death.¹⁸ NICE recommends reserving antipsychotics for psychosis or agitation in dementia only after a number of precautions, including a careful risk-benefit analysis, discussion with the patient and carers, and careful monitoring.⁷ Other psychotropic

medication has been proposed for BPSD, including memantine,¹⁹ but evidence of efficacy in a clinical population is, at present, lacking.²⁰

RECENT DEVELOPMENTS

The neuropathology of Alzheimer's disease is relatively well described, however, disease modifying treatments have not yet been successful. A vaccine against beta-amyloid peptide in Alzheimer's plaques was designed with the intention of boosting amyloid clearance and therefore slowing disease progression. Although animal models suggested this would be a fruitful strategy, unfortunately in humans, the phase II trial had to be stopped because some participants developed meningoencephalitis, although there had been some response in those with higher antibody levels.²¹

Other immunotherapies are being considered in the light of this trial, with the hope that using smaller fragments of beta-amyloid or direct administration of antibodies will lead to fewer adverse events.²² The aggregation of tau has been proposed as a further target for disease modifying treatments and a phase III trial of methylthioninium chloride (methylene blue), which interferes with the aggregation of tau has been launched, after positive results from the phase II trial.²³

Other symptomatic treatments considered include latrepirdine, an antihistamine with cholinesterase inhibitory and possible neuroprotective properties, which produced promising results in phase II trials in Russia, but these results were not replicated in phase III trials.²⁴ Trials of huperzine A, a plant extract with acetylcholinesterase inhibitory properties, as well as potentially shifting metabolism of the amyloid precursor protein to a non-amyloidogenic pathway, are underway.²⁴

Further research is warranted to compare and combine psychological approaches, such as cognitive stimulation therapy, with acetylcholinesterase inhibitors.¹³

PRIMARY CARE TEAM

Dementia is a growing problem, partly because people are living longer and also because the baby boomer generation is entering old age. Therefore, any advances in the treatment and management of dementia are likely to be devolved »

quickly to primary care. For example, the first of the treatments used in Alzheimer's dementia, the acetylcholinesterase inhibitors, are currently initiated in specialist clinics, but are likely to be devolved to primary care in the foreseeable future. It will, therefore, be essential for the whole primary care team to stay abreast of developments and acquire, or further develop, the skills needed to support patients with dementia.

'All carers should receive a specific assessment of their own needs'

Primary care is optimally placed to screen for cognitive impairments, e.g. by administration of the MoCA as a standard screen in the elderly, to provide essential longitudinal information that will make a diagnosis of dementia safer. Primary care also has a crucial role in primary and, particularly secondary, prevention programmes to tackle excessive weight, lack of activity, smoking, and other lifestyle risk factors for dementia including Alzheimer's disease.²⁵

Equally important is the treatment of medical conditions, which increase dementia risk, e.g. hypertension, diabetes, cardiovascular disease, and the treatment and prevention of complicating physical disease, including vaccination for influenza or pneumonia.

Primary care should also provide a hub of information, with easy referral pathways into social work, voluntary agencies and further clinical resources to promote better health for patients, and their carers.

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Useful information

Alzheimer's UK
www.alzheimers.org.uk

Alzheimer's Research UK
www.alzheimersresearchuk.org

Age UK
www.ageuk.org.uk

Living well with dementia: A national dementia strategy (2011)
www.dh.gov.uk/health/2011/07/dementia-strategy/

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