

# Diagnosing dementia

Although an age-related decline in cognitive ability is noted in the writings of Ancient Egyptian, Roman and Greek authors, dementia has only been considered as a pathological process since the 17th century. Since then, the emergence of psychiatric classification, the discovery of biomarkers and the development of individual aetiological criteria have contributed to the ongoing evolution of the dementia concept, perhaps best evidenced by the serial revisions of the dementia syndrome in successive editions of *International Classification of Diseases* (ICD) and the *Diagnostic and Statistical Manual of Mental Disorders* (DSM).

Despite its rise to prominence in medical, social and political agendas alike, dementia remains under-recognized, particularly in the acute hospital setting; Sampson et al (2009) reported that 42% of acute medical admissions over 70 years old had dementia, although only half of these cases had been formally diagnosed.

This article discusses key components of the diagnostic process for dementia, important differential diagnoses, and considers rating scales and tools which aid the assessment in the acute hospital environment.

## Clinical assessment

Despite the evolution of dementia over the past century, the core characteristics described

by Emil Kraepelin remain: progressive cognitive impairment (representing a decline in previous abilities) sufficient to affect everyday functioning that persists, differentiating dementia from the more acute, and usually transient, impairments of delirium.

In a general hospital setting, the identification and diagnosis of the dementia syndrome is usually best attempted before consideration is given to subtype diagnosis later in a specialist setting. The main diagnostic subtypes are Alzheimer's disease, vascular dementia, dementia with Lewy bodies and frontotemporal dementia. While this review discusses relevant features of each of these, an understanding of subtypes is best achieved by consulting their respective criteria (Román et al, 1993; McKeith et al, 2005; McKhann et al, 2011; Rascovsky et al, 2011).

Central to dementia diagnosis is a comprehensive clinical history, using as many sources of information as possible. No single neuroimaging investigation or cognitive test is sufficient for making a dementia diagnosis. In particular, retrieval of an accurate collateral history is essential, as the need to demonstrate evidence of a decline from previous cognitive ability and functioning requires a thorough understanding of the patient's premorbid state.

Patients in whom dementia is suspected should be referred to specialist memory assessment services (National Institute for Clinical Excellence, 2006), often provided by mental health and geriatric medicine teams. These services provide multidisciplinary person-centred care to support patients and their carers through all stages from diagnosis to planning for the future.

## Cognitive impairment

Although amnesia was previously a required deficit for dementia diagnosis, this is no longer the case. Neither the National Institute on Aging–Alzheimer's Association (NIA-AA) nor DSM-5 criteria require the presence of amnesia for a diagnosis of all-cause dementia to be made; rather, impairment in any two

of five cognitive domains is sufficient (*Figure 1*). Assessment of deficits in these domains is facilitated by the use of cognitive rating scales. Despite these changes to criteria, however, retrospective memory loss remains, clinically, the most characteristic impairment of dementia.

Of the many cognitive rating scales available, only the Abbreviated Mental Test Score (Jitapunkul et al, 1991) had more than a single study examining its properties included in a meta-analysis for dementia screening in general hospital inpatients, with a sensitivity of 81%, and specificity of 84% reported (Jackson et al, 2013). Shorter than the Folstein Mini-mental state examination (MMSE) (Folstein et al, 1975), it is also freely available to use without the copyright restrictions that the MMSE has been subject to in recent years.

The MMSE nevertheless remains the most commonly used cognitive measurement in clinical practice, although it is better suited to assessment within specialist services. It is succinct and covers most of the necessary domains but, along with other cognitive scales, does not have a cut-off score sufficient for diagnosis. The MMSE poorly assesses executive functioning and so the clock drawing task is frequently used as an adjunct. The Montreal Cognitive Assessment (Nasreddine et al, 2005) is comparable in length to the MMSE but also includes frontal lobe tests and is more sensitive to mild cognitive impairment. The Addenbrooke's

**Figure 1. Impairment in two of the five cognitive domains listed by National Institute on Aging–Alzheimer's Association is required for dementia diagnosis. From McKhann et al (2011).**

- Impaired ability to acquire and remember new information
- Impaired reasoning and handling of complex tasks, poor judgement
- Impaired visuospatial abilities
- Impaired language function
- Changes in personality, behaviour or compartment

**Dr Joseph PM Kane** is Clinical Research Associate in the Institute of Neuroscience, Newcastle University, Newcastle upon Tyne NE4 5PL

**Dr Sarah Richardson** is Alzheimer's Society Clinical Training Fellow in the Institute of Neuroscience, Newcastle University

**Dr Louise Allan** is Clinical Senior Lecturer in the Institute of Neuroscience, Newcastle University

**Professor Alan Thomas** is Professor of Old Age Psychiatry in the Institute of Neuroscience, Newcastle University

Correspondence to: Dr JPM Kane (joseph.kane@newcastle.ac.uk)

Cognitive Examination III (Hsieh et al, 2013) offers a much more comprehensive account of cognitive function, providing subscores for respective domains. However, it is considerably longer and more challenging, making it less suitable for routine use in the acute medical environment.

### Functional impairment

Like cognitive ability, functional impairment must be demonstrated as a decline from the patient's baseline functioning and is thus best informed by a collateral history. Successive iterations of diagnostic criteria have lowered the degree of impairment required to satisfy functional impairment; where impairment in basic activities of daily living (e.g. washing, dressing) had previously been necessary, loss of independence in more complex instrumental activities of daily living, like household financial management or navigating public transport, can now represent impairment sufficient to meet a diagnosis of dementia (McKhann et al, 2011). Again, rating scales can help to identify the presence of functional impairments. The Bristol Activities of Daily Living Scale (Bucks et al, 1996) can help quantify a patient's functional ability.

As for cognitive ability, clinical judgement is required to determine whether or not reported deficits represent a decline in ability. For example, it is not uncommon for tasks like meal preparation or financial management to have been the domain of the patient's spouse before the onset of cognitive impairment, and therefore not be a meaningful measure of baseline functioning. When determining loss of function it is crucial to distinguish changes which are the result of physical impairments from those which result from cognitive decline, since only the latter are relevant to dementia diagnosis.

### Delirium

As the main differential diagnosis in the patient in whom dementia is suspected, every attempt should be made to exclude delirium before a diagnosis of dementia is made. Highly prevalent in the acute hospital setting, delirium affects 29–64% of medical inpatients (Inouye et al, 2014) but is underdiagnosed, with 72% of cases going undetected (Collins et al, 2010).

Delirium is characterized by acute onset, over days or hours, in contrast to the months or years suggestive of dementia. Therefore informant information about functioning

before the illness leading up to hospital admission is crucial to distinguishing delirium from dementia; the Informant Questionnaire on Cognitive Decline in the Elderly (Jorm and Jacomb, 1989) can be helpful in determining changes in the patient's cognitive ability based on collateral report.

Dementia is a major risk factor for delirium and so delirium commonly occurs in addition to a pre-existing (but sometimes undiagnosed) dementia. Thorough assessment and follow up of these patients should occur, whenever possible, in the community setting following discharge. Adequate time must be afforded for resolution of delirium in such cases, particularly if other factors likely to influence cognitive impairment are implicated. In those with pre-existing dementia, seemingly innocuous factors such as constipation, or the distress suffered as a consequence of it, may precipitate or exacerbate delirium, often in the absence of derangement of routine blood investigations. Recently commenced medications should be closely scrutinized, with anticholinergic or opiate agents frequently implicated.

Frequent and rapid fluctuations in mental state, in contrast to the more gradual changes observed in dementia, are observed in delirium, although fluctuations are also a core feature of dementia with Lewy bodies (McKeith et al, 2005). Visual hallucinations and delusions are also characteristic of both dementia with Lewy bodies and delirium, further underlining the importance of careful exploration of the clinical course of such features, preferably with a reliable informant, and a thorough neurological examination to assess for the presence of parkinsonian features.

Sustained attention deficits are the hallmark neuropsychological characteristic of delirium and a relatively consistent feature during the course of an episode of delirium. Although this may be demonstrated through impairment in the MMSE's 'serial sevens' task or the attentional subsection of the Addenbrooke's Cognitive Examination Revised (ACE-R), the presence of severe attentional deficits may make it difficult for either to be completed.

Delirium usually resolves within a few days to weeks, although in many cases resolution can take up to 6 months. However, there is growing evidence that delirium is not as transient and benign

as previously thought, with evidence that delirium increases the risk of developing dementia eightfold (Davis et al, 2012).

### Depression

Depressive illness is an important consideration as a non-cognitive feature of dementia, as a differential diagnosis for dementia and as a risk factor for dementia (Bennett and Thomas, 2014); late-onset depression is associated with a twofold increased risk of developing dementia (Ownby et al, 2006).

It is well recognized that cognitive impairment is a core feature of depressive illness in patients of any age and such deficits are more severe in late life depression (Thomas et al, 2009). While consideration should therefore be given to the possible presence of depression, only when depression is itself severe is the cognitive impairment likely to be confused with dementia.

While depression is commonly observed as a feature of both vascular dementia and dementia with Lewy bodies, other features of dementia subtypes can also be mistaken for presentations of mood disorders. Spontaneous, short-lived episodes of weeping or elevated mood can suggest the presence of emotional lability associated with cerebrovascular disease, while elevated mood can be indicative of frontal dementias. Apathy is prevalent in all subtypes, even at the early stages (Mega et al, 1996) and is frequently mistaken for depression; they should be distinguished by the presence of sadness and anhedonia in depression.

### Physical examination and investigations

Patients with suspected dementia should undergo thorough physical examination, with particular scrutiny paid to the neurological assessment; not only to determine the presence of reversible dementias, but also to recognize the characteristics of dementia subtypes such as dementia with Lewy bodies and frontotemporal dementia.

Spontaneous parkinsonism, a core feature of dementia with Lewy bodies, should encourage examination of pyramidal and extra-pyramidal motor systems, which might also determine evidence of vascular dementia or motor neurone disease. Myoclonus may indicate epilepsy or Creutzfeldt–Jakob disease. Gait assessment can identify a shuffling gait (dementia with Lewy bodies)

as well as the broad-based gait of normal pressure hydrocephalus, while examination and characterization of any tremors can also be invaluable in determining underlying pathology. Frontal gait ataxia may indicate the diagnosis of vascular dementia.

Reflexes are often challenging to assess in patients with cognitive impairment, but the characteristic presence of primitive reflexes (grasp, sucking and snout reflexes) in frontal dementias can be a helpful diagnostic sign, although they are common in advanced dementia of all subtypes. Sensory examination, also difficult to determine in patients with cognitive impairment, may reveal abnormalities suggestive of cerebrovascular lesions, peripheral diabetic neuropathy or vitamin B<sub>12</sub> deficiency, as well as the important, if rarer, subacute combined degeneration of the spinal cord.

Full blood count, erythrocyte sedimentation rate or C-reactive protein, renal function, thyroid function, calcium, glucose, vitamin B<sub>12</sub>, serum folate, and liver function tests are helpful before secondary referral as a means of excluding systemic illnesses that might cause, or exacerbate, cognitive impairment. Other tests, such as fasting lipids, syphilis serology, HIV testing, mid-stream urine, chest X-ray and electrocardiography are used if indicated by clinical findings, rather than forming part of an initial screen.

The National Institute for Clinical Excellence (2006) advocates the use of computed tomography or magnetic resonance imaging for exclusion of intracranial pathology like tumours, normal pressure hydrocephalus and subdural haematomas. Magnetic resonance imaging can also be useful in providing coronal views of the hippocampi that allow the identification of the atrophy characteristic of Alzheimer's disease; modern computed tomography scanners can often provide coronal reconstructions of the hippocampi to help in the same way. Magnetic resonance imaging can also be helpful in detecting more subtle neuropathological changes, like frontal lobe atrophy, suggestive of frontotemporal dementia, and cerebrovascular disease in the white matter, like lacunar infarcts and ischaemic white matter disease.

Functional perfusion imaging with single photon emission computed tomography and positron emission tomography where available, can highlight characteristic patterns for the different pathological causes

of dementia, but are advisable only after consultation with specialist dementia services.

## Conclusions

Dementia diagnosis in the acute inpatient environment is challenging, particularly given the high prevalence of delirium among medical admissions, and accessing local specialist services following discharge is strongly advised. A comprehensive clinical history, built around the framework of identifying cognitive impairment in two domains and functional impairment sufficient to interfere with independence, and the exclusion of a diagnosis of delirium, provides the most effective approach to dementia diagnosis, after which subtype diagnosis may follow. **BJHM**

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## KEY POINTS

- Dementia is characterized by cognitive impairment, representing a decline in previous abilities, adversely affecting everyday functioning, and differentiated from delirium.
- The presence of depression, and its relationship to cognitive impairment, should also be considered.
- A thorough clinical history with access to a reliable informant is crucial and referral to specialist memory services recommended.
- Amnesia, while common in Alzheimer's dementia, need not be present for dementia diagnosis to be applicable; rather, impairment in two of five cognitive domains is sufficient for diagnosis.
- After identification of 'all-cause dementia', subtype diagnosis may follow.

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