Approach to assessment of cognitive disorders

Masud Husain

Dept Experimental Psychology & Nuffield Dept Clinical Neurosciences, University of Oxford
Take a history from patient and someone who knows them

*Probably the most crucial part of the assessment*

- Often best, if possible, to start with both the patient and an informant who knows them well
- I start by taking a brief history from the patient
- Put them at ease. Listen carefully and observe how the patient expresses themselves
- What is the interaction between patient and informant?
Take a history from patient and someone who knows them

*Probably the most crucial part of the assessment*

- Often best, if possible, to start with both the patient and an informant who knows them well
- I start by taking a brief history from the patient
- Put them at ease. Listen carefully and observe how the patient expresses themselves
- What is the interaction between patient and informant?
- Then take the history from the informant alone, without the patient in the room
- Did the patient fail to mention key facts?
- Now take a brief history independently from the patient
- Check whether the two accounts are concordant
- Is the patient appropriate in their interactions with you? Are they slow to respond?
- Are they overly familiar, disinhibited, indifferent, low in mood?
Key points to extract

*They’re functions that are thought to be deployed when control needs to be exerted*

- What are the problems – if any – as far as the patient and informant are concerned?
- How long has there been a problem?
- Is it progressive? Or was it sudden-onset and has been stable since? Does it fluctuate?
- How seriously do they impact on everyday life? What’s the worst thing that’s happened?
Key points to extract

*They’re functions that are thought to be deployed when control needs to be exerted*

- What are the problems – if any – as far as the patient and informant is concerned?
- How long have they been a problem?
- Is it progressive? Or was it sudden-onset and has been stable since?
- How seriously do they impact on everyday life? What’s the worst thing that’s happened?
- Are there important life events / stresses at work or home? Or in physical health?
- Who is is at home? What are the interactions like?
- Sleep pattern – altered behaviour (e.g. as in REM sleep behaviour disorder), sleep apnoea
- Mood – including ‘biological symptoms’ of depression
- Would people say there has been a change in personality or behaviour?
- Social / emotional engagement
Background history

*Important other factors that might have a bearing*

- **Past medical history** | Vascular risk factors (hypertension, diabetes, smoking, raised cholesterol), systemic disorders, infections (e.g. HIV), sleep disorders, etc.
- **Past psychiatric history** | Anxiety, mood disorders, etc.
- **Drug history** | Prescribed and recreational drug use, alcohol
- **Family history** | Is there a family history of young-onset dementia (<65 yrs age)?
Patient video
Cognitive screen

To obtain a brief overview of cognitive performance across several domains

- There are a range of screening tests which vary in time taken to administer and complexity
- **MMSE** | Mini-mental state examination
- **MOCA** | Montreal Cognitive Assessment
- **ACE** | Addenbrooke’s Cognitive Examination
**ATTENTION**

- Ask: "What is the day?" __________
- Ask: "Which season is it?" ____________
- Ask: "Could you take 7 away from 1000?" I'd like you to keep taking 7 away from each new number until I tell you to stop." ____________
- Stop after five subtractions (93, 86, 79, 72, 65) 
  Score only the third trial. __________

**MEMORY**

- Ask: "Which 3 words did I ask you to repeat and remember?" _______ _______ _______

**FLUENCY**

- Letters
  Say: "I'm going to give you a letter of the alphabet and I'd like you to generate as many words as you can beginning with that letter, but not names of people or places. For example, if I give you the letter "C", you could give me words like 'cat, cry, clock' and so on. But, you can't give me words like Catherine or Canada. Do you understand? Are you ready? You have one minute. The letter I want you to use is the letter "P".
  Score (Score 0 – 2)

<table>
<thead>
<tr>
<th>Letter</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Animals
  Say: "Now can you name as many animals as possible. It can begin with any letter.
  Score (Score 0 – 2)

<table>
<thead>
<tr>
<th>Animal</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MEMORY**

- Name of the woman who was Prime Minister ____________
- Name of the USA president who was assassinated in the 1960s ____________

**LANGUAGE**

- Place a pencil and a piece of paper in front of the subject. As a practice trial, ask the subject to "Pick up the pencil and then the paper." If incorrect, score 0 and do not continue further.
- If the subject is correct on the practice trial, continue with the following three commands below.
  - Ask the subject to "Place the paper on top of the pencil"
  - Ask the subject to "Pick up the pencil but not the paper"
  - Ask the subject to "Pass me the pencil after touching the paper"
  Note: Place the pencil and paper in front of the subject before each command.

**MEMORY**

- Name of the current Prime Minister ____________
- Name of the woman who was Prime Minister ____________
- Name of the USA president ____________

**LANGUAGE**

- Ask the subject to write two (or more) complete sentences about his/her last holiday/weekend/Christmas. Write in complete sentences and do not use abbreviations.
  Give 1 point if there are two (or more) complete sentences about the one topic; and give another 1 point if grammar and spelling are correct.

**MEMORY**

- If you have a chance to learn, we'll be doing that 3 times. I'd like you to repeat the name and address later.

<table>
<thead>
<tr>
<th>1st Trial</th>
<th>2nd Trial</th>
<th>3rd Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>__________</td>
<td>__________</td>
<td>__________</td>
</tr>
</tbody>
</table>

**ATTENTION**

- Score only the third trial. __________

**MEMORY**

- Name of the current Prime Minister ____________
- Name of the woman who was Prime Minister ____________
- Name of the USA president____________

**LANGUAGE**

- Ask the subject to repeat: 'caterpillar'; 'eccentricity'; 'unintelligible'; 'statistician'
  Score if all are correct; score 1 if 3 are correct, and score 0 if 2 or less are correct.

**LANGUAGE**

- Ask the subject to write two (or more) complete sentences about his/her last holiday/weekend/Christmas. Write in complete sentences and do not use abbreviations.
  Give 1 point if there are two (or more) complete sentences about the one topic; and give another 1 point if grammar and spelling are correct.
LANGUAGE
➤ Ask the subject to repeat: 'All that glitters is not gold'

➤ Ask the subject to repeat: 'A stitch in time saves nine'

LANGUAGE
➤ Ask the subject to name the following pictures:

➤ Using the pictures above, ask the subject to:
   • Point to the one which is associated with the monarchy
   • Point to the one which is a marsupial
   • Point to the one which is found in the Antarctic
   • Point to the one which has a nautical connection

LANGUAGE
➤ Ask the subject to read the following words: (Score 1 only if all correct)

   sew
   pint
   soot
   dough
   height

VISUOSPATIAL ABILITIES
➤ Infinity Diagram: Ask the subject to copy this diagram

VISUOSPATIAL
➤ Wire cube: Ask the subject to copy this drawing (for scoring, see instructions guide)

VISUOSPATIAL
➤ Clock: Ask the subject to draw a clock face with numbers and the hands at ten past five. (For scoring see instruction guide: circle = 1, numbers = 2, hands = 2 if all correct)
VISUOSPATIAL ABILITIES
- Ask the subject to count the dots without pointing to them

- Ask the subject to identify the letters

MEMORY
- Ask "Now tell me what you remember about that name and address we were repeating at the beginning"

S C O R E S
- TOTAL ACE-III SCORE

<table>
<thead>
<tr>
<th>Attention</th>
<th>Memory</th>
<th>Fluency</th>
<th>Language</th>
<th>Visuospatial</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>125</td>
<td>125</td>
<td>75</td>
<td>75</td>
</tr>
</tbody>
</table>
Structured information from informant

To obtain a brief overview of cognitive performance across several domains

- Questionnaires for them to fill in, e.g. Cambridge Behavioural Inventory
Cambridge Behavioural Inventory Revised (CBI-R)

For the Carer

Your Name: _____________________________ Today’s date: ___/___/___
Patient’s name: _____________________________ Relationship to the patient:

We would like to ask you a number of questions about various changes in the patient’s behaviour that you may have noticed. It is important that we obtain your view as it will help us in our assessment.

Please read the description of each problem carefully. Then circle the number under the heading “Frequency” that best describes the occurrence of the behavioural change.

Some of the everyday skill questions may not apply, if for instance the person you care for has never done the shopping. Please enter N/A (not applicable).

All questions apply to the patient’s behaviour OVER THE PAST MONTH.

<table>
<thead>
<tr>
<th>Memory and Orientation</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has poor day-to-day memory (e.g. about conversations, trips etc.)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Asks the same questions over and over again</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Loses or replaces things</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Forgets the names of familiar people</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Forgets the names of objects and things</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shows poor concentration when reading or watching television</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Forgets what day it is</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Becomes confused or muddled in unusual surroundings</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Everyday Skills</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Does not want to go out</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has difficulties using electrical appliances (e.g. TV, radio, cooker, washing machine)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has difficulties writing (letters, Christmas cards, lists etc.)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has difficulties using the telephone</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has difficulties making a hot drink (e.g. tea/coffee)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has problems handling money or paying bills</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Self Care</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Has difficulties grooming self (e.g. shaving or putting on make-up)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has difficulties dressing self</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has problems feeding self without assistance</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has problems bathing or showering self</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormal Behaviour</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Finds humour or laughs at things others do not find funny</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has temper outbursts</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Is uncooperative when asked to do something</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shows socially embarrassing behaviour</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Makes tactless or suggestive remarks</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Acts impulsively without thinking</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

Cambridge Behavioural Inventory Revised (CBI-R)

<table>
<thead>
<tr>
<th>Mood</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cries</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Appears sad or depressed</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Is very restless or agitated</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Is very irritable</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Beliefs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sees things that are not really there (visual hallucinations)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Hears voices that are not really there (auditory hallucinations)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has odd or bizarre ideas that cannot be true</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Eating Habits</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prefers sweet foods more than before</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Wants to eat the same foods repeatedly</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Her/his appetite is greater, s/he eats more than before</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Table manners are declining e.g. stuffing food into mouth</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sleep</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep is disturbed at night</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Sleeps more by day than before (cat naps etc.)</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stereotypic and Motor Behaviours</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Is rigid and fixed in her/his ideas and opinions</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Develops routines from which s/he can not easily be discouraged e.g. wanting to eat or go for walks at fixed times</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Clock watches or counts repeatedly</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Uses the same expression or catch phrase</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Motivation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Shows less enthusiasm for his or her usual interests</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shows little interest in doing new things</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Fails to maintain motivation to keep in contact with friends or family</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Appears indifferent to the worries and concerns of family members</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shows reduced affection</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

Any other comments:

Thank you for your time.
Structured information from informant

To obtain a brief overview of cognitive performance across several domains

- Questionnaires for them to fill in, e.g. **Cambridge Behavioural Inventory** or
- Structured interviews, e.g.:
  - **CDR | Clinical Dementia Rating**
  - **NPI | Neuropsychiatric Inventory**
Physical neurological examination

Assists in narrowing the differential diagnosis – the possible diagnoses that fit the case

- Many patients will have no physical neurological signs
- But if present such signs can help to make the diagnosis or differentiate between them

- Gait
- Speech
- Weakness
- Pyramidal or upper motor neuron signs
- Lower motor neuron signs
- Parkinsonism
- Limb apraxia
Physical neurological examination

Assists in narrowing the differential diagnosis – the possible diagnoses that fit the case

Ataxia
Spino cerebellar ataxia (particularly types 2, 12, and 17), paraneoplastic diseases, prion diseases (particularly familial forms and variant CJD), DRPLA (common in Japan), fragile x-associated tremor ataxia syndrome,^

familial British and Danish dementias, mitochondrial disorders, superficial siderosis, neuronal ceroid lipofuscinosis (Kufs disease), Niemann-Pick disease type C, multiple system atrophy (dementia usually mild, if present), Alexander's disease, and multiple sclerosis

Pyramidal signs
Multiple sclerosis, frontotemporal lobar degeneration with motor neuron disease, Alzheimer's disease (some presenilin mutations), spinocerebellar ataxias, phenylketonuria, familial British and Danish dementias, hereditary spastic paraparesis (SPG4), adrenoleukodystrophy, vanishing white matter disease, polyglucosan body disease, polycystic lipomembranous sclerosing leucoencephalopathy (Nasu-Hakola disease)

Dystonia/choria
Huntington's disease (and Huntington's disease-like syndromes 1–3), Kufs disease (characteristic facial dyskinesia), Wilson's disease, neuroacanthocytosis, pantothenate kinase-associated neurodegeneration (neurodegeneration with brain iron accumulation), Lesch-Nyhan syndrome, DRPLA, corticobasal degeneration, neuroferritinopathy, anti-NMDA receptor-mediated limbic encephalitis, variant CJD

Bucco-lingual mutilation
Neuroacanthocytosis, Lesch-Nyhan syndrome

Gaze palsy
Niemann Pick disease type C (vertical supranuclear; early downgaze loss), Gaucher's disease (horizontal supranuclear), progressive supranuclear palsy (vertical supranuclear), mitochondrial disorders, spinocerebellar ataxias (particularly type 2), paraneoplastic disorders, Whipple's disease

Limb apraxia
Alzheimer's disease, corticobasal syndrome

Akinetic-rigid syndrome
Lewy body disease (dementia with Lewy bodies and Parkinson's disease dementia), progressive supranuclear palsy, multiple system atrophy (dementia usually mild, if present), Huntington's disease (particularly juvenile onset), corticobasal degeneration, dementia pugilistica, Wilson's disease, pantothenate kinase-associated neurodegeneration (neurodegeneration with brain iron accumulation), frontotemporal lobar degeneration with parkinsonism-17, Alzheimer's disease (usually advanced)

Peripheral neuropathy
Neuroacanthocytosis, cerebrotendinous xanthomatosis, HIV infection, giant axonal neuropathy, alcohol-related diseases, metachromatic leukodystrophy, porphyria, adrenoleukodystrophy, GM2 gangliosidosis, polyglucosan body disease, Krabbe's disease, sialidosis, Fabry's disease, mitochondrial disorders, spinocerebellar ataxias (particularly type 3)

Myoclonus or early seizures
Prion disease, Alzheimer's disease, Lewy body disease, DRPLA, mitochondrial disorders, Gaucher's disease, GM2 gangliosidosis, neuroserpinopathy, polycystic lipomembranous sclerosing leucoencephalopathy, subacute sclerosing panencephalitis, progressive myoclonic epilepsy syndromes, Kufs disease, Lafora body disease, sialidosis

Deafness
Superficial siderosis, mitochondrial disorders, familial Danish dementia, alpha mannosidosis, sialidosis

Dysautonomia
Lewy body disease, multiple system atrophy, prion disease (familial insomnia), porphyria, adrenoleukodystrophy, anti-NMDA receptor-mediated limbic encephalitis
Patient video
Patient video
Formal neuropsychological assessment

Very few patients undergo this

- This takes time to perform: 1-3 hrs depending upon protocols used at different centres
- History taken and in-depth examination of neuropsychological function performed
- Different centres use different batteries
- Most will try to obtain an estimate of premorbid intelligence (e.g., using NART in the UK)
- Verbal and performance IQ five some general estimates
- Domain specific tests of: attention, memory, visuospatial, language and executive functions commonly used
- In addition, if appropriate, tests of praxis, visual object recognition and semantic knowledge
Clinical diagnosis rests on first defining the syndrome

Ancillary investigations can help refine the diagnosis

- What are the key features of the history – from both patient and informant?
- What are the findings on cognitive assessment?
- Are there any physical signs?
- Most diagnoses are made on the basis of these factors
Investigations

To exclude treatable causes and to find supporting evidence for a clinical diagnosis

- **Screening blood tests**: to exclude, for example, metabolic / hormonal / vitamin / inflammatory / chronic infectious causes
- **Structural brain imaging**, ideally MRI but often CT (to exclude, for example, a tumour)
- **Cerebrospinal fluid (CSF)** examination via lumbar puncture: to exclude inflammatory / infectious cause but also to measure amyloid-beta and tau protein levels
- **FDG PET (fluorodeoxyglucose positron emission tomography) brain imaging** to examine regional brain metabolism
- **Amyloid and / or tau PET brain imaging** in some specialized centres
### What is dementia?

*This is a clinical definition* | Diagnostic and Statistical Manual of Mental Disorders

<table>
<thead>
<tr>
<th>DSM-IV criteria for dementia</th>
<th>DSM-5 criteria for major neurocognitive disorder (previously dementia)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A1.</strong> Memory impairment</td>
<td><strong>A.</strong> Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains*:</td>
</tr>
<tr>
<td></td>
<td>- Learning and memory</td>
</tr>
<tr>
<td></td>
<td>- Language</td>
</tr>
<tr>
<td></td>
<td>- Executive function</td>
</tr>
<tr>
<td></td>
<td>- Complex attention</td>
</tr>
<tr>
<td></td>
<td>- Perceptual-motor</td>
</tr>
<tr>
<td></td>
<td>- Social cognition</td>
</tr>
<tr>
<td><strong>A2.</strong> At least one of the following:</td>
<td><strong>B.</strong> The cognitive deficits interfere with independence in everyday activities. At a minimum, assistance should be required with complex instrumental activities of daily living, such as paying bills or managing medications.</td>
</tr>
<tr>
<td>- Aphasia</td>
<td></td>
</tr>
<tr>
<td>- Apraxia</td>
<td></td>
</tr>
<tr>
<td>- Agnosia</td>
<td></td>
</tr>
<tr>
<td>- Disturbance in executive functioning</td>
<td></td>
</tr>
<tr>
<td><strong>B.</strong> The cognitive deficits in A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning</td>
<td><strong>C.</strong> The cognitive deficits do not occur exclusively in the context of a delirium</td>
</tr>
<tr>
<td><strong>C.</strong> The cognitive deficits do not occur exclusively during the course of delirium</td>
<td><strong>D.</strong> The cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia)</td>
</tr>
</tbody>
</table>
What is dementia?

National Institute of Aging – Alzheimer’s Association guidelines require two domains

1. Interferes with the ability to function at work or at usual activities; and
2. Represents a decline from previous levels of functioning and performing; and
3. Are not explained by delirium or major psychiatric disorder;
4. Cognitive impairment is detected and diagnosed through a combination of (1) history-taking from the patient and a knowledgeable informant and (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing. Neuropsychological testing should be performed when the routine history and bedside mental status examination cannot provide a confident diagnosis.
5. The cognitive or behavioral impairment involves a minimum of two of the following domains:
   a. Impaired ability to acquire and remember new information—symptoms include: repetitive questions or conversations, misplacing personal belongings, forgetting events or appointments, getting lost on a familiar route.
   b. Impaired reasoning and handling of complex tasks, poor judgment—symptoms include: poor understanding of safety risks, inability to manage finances, poor decision-making ability, inability to plan complex or sequential activities.
   c. Impaired visuospatial abilities—symptoms include: inability to recognize faces or common objects or to find objects in direct view despite good acuity, inability to operate simple implements, or orient clothing to the body.
   d. Impaired language functions (speaking, reading, writing)—symptoms include: difficulty thinking of common words while speaking, hesitations; speech, spelling, and writing errors.
   e. Changes in personality, behavior, or comportment—symptoms include: uncharacteristic mood fluctuations such as agitation, impaired motivation, initiative, apathy, loss of drive, social withdrawal, decreased interest in previous activities, loss of empathy, compulsive or obsessive behaviors, socially unacceptable behaviors.

Neurological diseases

Common causes of dementia

Alzheimer’s disease 62%
Vascular dementia 17%
Mixed dementia 10%
Rarer causes of dementia 5%
Dementia with Lewy bodies 4%
Frontotemporal dementia 2%

Alzheimer’s Society (2019b)
Common causes of dementia

Neurological diseases

Alzheimer's disease 62%
Vascular dementia 17%
Mixed dementia 10%
Frontotemporal dementia 2%
Rarer causes of dementia 5%
Dementia with Lewy bodies 4%

Figure 1: Epidemiology of young-onset dementia
Data from the community study of Harvey and colleagues.6
Neurological diseases

Causes of young-onset dementia (<65 yrs old)

Huntington’s disease
Dementia in multiple sclerosis
Dementia in Down’s syndrome
Corticobasal degeneration
Prion disease
Dementia in Parkinson’s disease
Dementia due to carbon monoxide poisoning
Other causes

MANY

Figure 1: Epidemiology of young-onset dementia
Data from the community study of Harvey and colleagues.6

Neurological diseases

*Causes of young-onset dementia (<65 yrs old)*

1 out of 20

people living with dementia are under the age of 65.

---

**Figure 1: Epidemiology of young-onset dementia**

Data from the community study of Harvey and colleagues.

- Alzheimer’s disease 34%
- Vascular dementia 18%
- Other 19%
- Alcoholic dementia 10%
- Dementia with Lewy bodies 7%
- Frontotemporal lobar degeneration 12%

Demographics of dementia

*Increased risk with age*

- **1 in 688 people** under 65 have dementia.
- **1 in 14 people** over 65 have dementia.
- **1 in 6 people** over 80 have dementia.
What is Alzheimer’s disease?

A neurodegenerative condition associated with brain atrophy and amyloid and tau pathology

Figure 2  Light micrograph of Alzheimer disease neuropathology. Section from the cortex of a patient with Alzheimer disease showing tangles and plaques. The intraneuronal tangle (arrow) is stained dark brown with an antibody that specifically targets paired helical filaments. These filaments are also seen as the dense brown material (dystrophic processes) embedded in the extracellular plaque (arrowhead). The lighter reddish staining of the plaque is from another antibody directed specifically against \( \beta \)-amyloid.

But we can’t get a pathological diagnosis unless we perform a brain biopsy which is associated with risks, so we have guidelines for making a clinical diagnosis.

Clinical diagnosis of Alzheimer’s disease

*Doesn’t have to be associated with memory loss, although this is the typical presentation*

Criteria for Probable Alzheimer’s disease (AD)

1. Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
   A. Insidious onset. Symptoms have a gradual onset over months to years, not sudden over hours or days;
   B. Clear-cut history of worsening of cognition by report or observation; and
   C. The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
      a. Amnestic presentation: It is the most common syndromic presentation of AD dementia. The deficits should include impairment in learning and recall of recently learned information. There should also be evidence of cognitive dysfunction in at least one other cognitive domain, as defined earlier in the text.
      b. Nonamnestic presentations:
         - Language presentation: The most prominent deficits are in word-finding, but deficits in other cognitive domains should be present.
         - Visuospatial presentation: The most prominent deficits are in spatial cognition, including object agnosia, impaired face recognition, simultanagnosia, and alexia. Deficits in other cognitive domains should be present.
         - Executive dysfunction: The most prominent deficits are impaired reasoning, judgment, and problem solving. Deficits in other cognitive domains should be present.

Clinical diagnosis of Alzheimer’s disease

Doesn’t have to be associated with memory loss, although this is the typical presentation

Criteria for Probable Alzheimer’s disease (AD)

D. The diagnosis of probable AD dementia should not be applied when there is evidence of (a) substantial concomitant cerebrovascular disease, defined by a history of a stroke temporally related to the onset or worsening of cognitive impairment; or the presence of multiple or extensive infarcts or severe white matter hyperintensity burden; or (b) core features of Dementia with Lewy bodies other than dementia itself; or (c) prominent features of behavioral variant frontotemporal dementia; or (d) prominent features of semantic variant primary progressive aphasia or non-fluent/agrammatic variant primary progressive aphasia; or (e) evidence for another concurrent, active neurological disease, or a non-neurological medical comorbidity or use of medication that could have a substantial effect on cognition.

## Typical presentations of common dementias

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Typical presentation</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alzheimer’s disease (AD)</strong></td>
<td>Memory disorder PLUS other domains affected</td>
<td>MRI: Hippocampal and biparietal atrophy. <strong>CSF:</strong> Raised tau; decreased amyloid-beta. <strong>FDG PET:</strong> Temporoparietal hypometabolism</td>
</tr>
<tr>
<td></td>
<td>BUT note that AD can also present with:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1) Visuospatial deficits and visual agnosia (**PCA</td>
<td>Posterior cortical atrophy**)</td>
</tr>
<tr>
<td></td>
<td>2) Language dysfunction (<strong>logopenic primary progressive aphasia</strong>)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3) Executive dysfunction (<strong>atypical frontal variant AD</strong>)</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular dementia</strong></td>
<td>Executive function deficits and slow processing speed</td>
<td></td>
</tr>
<tr>
<td><strong>Mixed dementia (AD + vascular dementia)</strong></td>
<td>Memory disorder PLUS other domains affected PLUS executive function deficits PLUS slow processing speed</td>
<td>MRI: Hippocampal and biparietal atrophy plus substantial small vessel cerebrovascular disease</td>
</tr>
<tr>
<td><strong>Lewy body dementia (LBD) or Parkinson’s disease dementia (PDD)</strong></td>
<td>Fluctuating attention, executive function and visuospatial deficits, visual hallucinations PLUS possibly physical signs of Parkinsonism</td>
<td>DAT (Dopamine transporter) scan may be abnormal</td>
</tr>
<tr>
<td><strong>Frontotemporal dementia (FTD)</strong></td>
<td>Three different presentations: behaviour variant, progressive non-fluent aphasia, semantic dementia</td>
<td>MRI: Different findings according to different presentations</td>
</tr>
</tbody>
</table>
Structural MRI | Alzheimer’s disease

Bilateral hippocampal atrophy and biparietal atrophy

This can also be observed in PCA (posterior cortical atrophy)

## Typical presentations of common dementias

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Typical presentation</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alzheimer’s disease (AD)</strong></td>
<td>Memory disorder PLUS other domains affected</td>
<td>MRI: Hippocampal and biparietal atrophy. CSF: Raised tau; decreased amyloid-beta. FDG PET: Temporoparietal hypometabolism</td>
</tr>
<tr>
<td></td>
<td>BUT note that AD can also present with:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1) Visuospatial deficits and visual agnosia (PCA</td>
<td>Posterior cortical atrophy)</td>
</tr>
<tr>
<td></td>
<td>2) Language dysfunction (logopenic primary progressive aphasia)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3) Executive dysfunction (atypical frontal variant AD)</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular dementia</strong></td>
<td>Executive function deficits and slow processing speed</td>
<td>MRI: Substantial small vessel cerebrovascular disease</td>
</tr>
<tr>
<td><strong>Mixed dementia (AD + vascular dementia)</strong></td>
<td>Memory disorder PLUS other domains affected and executive function deficits and slow processing speed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MRI: Hippocampal and biparietal atrophy plus substantial small vessel cerebrovascular disease</td>
<td></td>
</tr>
<tr>
<td><strong>Lewy body dementia (LBD) or Parkinson’s disease dementia (PDD)</strong></td>
<td>Fluctuating attention, executive function and visuospatial deficits, visual hallucinations PLUS possibly physical signs of Parkinsonism</td>
<td>DAT(Dopamine transporter) scan may be abnormal</td>
</tr>
<tr>
<td><strong>Frontotemporal dementia (FTD)</strong></td>
<td>Three different presentations: behavioural variant, progressive non-fluent aphasia and semantic dementia</td>
<td>MRI: Different findings according to different presentations</td>
</tr>
</tbody>
</table>
**Structural MRI | Vascular dementia**

*White matter signal change associated with small vessel cerebrovascular disease*

<table>
<thead>
<tr>
<th>Recent small subcortical infarct</th>
<th>White matter hyperintensity</th>
<th>Lacune</th>
<th>Perivascular space</th>
<th>Cerebral microbleeds</th>
</tr>
</thead>
</table>

Example image

See Chapter 25: Biessels & Scheltens in Husain & Schott textbook
## Typical presentations of common dementias

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Typical presentation</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alzheimer’s disease (AD)</strong></td>
<td>Memory disorder PLUS other domains affected</td>
<td><strong>MRI:</strong> Hippocampal and biparietal atrophy. <strong>CSF:</strong> Raised tau; decreased amyloid-beta. <strong>FDG PET:</strong> Temporoparietal hypometabolism</td>
</tr>
<tr>
<td></td>
<td>BUT note that AD can also present with:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1) Visuospatial deficits and visual agnosia (PCA</td>
<td>Posterior cortical atrophy)</td>
</tr>
<tr>
<td></td>
<td>2) Language dysfunction (logopenic primary progressive aphasia)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3) Executive dysfunction (atypical frontal variant AD)</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular dementia</strong></td>
<td>Executive function deficits and slow processing speed</td>
<td><strong>MRI:</strong> Substantial small vessel cerebrovascular disease</td>
</tr>
<tr>
<td><strong>Mixed dementia (AD + vascular dementia)</strong></td>
<td>Memory disorder PLUS other domains affected and executive function deficits and slow processing speed</td>
<td><strong>MRI:</strong> Hippocampal and biparietal atrophy plus substantial small vessel cerebrovascular disease</td>
</tr>
</tbody>
</table>
# Typical presentations of common dementias

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Typical presentation</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Alzheimer’s disease (AD)</em></td>
<td>Memory disorder PLUS other domains affected</td>
<td><strong>MRI</strong>: Hippocampal and biparietal atrophy. <strong>CSF</strong>: Raised tau; decreased amyloid-beta. <strong>FDG PET</strong>: Temporoparietal hypometabolism</td>
</tr>
<tr>
<td>BUT note that AD can also present with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Visuospatial deficits and visual agnosia (PCA</td>
<td><strong>PCA</strong></td>
<td>Posterior cortical atrophy)</td>
</tr>
<tr>
<td>2) Language dysfunction (logopenic primary progressive aphasia)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Executive dysfunction (atypical frontal variant AD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Vascular dementia</em></td>
<td>Executive function deficits and slow processing speed</td>
<td><strong>MRI</strong>: Substantial small vessel cerebrovascular disease</td>
</tr>
<tr>
<td><em>Mixed dementia (AD + vascular dementia)</em></td>
<td>Memory disorder PLUS other domains affected and executive function deficits and slow processing speed</td>
<td><strong>MRI</strong>: Hippocampal and biparietal atrophy plus substantial small vessel cerebrovascular disease</td>
</tr>
<tr>
<td><em>Lewy body dementia (DLB) or Parkinson’s disease dementia (PDD)</em></td>
<td>Fluctuating attention, executive function and visuospatial deficits, visual hallucinations PLUS possibly physical signs of Parkinsonism</td>
<td><strong>DAT (Dopamine transporter) scan</strong> may be abnormal</td>
</tr>
</tbody>
</table>
DAT scan | Parkinson’s / Dementia with Lewy bodies (DLB)

Dopamine transporter scan

Asymmetric involvement often the early hallmark
### Typical presentations of common dementias

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Typical presentation</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alzheimer’s disease (AD)</strong></td>
<td>Memory disorder PLUS other domains affected</td>
<td><strong>MRI</strong>: Hippocampal and biparietal atrophy. <strong>CSF</strong>: Raised tau; decreased amyloid-beta. <strong>FDG PET</strong>: Temporoparietal hypometabolism</td>
</tr>
<tr>
<td>BUT note that AD can also present with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Visuospatial deficits and visual agnosia (**PCA</td>
<td>Posterior cortical atrophy**)</td>
<td></td>
</tr>
<tr>
<td>2) Language dysfunction (<strong>logopenic primary progressive aphasia</strong>)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Executive dysfunction (<strong>atypical frontal variant AD</strong>)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vascular dementia</strong></td>
<td>Executive function deficits and slow processing speed</td>
<td><strong>MRI</strong>: Substantial small vessel cerebrovascular disease</td>
</tr>
<tr>
<td><strong>Mixed dementia (AD + vascular dementia)</strong></td>
<td>Memory disorder PLUS other domains affected and executive function deficits and slow processing speed</td>
<td><strong>MRI</strong>: Hippocampal and biparietal atrophy plus substantial small vessel cerebrovascular disease</td>
</tr>
<tr>
<td><strong>Lewy body dementia (DLB) or Parkinson's disease dementia (PDD)</strong></td>
<td>Fluctuating attention, executive function and visuospatial deficits, visual hallucinations PLUS possibly physical signs of Parkinsonism</td>
<td><strong>DAT (Dopamine transporter) scan</strong> may be abnormal</td>
</tr>
<tr>
<td><strong>Frontotemporal dementia (FTD)</strong></td>
<td>Three different presentations: <strong>behavioural variant</strong>, <strong>progressive non-fluent aphasia</strong> and <strong>semantic dementia</strong></td>
<td><strong>MRI</strong>: Different findings according to different presentations</td>
</tr>
</tbody>
</table>
Cognitive and behavioural ‘fingerprints’

For some dementia syndromes
Cognitive and behavioural ‘fingerprints’

For some dementia syndromes

Cognitive and behavioural ‘fingerprints’

For some dementia syndromes

FTD: Progressive non-fluent aphasia

Cognitive and behavioural ‘fingerprints’ for some dementia syndromes.
Cognitive and behavioural ‘fingerprints’

For some dementia syndromes
Cognitive and behavioural ‘fingerprints’

For some dementia syndromes

[Image of diagrams showing cognitive and behavioural 'fingerprints' for different dementia syndromes, such as Semantic dementia, Alzheimer's disease, Progressive non-fluent aphasia, Behavioural variant frontotemporal lobar degeneration, Posterior cortical atrophy, with detailed breakdowns of cognitive functions like Verbal memory, Speech, Nonverbal knowledge, Action, Literacy, Calculation, Object representation, Executive, Emotion, Nonverbal memory, Space, and loss of function across cognitive domains.]

‘Pseudodementia’

*Important to remember that the commonest cause of cognitive symptoms is NOT dementia*

- Depression and mood disorders
Psychiatric diseases
Associated with cognitive dysfunction
Case History

*Middle aged woman with memory complaints*

- 50yr old left-handed woman presenting with attention and memory complaints
- Looses the thread of conversations, difficulty remembering plans, can no longer multi-task
- Forgets where she puts things down; no major serious events due to memory symptoms
- Low mood, lost her confidence, irritable and less motivated
- Two years previously walked out of her job because it seemed overwhelming
- **Past history** | Depression, fibromyalgia and osteoarthritis
- **Medication** | Antidepressant and analgesics
- **ACE-III score** | Total 65/100 (attention 14/18, memory 9/26, fluency 7/14, language 20/26, visuospatial 15/16).
- **Neurological examination** | Normal – including no evidence of limb apraxia
- **Investigations** | MRI brain and screening blood tests normal
- **Impression** | ‘Pseudeodementia’ / cognitive impairment associated with depression
Case History

*Middle aged woman with memory complaints*

- Returns 16 months later. She is unable to give a history
- Family feel her symptoms have worsened significantly. Can no longer be left on her own
- Has to be prompted to do things and accompanied to events
- She says her mood is good and family say that it fluctuates
- **ACE-III score** | Total 39/100 (attention 7/18, memory 3/26, fluency 1/14, language 19/26, visuospatial 9/16).
- **Neurological examination** | Limb apraxia with difficulty copying meaningless gestures
- **MRI brain** | MRI within normal limits
- **FDG PET scan** | Marked left temporoparietal hypometabolism including left medial temporal lobe. Smaller region of hypometabolism in right posterior temporal parietal zone and left frontal lobe.
- **CSF** | Tau/a-beta amyloid ratio raised at 1.79 (normal range less than 1.00) with raised total tau and reduced a-beta amyloid.
Patient video
Reading

Core text is available online

- **Chapters 10, 11 and 21** cover the assessment and investigation of the person presenting with cognitive symptoms

- **Chapter 33** deals with different presentations of Alzheimer’s disease


For next week

Read the chapter on Disorders of Attention

- **Ch 15** *Disorders of Attentional Processes*
  by Paolo Bartolomeo