Patterns of Cognitive Impairment in Dementia

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Objectives
(1) Review current diagnostic criteria for Alzheimer's disease and other common dementia syndromes
(2) Describe assessment methods and neuropsychological impairments observed in Alzheimer's disease and other dementia syndromes
(3) Discuss challenges in differential diagnosis including reversible conditions that mimic dementia and factors that may influence cognitive test performance

What is dementia? National Institute on Aging-Alzheimer’s Association criteria (2011)

• Presence of cognitive or behavioral symptoms that:
  • Interfere with ability to function at work or at usual activities
  • Represent a decline from previous levels of functioning
  • Is not explained by delirium or major psychiatric disorder
  • Cognitive impairment is detected through a combination of:
    • (1) history-taking from the patient and a knowledgeable informant and
    • (2) 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.

• Cognitive or behavioral impairment involves a minimum of two of the following domains:
  Note: DSM-5 criteria for major neurocognitive disorder identical except impairment in one or more domains

What is dementia? National Institute on Aging-Alzheimer’s Association criteria (2011)

Cognitive Domains and Assessment

<table>
<thead>
<tr>
<th>LANGUAGE</th>
<th>READING ABILITIES</th>
<th>ATTENTION/ WORKING MEMORY</th>
<th>PROCESSING/MOTOR SPEED</th>
<th>LEARNING</th>
<th>MEMORY</th>
<th>EXECUTIVE FUNCTIONING</th>
</tr>
</thead>
<tbody>
<tr>
<td>WAIS-IV Reading</td>
<td>Digit Span</td>
<td>Digit Symbol/Coding</td>
<td>Word List Immediate Recall</td>
<td>Word List Delayed Recall</td>
<td>Trailmaking Test A</td>
<td>Trailmaking Test B</td>
</tr>
<tr>
<td>Boston Naming Test</td>
<td>Judgment of Line Orientation</td>
<td>Letter Number Sequencing</td>
<td>Story Immediate Recall</td>
<td>Story Delayed Recall</td>
<td>Wisconsin Card Sorting Test</td>
<td>Stroop</td>
</tr>
<tr>
<td>Semantic Fluency</td>
<td>Clock Drawing</td>
<td>Block Design</td>
<td>Figure Delayed Recall</td>
<td>Figure Delayed Recall</td>
<td>Letter Fluency</td>
<td></td>
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Differentiation of dementia from MCI

“Determination of whether or not there is significant interference in the ability to function at work or in usual daily activities”

This is inherently a clinical judgment made by a skilled clinician on the basis of the individual circumstances of the patient and the description of daily affairs obtained from the patient and from a knowledgeable informant
**What is “Impaired”?**

68% of population fall within 1 SD
95% of population fall within 2 SD

*Increase in certainty of impairment: Greater the impairment. More tests that are impaired.*

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**Dementia due to Alzheimer’s disease**

**Probable AD**
- Dementia has the following characteristics:
  - Insidious onset - Gradual onset over months to years not sudden over hours or days
  - Clear-cut history of worsening of cognition by report or observation
  - Initial and most prominent cognitive deficits are evidence on history and exam in memory
  - Does not meet criteria for other neurodegenerative disorder (e.g., VaD, DLB, FTD)
  - Off (per DSM-5) has evidence of a causative Alzheimer’s disease genetic mutation from family history or genetic testing (e.g., presenilin 1 or 2 or APP)

**Possible AD**
- Typical course (e.g., sudden onset or no evidence of progressive decline)
- Etiologically mixed presentation
- Concomitant cerebrovascular disease (e.g., history of stroke temporally related to cognitive impairment, presence of multiple or extensive infarcts or severe white matter hypointensities)
- Features of dementia with brain atrophy
- Another neurological disease or medical conditions/medications that could substantially affect cognition

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**Memory impairment in AD – “Cortical pattern”**

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<th>PRESENTATION</th>
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<th>DELAYED RECALL</th>
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<tr>
<td>LEARNING/ENCODING</td>
<td>RETENTION/STORAGE</td>
<td>FROM STORAGE</td>
</tr>
<tr>
<td>NEW INFORMATION</td>
<td>INFORMATION</td>
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1. Rapid forgetting
2. Information still not accessible even when reduce retrieval demands via recognition test
3. Reduced primacy effect (e.g., more difficulty recalling beginning of word list)
4. More likely to produce intrusion errors

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**Memory impairment in non-AD – “Subcortical pattern”**

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1. Able to learn and store information, but difficulty retrieving from storage resulting in delayed recall impairment
2. Information is accessible when reduce retrieval demands via recognition test

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**Semantic memory and executive functioning impairments in typical AD**

- **Semantic Memory**
  - Language impairment
  - Loss of general knowledge
- **Executive Functioning**
  - Set-shifting
  - Novel problem-solving

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**Clinical case example**

- 81 year-old gentleman diagnosed with a mild neurocognitive disorder (mild cognitive impairment) 1.5 years ago with deficits in delayed memory, but only mild functional changes (e.g., needs reminders for medications).
  - Had a brain injury a few months prior to that evaluation during an MVA resulting in subarachnoid and frontal-temporal lobe hemorrhage and confusions.
  - However, wife reported concern about memory loss prior to the injury
  - Had a brain injury a few months prior to that evaluation during an MVA resulting in subarachnoid and frontal-temporal lobe hemorrhage and confusions.
  - Recommended to return for follow-up evaluation to assess progression of symptoms

At the current appointment, patient denied any problems with memory or other cognitive abilities. This was in contrast to his wife who reported continued cognitive and functional decline during the past 1.5 years, including frequent repetitive statements, forgetting to pay bills, unable to use new appliances, wearing the same clothes and not showering regularly, and increased sleeping. He had difficulty describing what he does in a typical day, just noting that he takes a short nap in the afternoon.
COGNITIVE PATTERNS IN DLB

“Although dementia screens such as the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment are useful to characterize global impairment in DLB, neuropsychological assessment should include tests covering the full range of cognitive domains potentially affected. Disproportionate attentional, executive function, and visual processing deficits relative to memory and naming are typical.”

McKeith et al. (2017) Neurology

COGNITIVE PATTERNS IN DLB

• Disproportionately severe visuospatial and visuo-constructive deficit in patients with DLB compared to those with AD
• The spatial and perceptual difficulties of DLB often occur early
• Useful tasks may include:
  - Figure copy (e.g., intersecting pentagons, complex figure copy)
  - Visual assembly (e.g., block design, puzzle tasks)
  - Spatial matching (e.g., line orientation, size matching tasks)
  - Perceptual discrimination (e.g., incomplete figures, incomplete letters)

FDG/PET occipital hypometabolism correlates with visual cortex neupathology in DLB. Larger studies, earlier in disease suggest sensitivity (70%) and specificity (74%) slightly lower than needed for an indicative biomarker

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CLINICAL CASE EXAMPLE

• Summary: Patient's continued cognitive and functional decline are consistent with a major neurocognitive disorder (dementia). Although the prior brain injury may have exacerbated symptoms, his progressive worsening of symptoms during the past 1.5 years provides evidence for an underlying neurodegenerative disorder. His cognitive profile of rapid forgetting are suggestive of Alzheimer's disease.
COGNITIVE PATTERNS IN DLB

MEMORY AND LANGUAGE

- Memory and object naming tend to be less affected in DLB, although some patients' difficulties may be secondary to speed or retrieval task demands.
- Best evaluated through story recall, verbal list learning, and confrontation naming tasks.

Relative preservation of medial temporal lobe in DLB.

MEMORY AND LANGUAGE

Vascular Dementia (VaD) – Diagnostic Criteria

1. Memory impairment + at least one other domain
2. VAD Impairment
3. Evidence of CVD
4. Causal relationship between dementia & CVD

Vascular Dementia: NINDS- AIREN (1993)

- Memory impairment + at least one other domain
- VAD Impairment
- Evidence of CVD
- Causal relationship between dementia & CVD

Vascular Dementia: AHA/ASA (2011)

- Evidence of stroke or subclinical vascular injury
- ≥ 2 cognitive domains + IADL impairment
- Causal relationship between dementia & CVD

Vascular Dementia: DSM-V (2013)

- Major neurocognitive disorder criteria met
- Onset of deficits temporally related to cerebrovascular event
- Evidence of CVD from history, physical exam, and/or neuroimaging sufficient to account for neurocognitive deficits

Both clinical and genetic evidence of CVD is present.

PROBABLE VAD: AT LEAST ONE OF 3 FEATURES

- Imaging evidence
- Temporal relationship or relationship in severity/pattern of impairment and presence of diffuse, subcortical CVD
- No gradually progressive deficits before or after stroke

VASCULAR IMPAIRMENT OF COGNITION CLASSIFICATION CONSENSUS STUDY (VICCCS; SKROOT, 2017)

Proposed mechanisms of cause:
- Cerebral amyloid angiopathy
- Mixed dementia
- White matter hyperintensities
- Microbleeds/microhemorrhages
- Microinfarcts
- Arteritis/vasculitis

PATTERN OF COGNITIVE IMPAIRMENT IN VAD

- Heterogeneous syndrome
- Depends on location/nature of pathology
- No uniform pattern of NP performance will characterize all patients with VaD

- Most common pattern (due to common disruptions to deep frontal white matter, frontal-subcortical circuits, and basal ganglia)
  - Executive dysfunction
  - Slowed processing speed
  - Attention deficits

- More frequent and earlier impairments in mobility, incontinence and depression
- May have greater functional impairment than AD when level of cognitive impairment is equal

Clinical Case Example

- 85 year-old retired mechanic presenting to the clinic due to memory decline that has been particularly noticeable during the past year.
- Several vascular risk factors including history of TIA's (x3 w/ left hand numbness), atrial fibrillation, AAA, cerebral atherosclerosis, iliac artery aneurysm, carotid stenosis, hyperlipidemia, COPD. He has gait ataxia and tremor that are thought to be related to vascular disease per Neurology evaluation.
- MRI head imaging showed stable (since 2015) generalized mild to moderate parenchymal volume loss, mild chronic microangiopathic change, and old microhemorrhage in the right mid temporal lobe.

AD: Memory scores 1 SD lower than executive function scores
- Correlations between memory tests and neuropathology ~.50

AD/VaD mixed cases were neuropsychologically similar to AD

VaD: Executive function not significantly lower than memory scores

- Memory more impaired than executive function in mild to moderate AD
- Two domains may be equally affected in VaD
**Clinical Case Example**

- Diagnostic impression = Major vascular neurocognitive disorder (VaD)
- His cognitive impairment likely reflects a decline from his prior level of functioning, interferes with his ability to perform everyday activities independently, and therefore is consistent with a diagnosis of major neurocognitive disorder. His cognitive profile of impaired attention and executive functioning with milder memory deficits, as well as the presence of significant vascular risk factors and cerebrovascular disease noted on MRI is most consistent with an etiology of cerebrovascular disease (e.g., vascular dementia).

**Reversible causes of cognitive impairment**

- Depression
- Delirium
- Thyroid dysfunction
- Vitamin deficiencies – B12
- Infections
- Medication side effects
  - Anticholinergics
- Sleep disorders (e.g., sleep apnea, insomnia)
- Alcohol abuse
- Chronic pain

**Summary**

<table>
<thead>
<tr>
<th></th>
<th>AD</th>
<th>DLB</th>
<th>VaD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Gradual</td>
<td>Gradual</td>
<td>Temporarily related to stroke, or gradual if related to SVD</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>Gradual</td>
<td>Gradual</td>
<td>“Stepwise” or gradual</td>
</tr>
<tr>
<td><strong>Cognitive pattern</strong></td>
<td>Memory more impaired than other domains (both recall &amp; recognition)</td>
<td>Semantic/language and executive dysfunction</td>
<td>Similar level of impairment on memory and executive functioning measures (intact recognition)</td>
</tr>
<tr>
<td><strong>Additional features that may be present</strong></td>
<td>Visual hallucinations</td>
<td>Parkinsonism</td>
<td>REM-sleep behavior disorder</td>
</tr>
<tr>
<td><strong>Neuropathology</strong></td>
<td>Beta-amyloid plaques</td>
<td>Tau tangles</td>
<td>Amyloid deposits</td>
</tr>
<tr>
<td></td>
<td>Infarcts, hemorrhages, arteriosclerosis, cerebral amyloid angiopathy, hypoperfusion</td>
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Summary

- Although most dementia results from a mixed pathology, evidence suggests there are distinct cognitive patterns across syndromes which may help determine the most prominent etiology.

- Cognitive patterns may assist with differential diagnosis, determining severity of overall cognitive impairment, and providing evidence of strengths and weaknesses that may be useful in advance care planning for those with dementia.

- When determining presence and severity of cognitive impairment, important to consider:
  - Premorbid intellectual functioning level of individual patient – is this a decline?
  - Is the normative sample for tests representative of the patient – similar demographics?
  - Are there any other factors may explain impairment on cognitive tests?

Thank You!

Questions?

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