1. Cognitive Disorders

Cognitive Disorders

Nancy Peterson Moczynski, Ph.D.
2005

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2. What Is Cognition?

What Is Cognition?

- Perception
- Attention
- Memory
- Reasoning
- Problem-solving

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3. Terms

**Terms**

- Syndrome: cluster of signs and symptoms
- Disorder (or disease): underlies a syndrome

4. Examples of Cognitive Syndromes and Disorders

**Examples of Cognitive Syndromes & Disorders**

- Mental Retardation
- Delirium
- Dementia
- Amnestic Disorder
- Down’s Syndrome
- Dilantin Toxicity
- Progressive Multifocal Leukoencephalopathy (PML)
- Korsakoff’s

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5. Delirium

Delirium

- Is an acute confusional state secondary to some medical or neurologic disorder
- Is treated as a medical emergency because the causal disorder may be fatal if untreated

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6. Delirium: Core Deficits

Delirium: Core Deficits

- Cognitive Impairment
- Altered consciousness (reduced awareness of the environment and difficulty maintaining attention)
- Waxing and Waning of Mental Status

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7. Prevalence of Delirium

Prevalence of Delirium

- 20% in the general hospital population
- Higher in elderly
- Common after surgery
- Increased risk among those with dementia or sensory deficits

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8. Associated Signs and Symptoms

Associated Signs and Symptoms

- Delusions
- Hallucinations
- Aggression
- Mood changes
- Sleep/wake problems
- Limited or absent memory formation

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9. EEG

- EEG is very sensitive to delirium
- Findings:
  - Slow background
  - Generalized slowing
  - Used to confirm diagnosis, follow course
  - Limited information about etiology

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10. 24-hour Course

- Acute onset
- Variable conscious awareness
- "Lucid" intervals
- Sundowning

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11. Etiologies

- MI
- Congestive heart failure
- Cardiac dysrhythmia
- Pneumonia
- UTI
- Fluid/electrolyte derangement
- Medication toxicity
- Alcohol/sedative withdrawal
- Etc., etc.

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12. Morbidity

- Falls
- Self-extubation
- Non-compliance
- Dangerous behaviors

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13. Mortality

**Mortality**

- Mostly from underlying disease
- Rate is disease dependent

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14. Course and Prognosis

**Course and Prognosis**

- Reversible w/ treatment of underlying medical condition
- Without Tx, continuing disability or death
- With Tx, improvement in MS in days to weeks

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15. Dementia: DSM IV

Dementia: DSM IV

- Decline in two or more areas of functioning, one of which is memory
- Other areas of decline may include
  - Language (aphasia)
  - Motor (apraxia)
  - Agnosia (failure in recognition)
  - Executive function (Abstract reasoning, Judgment, planning)

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16. Another Definition

Another Definition:

- Acquired impairment which interferes with social or occupational function caused by brain dysfunction

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17. Course

**Course**

- Dementia may be:
  - Progressive
  - Static
  - Remitting

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18. Causes of Dementia

**Causes of Dementia:**

- Alzheimer's Disease
- Vascular disease
- Lewy Body dementia
- Huntington’s Disease
- HIV
- Head Trauma
- Parkinson’s
- Frontal Lobe Dementia

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19. Salient Features of Several Dementias

Salient Features of Several Dementias

- AD: - Memory
- Lewy Body Dementia:
  - Dementia
  - Parkinsonism
  - Psychosis
- Frontal Lobe Dementia
  - Executive System Decline worse than memory
- Huntington’s
  - Choreiform Movements
  - Mood and Personality Changes
  - Cognitive Decline
- HIV Dementia
  - Motor Slowing
  - Slowed info processing
  - Poor abstraction

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20. Prevalence of Dementia

Prevalence of Dementia

- Rates vary from 2.5% to 24.6% of the population over 65
- Prevalence doubles every 5 years after the age of 65

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Alzheimer's Disease: Definition

AD is a progressive dementia of insidious onset, usually between the ages of 40 and 90, most often after the age of 65.

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Alzheimer's: DSM IV Criteria

- Development of multiple cognitive deficits manifest by both
  - memory impairment
  - 1 or more of following
    - aphasia
    - apraxia (inability to perform learned purposeful movements)
    - agnosia
    - disturbance in executive function
- These cause significant impairment in social or occupational function & represent a decline
- Onset is gradual

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23. AD Criteria: Absence of Another Explanation

**AD Criteria: Absence of Another Explanation**

- not due to something else
- not delirium

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24. Prevalence

**Prevalence**

- Of all dementia cases, an estimated 65-72% are attributed to AD alone
  - these figures vary significantly
  - Some estimates are as high as 80%
- Incidence increases sharply with age
  - 10.3% of population over 65
  - 26-47% of those over 85

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25. Genetic Factors

Genetic Factors

- There is some evidence for the contribution of genetic factors
- 1st degree relatives of AD patients have a 2 to 6 times greater risk of developing dementia compared to 1st degree relatives of healthy controls
- In addition, the E4 allele of apolipoprotein E is found in 50-60% of AD cases

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26. Multiple Genetic Loci

Multiple Genetic Loci

- Presenilin 1
- Presenilin 2
- Apolipoprotein E4
- Amyloid precursor protein

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27. Etiology/Pathology: AD

Etiology/Pathology: AD

- AD is characterized by:
  - degeneration of specific nerve cells
  - presence of neuritic plaques
  - presence of neurofibrillary tangles
- Temporal and Parietal lobes are disproportionately involved

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28. Pathology Specifics

Pathology Specifics

- Neurofibrillary Tangles (NFT’s)
  - are intraneuronal lesions made of a mass of proteins
  - the quantity of NFT’s is associated with overall indicators of cognitive impairment
- Senile Plaques (SP’s)
  - made of beta amyloid protein deposits
  - often with glial cells and dystrophic neurites

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29. Location of NFT’s and SP’s

Location of NFT’s and SP’s

- Both are found throughout cortex
- More are found in the hippocampus than other structures
- Found mostly in cells important in afferent (towards CNS) and efferent (away from) information (Layers II and IV)

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30. Location of Cell Loss

Location of Cell Loss

- As disease progresses, fronto/temporal and parietal association areas are increasingly involved
- There is also subcortical neuronal loss in the nucleus basalis of mynert (basal forebrain- subthalamus to base of the 3rd ventricle; chonlinergic innervation) and in the locus coeruleus (dorsal pons; NE)

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31. Clinical Course: AD

Clinical Course: AD

- Dominant Feature: Memory loss
- Pts often present to family MD with absent mindedness (initially ignored) followed by forgetting of day-to-day events, or a tendency to repeat, and possibly word-finding difficulties

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32. Disease progression: AD

Disease progression: AD

- Memory for new events is initially problematic, while memories from the past- i.e. youth and early adult- remain intact

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33. Over time, long-term memory becomes more impaired

**Over time, long-term memory becomes more impaired**

- The patient may become unable to find their way home
- unable to identify voices on the telephone
- ultimately family and friends can no longer be recognized
- Illness ends in death, usually after 8 to 10 years

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34. AD: Neuropsychological Test Findings

**AD: Neuropsychological Test Findings**

- Cognitive Functions most closely associated with AD (Cahn et al., 1995)
  - Memory: auditory and visual delayed
  - Complex/divided attention (Trails B)
  - Naming/language

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35. AD: Memory

**AD: Memory**

- Explicit memory seems to be most affected
  (Carlesimo; Oscar-Berman, 1992)
  - List Learning
  - Story Learning
  - Figure Learning
- Partial deficit in implicit learning of verbal and visuospatial material (priming)
- Implicit visuo-motor skills INTACT (pursuit rotor learning)

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36. Frontal Lobe Dementia: Definition

**Frontal Lobe Dementia: Definition**

- FLD is associated with deterioration in frontal lobe functioning not due to AD pathology
- Variability in the literature suggests that FLD is a heterogeneous disorder
- It is considered by some to be a class of disorders rather than a single entity

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37. FLD: Subtypes

**FLD: Subtypes**

- FLD is also sometimes referred to as **frrontotemporal dementia**
- Subtypes (Defined only at autopsy) include
  - Pick's disease
  - Non-specific Frontal degeneration
  - Frontal degeneration with anterior spinal neuron loss
  - Progressive subcortical gliosis

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38. FLD: Diagnostic Criteria

**FLD: Diagnostic Criteria**

- There are no specific criteria in DSM IV for FLD in general
- For Pick's Disease, Dx is established at autopsy by the presence of Pick bodies

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39. **FLD: Prevalence**

**FLD: Prevalence**

- FLD accounts for 8-10% of non-traumatic cases of dementia
- It has been characterized (e.g. by Mendex, et al., 1996) as one of the most common neurogenerative dementias, particularly among those under age 65
- It appears more prevalent among women than men

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40. **Pathology: FLD**

**Pathology: FLD**

- There is cell loss in the frontal lobes and anterior temporal lobes
- Blood flow in the frontal lobes is low
- In Pick’s disease
  - Pick bodies are present
  - These are intranuronal argyrophilic inclusion bodies

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41. FLD: Symptoms/Clinical Course

FLD: Symptoms/Clinical Course

- Mean age at onset is approximately 54
- Mean duration is 7.6 years, but is HIGHLY variable
- Clinical onset is slow and insidious

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42. Early Personality and Behavior Changes

Early Personality and Behavior Changes

- Disinhibition
- Lack of judgement
- Restlessness
- Irritability
- Impaired control and modulation of emotions

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43. Symptoms in Some Cases

Symptoms in Some Cases Also Include:

- Apathy
- Withdrawal
- Disinterest

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44. FLD: Salient Cognitive Findings

FLD: Salient Cognitive Findings

- perseveration
- selective attention
- set shifting
- concept and strategy formation
- planning
- abstraction
- self-monitoring
- mental flexibility
- response inhibition

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45. **FLD: Relatively Preserved Abilities**

- memory,
- language
- visuo-spatial
- motor capacities
- orientation

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46. **As FLD Progresses:**

- You can see:
  - Frontal release signs
  - Weakness
  - Motor perseveration
  - Impersistance
- In later stages FLD is difficult to distinguish from AD

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47. FLD vs. AD

**FLD vs. AD**

- FLD *worse* on vocabulary and *better* on Block Design and paired associated learning
- In general
  - AD worse on memory
  - FLD worse on executive functions

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48. HIV dementia: Definitions

**HIV dementia: Definitions**

- Mild Cognitive Motor Disturbance (MCMD)
- HIV Associated Dementia (HAD)

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49. **Prevalence**

Prevalence

- MCMD occurs in as many as 25% to 30% of HIV-1 infected individuals in the early symptomatic stage.
- 33-40% of patients with AIDS develop some form of HIV-related cognitive impairment by the time of death.
- Full blown dementia occurs in approximately 15% overall.

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50. **Anatomy/Pathology**

Anatomy/Pathology

- Structures involved are primarily white matter and deep gray matter, with the cerebral cortex relatively free from infection.
- Basal ganglia, thalamus, pons, and brain stem are typically involved.

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51. Anatomy/Pathology

Anatomy/Pathology

- Dementia is related to the presence of virus in the macrophages and multinucleated giant cells.
- There is evidence that some strains of HIV are more neurovirulent than others.
- The pathogenetic mechanisms involved in the production of HIV dementia remain obscure.

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52. Quantitative MRI and Morphometric Studies

Quantitative MRI & Morphometric Studies

- Cerebral atrophy is common
- Loss of neuronal numbers (esp. frontal and temporal)
- Loss of dendritic arborization
- Diffuse pallor of the myelin

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Clinical Course

- WITHOUT Treatment, dementia can be rapidly progressive, with a mean survival of 6 months
- However, progression is quite variable, with some patients remaining only mildly demented until death.

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Cognitive Dysfunction in HAD

- Cognitive deficits may involve:
  - fine motor skills
  - speed of processing
  - attention
  - abstraction
  - ability to shift sets and form concepts
  - memory

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55. Dementias In Summary

**Dementias In Summary**

- Cortical Dementias
  - AD
  - Frontal Lobe Dementia
- Subcortical Dementias
  - HIV Associated Dementia

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56. Alzheimer's Disease

**Alzheimer’s Disease**

- Memory
- Aphasia
- Apraxia

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57. Frontal Lobe Dementia

- Executive System Decline worse than Memory

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58. HAD

- Motor Disturbance
- Slowed Info Processing Speed
- Poor abstraction

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59. Dementias: Salient Features

Dementias: Salient Features

- **AD**: - Memory
- **Frontal Lobe Dementia**
  - Executive System Decline worse than memory
- **HAD**:
  - Motor Disturbance
  - Decreased info. Speed
  - Poor abstraction

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60. Cognitive Disorders: Summary

Cognitive Disorders: Summary

- **Delirium**: usually transient; effects level of conscious awareness and cognition
- **Dementia**: more stable, may be progressive, decline in multiple areas, subcortical and cortical syndromes

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Clinical Vignettes

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