

1. Cognitive Disorders



Cognitive Disorders

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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

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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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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



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



Morbidity

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

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Mortality



Mortality

- Mostly from underlying disease
- Rate is disease dependent

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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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Another Definition



Another Definition:

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

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Course



Course

- Dementia may be:
 - Progressive
 - Static
 - remitting

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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

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

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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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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Multiple Genetic Loci



Multiple Genetic Loci

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

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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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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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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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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; cholinergic innervation) and in the locus coeruleus (dorsal pons; NE)

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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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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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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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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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FLD: Subtypes



FLD: Subtypes

- FLD is also sometimes referred to as **frontotemporal 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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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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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 neurodegenerative dementias, particularly among those under age 65
- It appears more prevalent among women than men

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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 intranuclear argentophilic inclusion bodies

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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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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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Symptoms in Some Cases



Symptoms in Some Cases Also Include:

- Apathy
- Withdrawal
- Disinterest

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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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FLD: Relatively Preserved Abilities



FLD: **Relatively** Preserved Abilities

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

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As FLD Progresses:



As FLD Progresses:

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

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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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HIV dementia: Definitions



HIV dementia: Definitions

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

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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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Anatomy/Pathology



Anatomy/Pathology

- HIV-1 infection affects primarily subcortical and frontostriatal brain processes (Navia, Cho, and Petito, et al, 1986; Harrison, Newman, and Jall-Craggs, et al., 1998).
- 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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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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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



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 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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Dementias In Summary



Dementias In Summary

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

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Alzheimer's Disease



Alzheimer's Disease

- Memory
- Aphasia
- Apraxia

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Frontal Lobe Dementia



Frontal Lobe Dementia

- Executive System Decline worse than Memory

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HAD



HAD

- Motor Disturbance
- Slowed Info Processing Speed
- Poor abstraction

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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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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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