KW 27 : Dementia

Overview of Dementia

- DSM-IV Definition
  - Diagnostic Criteria
  - Exclusions
  - Subtypes
- Alzheimer's
  - Demographic Prevalence
  - Causes
  - Progression
- Parkinson's
- Categorizations:
  - Cortical vs. Subcortical
  - Degenerative vs. Nondegenerative

DSM-IV Cognitive Disorders

- Chapter: "Delirium, Dementia, and Amnestic and other Cognitive Disorders"
- Formerly called "Organic Mental Syndromes and Disorders" in DSM-III
- Types:
  - Delirium
  - Dementia
  - Amnestic Disorder
  - Cognitive Disorder NOS

DSM-IV Delirium

- Delirium : disturbance of consciousness & cognition develops in short timeframe.
  - caused by direct action of physiological condition, drug intoxication or withdrawal, poison
  - usually reversible
  - level of consciousness affected, fluctuating
  - disorientation
  - example: delirium due to extreme alcohol intoxication, delirium due to hypoglycemia

DSM-IV Dementia

- Dementia : development of multiple cognitive deficits, including memory, and at least one of the following: aphasia, apraxia, agnosia, disturbance in executive functioning, not due to delirium.

DSM-IV Dementia : Types

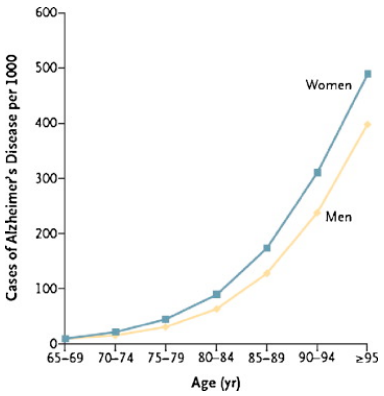
- Types
  - Alzheimer's
  - Vascular
  - HIV
  - Head Trauma
  - Parkinson's
  - Huntington's
  - Pick's
  - Creutzfeldt-Jakob
  - Other Medical Condition
  - Substance-Induced Persisting
  - Multiple etiologies
  - NOS

Dementia : Prevalence

Type	Proportion of all dementias
Alzheimer's	46%
Vascular	22%
Parkinson's	2%
Other (including Mixed)	30%

Prevalence of AD

- 20% of adults aged 80-90
- As many as 50% of adults aged 95+
- Enormous societal cost



DSM-IV Dementia of the Alzheimer's Type

- A: Development of multiple cognitive deficits including
  - memory impairment AND
  - one of the following: aphasia, apraxia, agnosia, disturbance in executive functioning
- B: symptoms cause significant impairment in social/ occupational function and represent a significant decline
- C: course : gradual onset, continuing decline
- D: exclusions:
  - 1. cerebrovascular disease, Parkinson's, Huntington's, other neurological disorders
  - 2. hormonal & vitamin deficiencies, infections (HIV)
  - 3. substance-induced conditions
- E: not due to delirium
- F: not due to other Axis I disorder

DSM-IV Dementia of the Alzheimer's Type

- Exclusions:
- D: not due to...
  - 1. cerebrovascular disease, Parkinson's, Huntington's, other neurological disorders
  - 2. hormonal & vitamin deficiencies, infections (HIV)
  - 3. substance-induced conditions
- E: not due to delirium
- F: not due to other Axis I disorder

DSM-IV Dementia of the Alzheimer's Type

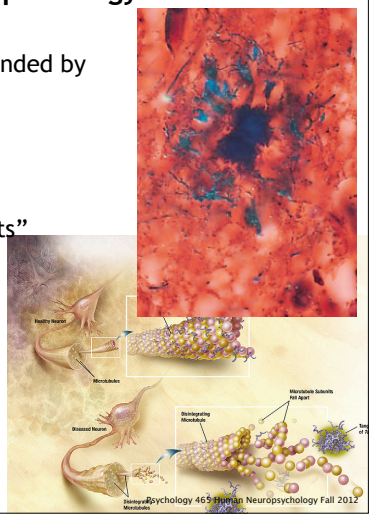
- Subtypes
  - With Early Onset (age < 65)
    - 290.10 Uncomplicated
    - 290.11 With Delirium
    - 290.12 With Delusions
    - 290.13 With Depressed Mood
  - With Late Onset (age >= 65)
    - 290.0 Uncomplicated
    - 290.3 With Delirium
    - 290.20 With Delusions
    - 290.21 With Depressed Mood

DSM-IV Dementia of the Alzheimer's Type

- Notes:
  - DSM-IV diagnosis is purely behavioral
  - Does not consider etiology, neuropathology

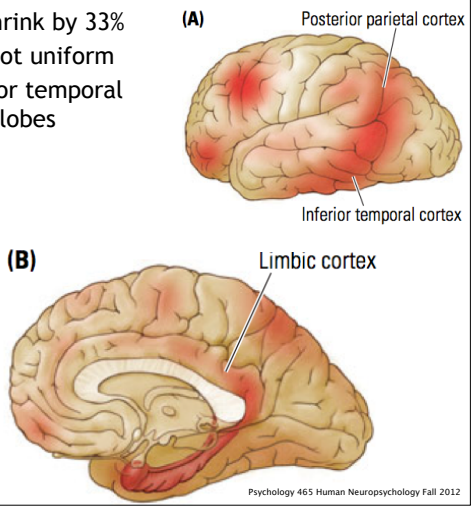
AD Neuropathology

- Neuritic (Amyloid) Plaques
  - central amyloid core surrounded by dead/dying cell fragments
  - not unique to AD
  - mainly in cortex
- Neurofibrillary Tangles
  - aka “paired helical filaments”
  - cortex & hippocampus



AD Cortical Atrophy

- Overall brain may shrink by 33%
- Cortical atrophy is not uniform
  - strongest in inferior temporal cortex and limbic lobes



AD Cortical Atrophy : loss of dendrites

- Much of cortical atrophy is due to dendritic De-arborization
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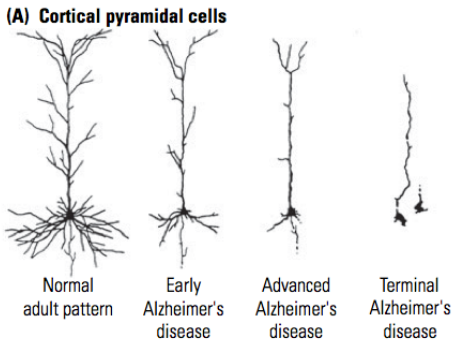


AD Neurotransmitter Changes

- Widespread loss of Acetylcholine
- other NTs also reduced
- complex picture

AD Causes

- Genetics
  - Familial Risk
    - sibling with AD: 3.8% risk
    - parent with AD: 10% risk
  - Genes for beta-amyloid and other precursor proteins are linked
    - genes on chromosome 21
    - Down’s syndrome = Trisomy 21
    - Down’s patients almost always have dementia by age 40
- Hot topic of research

AD Course - 7 year life expetency

Level	Description
Very Mild	Complaints of memory problems (often of losing objects and forgetting names) Clinical interview normal: NP testing may be normal (?)
Mild	Clear but subtle behavioral changes: gets lost, others notice memory problems, reading recall and learning new names poor, loses a valuable object. Social/occupational functioning suffers. Denial/anxiety.
Moderate	Problems with recent events, personal history, serial 7s, finances & travel. Anomia. Denial, flat affect, withdrawal.
Moderate-severe	Needs assistance. Can’t recall own address, some family names. Ox2. Counting backwards by 2s.
Severe	Forgets spouse’s name. Unaware of recent events. Some memory for childhood. Can’t count from 10. Personality change, delusions, apathy.
Very Severe	All verbal abilities lost. Incontinence. Can’t walk.

AD Prevention

- Prevention
  - no currently validated preventions exist
  - some small correlations found with:
    - diet
    - light alcohol use (red wine)
    - NSAIDs
    - THC
-

AD Treatment

- Medications:
  - Acetylcholine agonists : acetylcholinesterase inhibitors
    - four drugs in this class
  - NMDA receptor antagonist
    - prevents glutamate-mediated excitotoxicity (?)
  - Symptom relief
    - antipsychotics, tranquilizers, sleeping medications
      - long-term use has bad outcomes

Ogden Ch. 17: Sophie

- ID & Presenting Problem
  - Sophie 51yo female noticing memory problems, seeks help from her psychologist (who had helped her with her mother's death from AD)
- Background
  - Family Hx: Mother had AD at age 65 and died at age 70
  - Sophie : "strong, vital" journalist, radio talk-show host
- Sx & Hx
  - At age 49 - memory problems (forgetting the plot of a book by the end, unable to do radio interviews from memory)
  - Sought help from psychologist, who did WAIS & Rey Complex Figure.
  - WAIS "normal range" ReyO- 2SD below normal
- Initial Dx: normal aging and "anxiety" from testing : WRONG

Ogden Ch. 17: Sophie

- Sx & Hx continued:
  - after misdiagnosis, over next 18 months, symptoms increased. Fired from her job due to poor performance during radio interviews.
  - depressive symptoms (mild)
  - word-finding difficulties
  - No substance use/abuse/ no medical issues, no toxic exposures, no medicines
- Test results:
  - Medical workup : normal
  - CT : slightly enlarged ventricles for her age

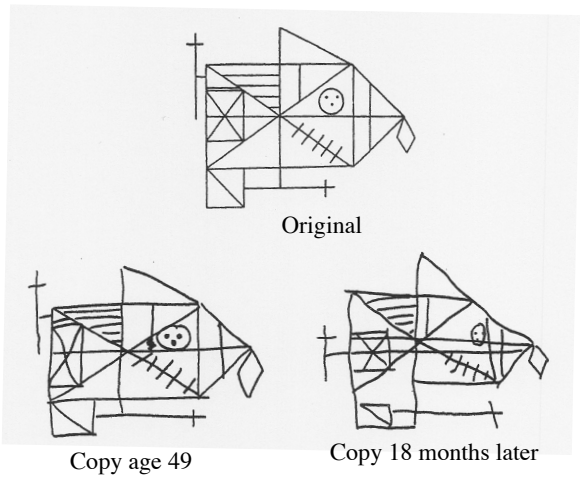
Sophie: Clinical Interview, MSE

- MSE:
  - "tiny woman with dark hair and eyes and delicate facial features"
  - "could have passed for 40 rather than 50"
  - "voice was strong and clear"
  - "vibrant personality"

Sophie: NP Testing

- WAIS IQ
  - FSIQ : subtests 1-2 SD below average (Z scores of -1.0 to -2.0)
  - Lowest scores on Visuo Spatial tests (Block Design, Object Assembly, Picture Arrangement) and tests of Abstract thinking (Similarities, Comprehension)
  - Slowed performance on Digit Symbol.
  - Word-finding difficulties on Vocabulary subtest.
- NART : estimated premorbid IQ : "Superior" (IQ of 120-129, equivalent to a Z score of +1.04 to +2.0)
- Rey Complex Figure test
  - notable worsening over 18 months
  - husband "she used to be very good at sketching"
  - Pt. crying "a small child could do better than that"

Sophie: Rey Complex Figure



Sophie: NP Testing 2

- Rey Figure Memory (45 minute delay)
  - a single rectangle
- Wechsler Memory Test
  - recall about 50% of expected for her age
- Recognition Memory : Words & Faces
  - scored 2SD below average, but thought she had done well
  - (Ogden says "she was not given feedback, and her mood lifted")

Sophie: Interpretation & Diagnosis

- Dx:
  - Alzheimer's disease, based on pattern:
    - memory impairment + other cognitive losses
    - gradual decline
    - mood changes (depression) are secondary to memory symptoms - e.g. not "pseudo-depression"
- Prognosis: poor
- Recommendations
  - counseling for family & Sophie
  - "settling her affairs" - making will, planning for nursing care, writing letters to family members, etc.
- Outcome:
  - steady deterioration, but was able to spend 4 years at home before nursing home then hospice

DSM-IV Dementia due to Parkinson's Disease

- Presence of Dementia, judged to be due to PD
- PD Symptoms
  - tremor
  - rigidity
  - bradykinesia
  - postural instability
  - Dementia in 20-60% of PD patients
  - Cognitive decline often exacerbated by Depression
- Note: the DSM-IV diagnosis is not terribly detailed.

PD Prevalence

- Prevalence:
  - About 0.1% to 1.0% of adults worldwide, risk increases with age
  - About 4% at age 80+

PD Motor Symptoms

- Positive Symptoms
  - tremor at rest
  - muscular rigidity
  - involuntary movements
    - akathesia, tics
- Negative Symptoms - disorders of
  - posture (unable to maintain posture, equilibrium / loss of balance)
  - righting (can't stand up or roll over)
  - locomotion (can't walk normally - shuffle with short footsteps)
  - speech : loss of prosody, gravelly speech
  - akinesia / bradykinesia : slow or lack of motor behavior

PD Cognitive Symptoms

- Up to 60% of PD patients have cognitive/emotional symptoms
- Emotional
  - reductions in libido, motivation, attention. Lack of activity (may sit quietly for hours). Apathy
  - Anxiety
  - Depression (25% having major depression)
- "Subcortical Dementia"
  - cognitive slowing
  - executive functioning
  - memory deficits
    - retrieval rather than learning
    - recognition better than recall

PD Course

- Insidious onset
  - slight tremor or stiffness at first
  - bradykinesia
  - masked facies (flattened affect)
  - stopped posture, shuffling gait
  - speech slows, monotone (lack of prosody)
  - trouble swallowing, drooling
- Progression is variable - typically 5 years from Dx to disability, 10-20 years until incapacitated

PD Causes

- Types:
  - idiopathic
  - postencephalitic
    - sleeping sickness of 1916-1917 to 1927
    - Oliver Sack's book *Awakenings*
  - drug-induced
    - antipsychotics
    - MPTP (bad batch of synthetic MPPP, a synthetic opioid)
- Causes:
  - degeneration of substantia nigra ("black area")
  - loss of dopamine projections to cortex

PD Treatment

- Drugs
  - Dopamine Agonists
    - L-Dopa - converted to dopamine in the brain
      - combined with carbidopa (which prevents peripheral conversion to DA). Patients suffer ON/OFF syndrome with severe motor symptoms (e.g. MJF, RJ)
    - amphetamines
    - MAOIs
  - Anticholinergics
    - block ACh which is overactive in low DA conditions
- Surgery
  - thalamotomy
  - stem cells
  - DBS : deep brain stimulation

PD Prevention

- Prevention:
  - consumption of both coffee and tobacco associated with reduced risk
    - highest caffeine drinkers had up to 80% reduction in risk of PD
    - tobacco, however, causes much other harm

Ogden Ch. 15: Parkinson's Disease : "Robert"

- ID & Presenting Problem
  - RJ 58 year old MD, referred by neurologist for baseline NP workup
- Background
  - Family Hx: father had hand tremor
- Sx & Hx
  - Noticed tremor in LH during a talk he was giving (ironically, about Parkinson's disease). Tremor in LH (he is Left handed) mostly while not using it
  - 4 months later, son (also MD) noticed it while golfing
  - family "encouraged" RJ to get evaluated by neurologist
- Initial Dx from neurologist
  - stage 1 PD: unilateral tremor, bradykinesia, rigidity

Ogden Ch. 15: Parkinson's Disease : "Robert"

- Tx:
  - started LDopa with very good results
  - tremor controlled
  - reduced work schedule, took on partner at work
  - Prozac for depression
- After 3 years
  - voice very faint, micrographia, wetting bed
  - seeing only easiest casies
- After 5 years
  - ON/OFF symptoms after taking L Dopa
    - ON: 30 minutes after taking choreatic dyskenesias
    - 60 minutes of normality
    - OFF: bradykinesia (could be stuck in a chair)

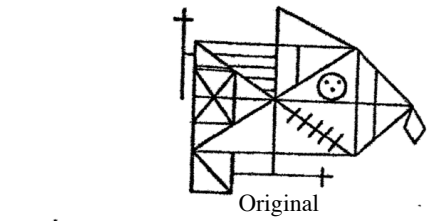
Robert : NP Testing

- Age 58
  - High overall IQ, especially on Verbal abilities
  - Mild visuospatial deficits
  - Cognitive slowing
  - Executive dysfunction
  - Rey Complex Figure test
    - copy : fair
    - memory poor but not as bad as Alzheimer's patient
- Age 60
  - no significant worsening in NP tests
  - however, gave up driving (having trouble changing lanes)

Ogden Ch. 15: Parkinson's Disease : "Robert"

- After 6 years, he had right-sided pallidotomy with good results
  - symptoms reduced, ON/OFF syndrome much better
  - could show facial expressions again
- After 7 years
  - tried DBS for left-side of brain, good results
  - by enabling "magic wand", could reduce symptoms

RJ: Rey Complex Figure



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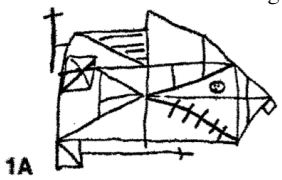

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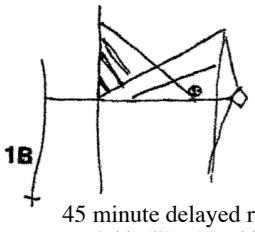
Copy age 58



1B

45 minute delayed recall