

Week 12

- KW27 - Dementia (Alzheimer's)
- 017 - Case Report (Sophie)

KW 27 : Dementia

Overview of Dementia

- DSM-5 Definition
 - Diagnostic Criteria
 - Etiological Subtypes
- Alzheimer's
 - Demographic Prevalence
 - Causes
 - Progression
- Parkinson's
- Huntington's
- Categorizations:
 - Cortical vs. Subcortical
 - Degenerative vs. Nondegenerative

DSM-5 Cognitive Disorders

- Chapter: "Neurocognitive Disorders"
- Formerly called "Delirium, Dementia, and Amnestic and other Cognitive Disorders" in DSM-IV
- Formerly called "Organic Mental Syndromes and Disorders" in DSM-III
- Types:
 - Delirium
 - Major Neurocognitive Disorder (NCD)
 - aka *Dementia*
 - Minor Neurocognitive Disorder (NCD)

DSM-5 Cognitive Domains

- Complex Attention
 - multi-tasking, STM, working memory
- Executive Function
 - plan and execute complex actions
- Learning and Memory
 - fails to track conversation, repeats self, can't remember short lists of items
- Language
 - expressive or receptive language, paraphasias
- Perceptual / Motor
 - driving, using tools, navigating
- Social Cognition
 - poor judgement, poor insight into social cognition

DSM-5 Delirium

- Delirium :
 - A - disturbance of attention (focus, sustain, shift) and awareness (consciousness & orientation)
 - B - develops in short timeframe (hours to days), tends to fluctuate
 - C - other cognitive domains affected
- example:
 - delirium due to extreme alcohol intoxication
 - delirium due to hypoglycemia

DSM-5 Minor NCD

- A - moderate cognitive *decline* in one or more areas
 - 1 - from patient, informant, or clinician
 - 2 - NP deficits : 1-2 SD below expectation
- B - little interference with ADLs
- C - not exclusively due to delirium
- D - not better explained by other disorder

DSM-5 Major NCD

- A - significant cognitive *decline* in one or more *domains*
 - 1 - from patient, informant, or clinician
 - 2 - substantial NP deficits (2+ SD below expectation)
- B - interference with ADLs
- C - not exclusively due to delirium
- D - not better explained by other disorder

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DSM-5 Cognitive Disorders Compared

	Delirium	Minor Neurocognitive Disorder	Major Neurocognitive Disorder
Timeframe	acute (hours to days)	insidious (months)	insidious (months)
Domains affected	Attention Consciousness Orientation (and others)	One or more	Two or more*
NP Deficits	(untestable)	1-2 SD below normal	2+ SD below normal
Activities of Daily Living affected?	Yes	Little	Yes

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DSM-5 NCD Descriptors

- Possible vs. Probable
- Behavioral Disturbance
 - without
 - with : psychosis, mood, agitation
- Severity
 - Mild - Instrumental ADLs preserved
 - *instrumental*: cooking, driving, computer, shopping, bills, medication
 - Moderate - basic ADLs preserved
 - *basic*: walking, bathing, dressing, toilet, eating
 - Severe - all ADLs impacted

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DSM-5 : Etiological SubTypes

- Types
 - Alzheimer's
 - Frontotemporal lobar degeneration (FTD)
 - Lewy Body Disease
 - Vascular Disease
 - Head Trauma (TBI)
 - Parkinson's
 - Huntington's
 - Creutzfeldt-Jakob
 - Other Medical Condition
 - Substance/Medication use

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Dementia : Prevalence

Type	Proportion of all dementias
Alzheimer's	*46%
Vascular	22%
Parkinson's	2%
Huntington's	< 1%
Other (including Mixed)	30%

* DSM-5 claims "60% to over 90%"

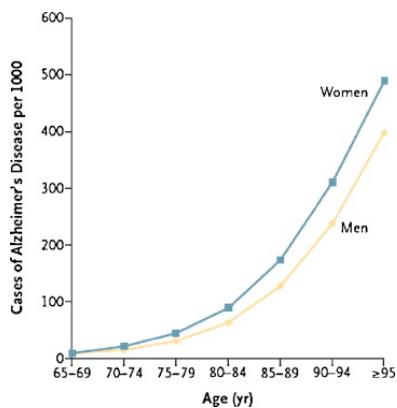
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Prevalence of AD

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

- Enormous societal cost



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DSM-5 : NCD due to Alzheimer's Disease

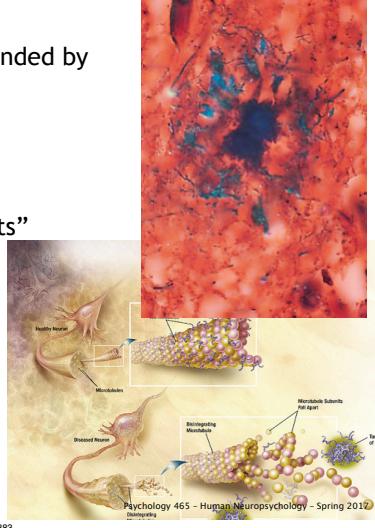
- A - NCD criteria are met
- B - insidious onset, gradual progression, 2 or more domains
- C - Probable AD criteria:
 - 1 - evidence of AD from family or genetic testing, or...
 - 2 - All of these
 - a - clear decline in 2 areas (memory and one other)
 - b - steadily progressive, gradual, no extended plateaus
 - c - no other etiology (e.g. vascular disease, other psychiatric disorders) etc.

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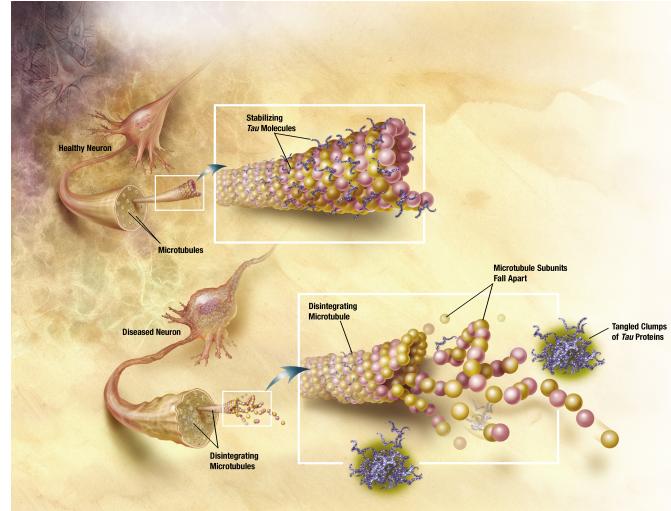
AD Neuropathology

- 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



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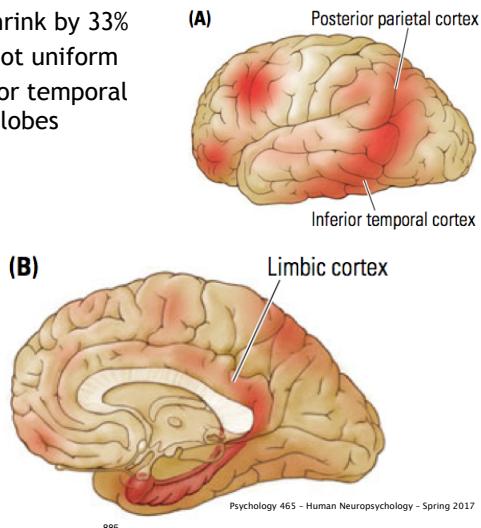
AD Neuropathology



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AD Cortical Atrophy

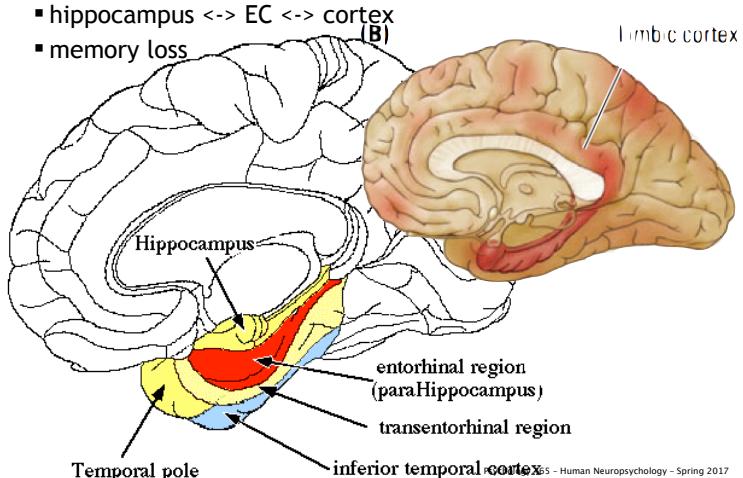
- Overall brain may shrink by 33%
- Cortical atrophy is not uniform
 - strongest in inferior temporal cortex and limbic lobes



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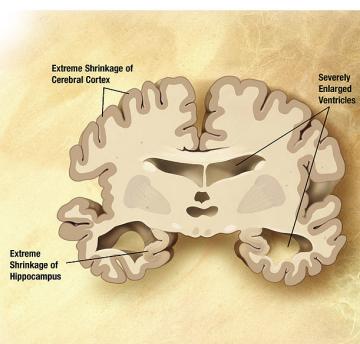
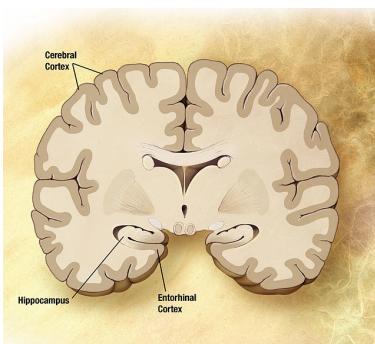
Entorhinal Cortex

- Entorhinal Cortex (EC) most affected
 - hippocampus <-> EC <-> cortex
 - memory loss



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Cortical Atrophy in AD

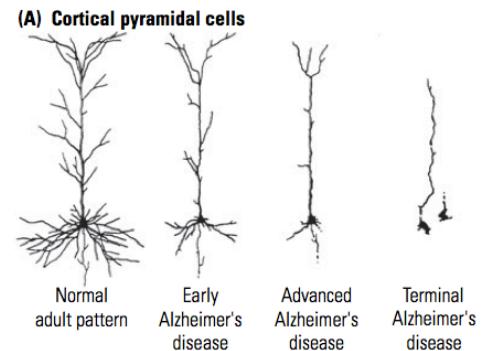


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AD Cortical Atrophy : loss of dendrites

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



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AD Neurotransmitter Changes

- Simplistic model
 - Widespread loss of Acetylcholine (ACh)
- Treatment with ACh esterase inhibitors
 - small benefit (at best)
- Realistic model
 - other NTs also reduced
 - complex picture

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AD Causes

- Genetics
 - Familial Risk
 - sibling with AD: 3.8% risk
 - parent with AD: 10.0% 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

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AD Stages/Course ~ 7 year life expectancy

Level	Description
1. No	Normal
2. Very Mild	Complaints of memory problems (often of losing objects and forgetting names) Clinical interview normal: NP testing may be normal (?)
3. 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. Clinical interview: may show issues NP testing: shows memory issues
4. Moderate	Problems with recent events, personal history, serial 7s, finances & travel. Anomia. Denial, flat affect, withdrawal.
5. Moderate-severe	Needs assistance. Can't recall own address, some family names. Ox2. Counting backwards by 2s.
6. Severe	Forgets spouse's name. Unaware of recent events. Some memory for childhood. Can't count from 10. Personality change, delusions, apathy.
7. Very Severe	All verbal abilities lost. Incontinence. Can't walk.

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AD Prevention

- Prevention
 - no currently validated preventions exist
 - some small correlations found with...
 - diet - "mediterranean" diet
 - + olive oils, beans, whole grains, fruits & vegetables, fish, dairy
 - - meats
 - exercise
 - physical
 - mental
 - light alcohol use (red wine)
 - NSAIDs
 - THC

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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

017 : Sophie (Alzheimer's Disease)

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Review

- “Dementia” - clinical term, used through DSM-IV
- Neurocognitive Disorder (NCD) - DSM 5
 - Minor (1-2 SDs, ADLs OK)
 - Major (2+ SDs, ADLs impacted)
- DSM 5 : NCD
 - first diagnose the *Severity*
 - then the *Etiology*
- Alzheimer’s Disease
 - Prevalence: 20% @ age 85, 50%+ @ age 95
 - ~ 7 years from Dx to death
 - memory loss, other cognitive Sx, beh./mood disturbance
 - cause : Unknown. APP / relation with Trisomy 21
 - plaques & tangles, loss of ACh + other NTs, atrophy
 - Tx: unimpressive

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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

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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

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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”

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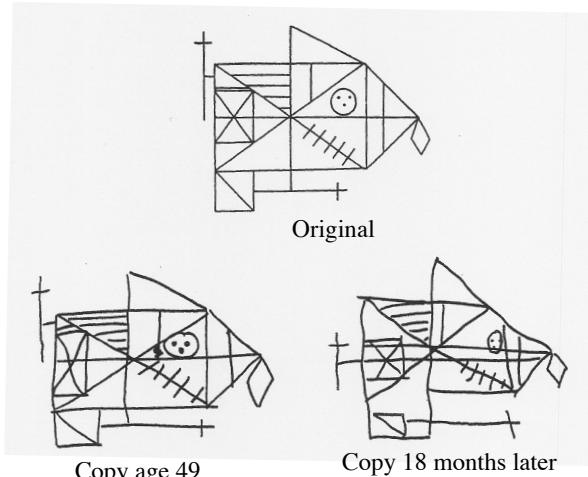
Sophie: NP Testing

- WAIS IQ
 - FSIQ : subtests 1-2 SD below average (Z scores of -1.0 to -2.0)
- Lowest scores on Visuospatial 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”

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Sophie: Rey Complex Figure



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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”)

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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

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