Overview of Dementia Etiologies

CAROLYN PARSEY, PHD

Clinical Neuropsychologist, UW Medicine Memory and Brain Wellness Center at Harborview

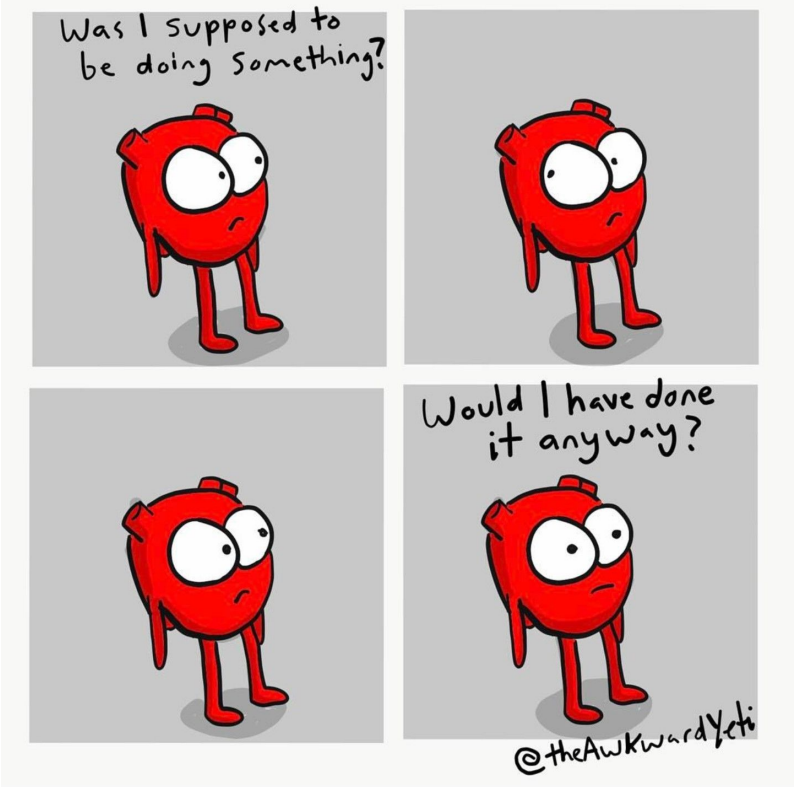
Assistant Professor, Department of Neurology, University of Washington School of Medicine

August 14, 2020

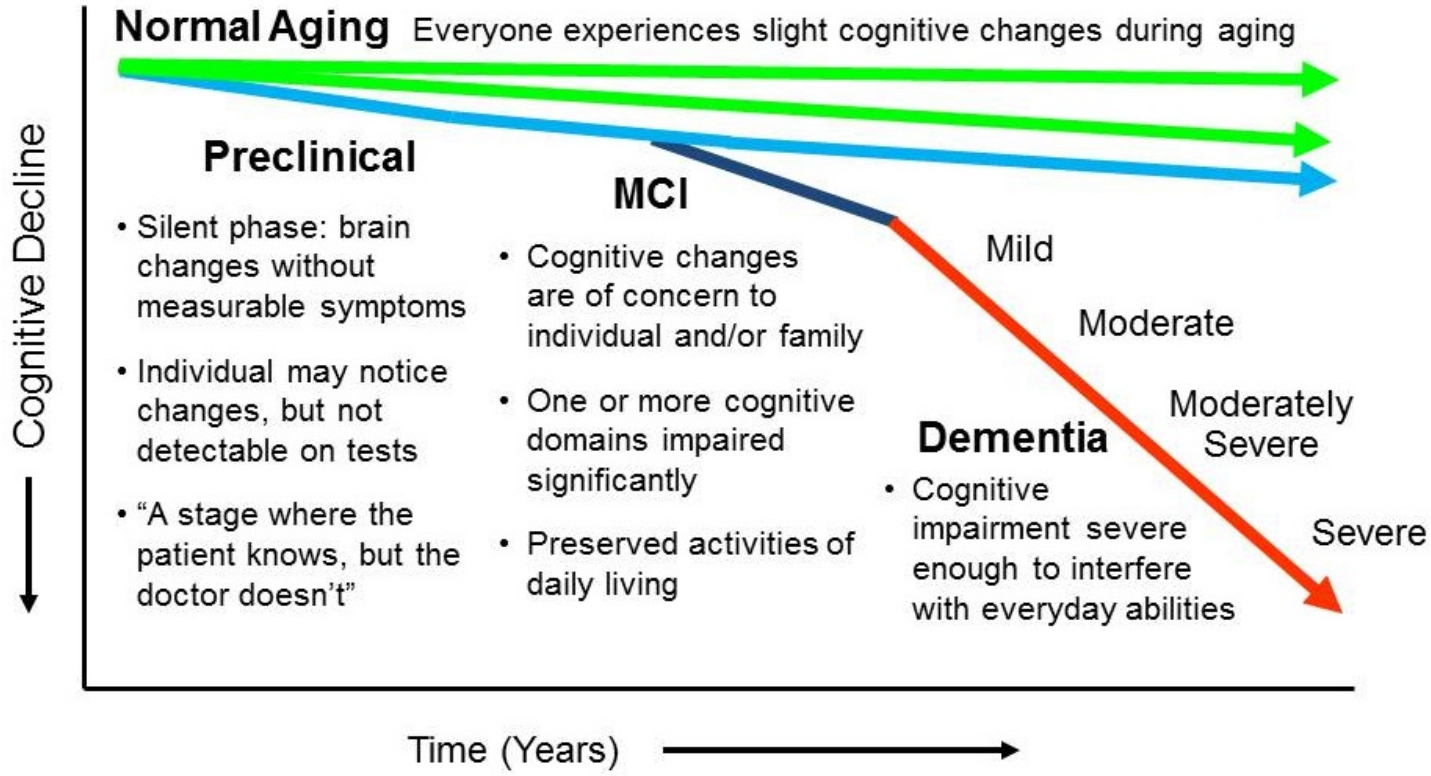
UW Medicine

TODAY'S ROAD MAP

- MCI subtypes (in brief)
- Four Common Etiologies of Dementia
  - Alzheimer's disease
  - Vascular-related
  - Frontotemporal
  - Lewy body

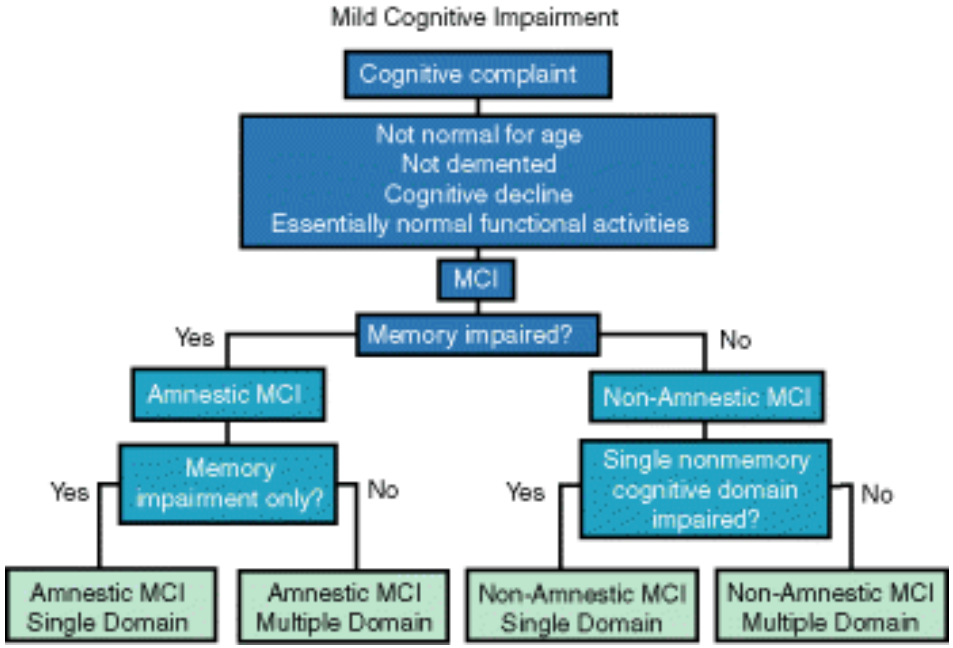


Cognitive Aging & Decline



Mild Cognitive Impairment (MCI)

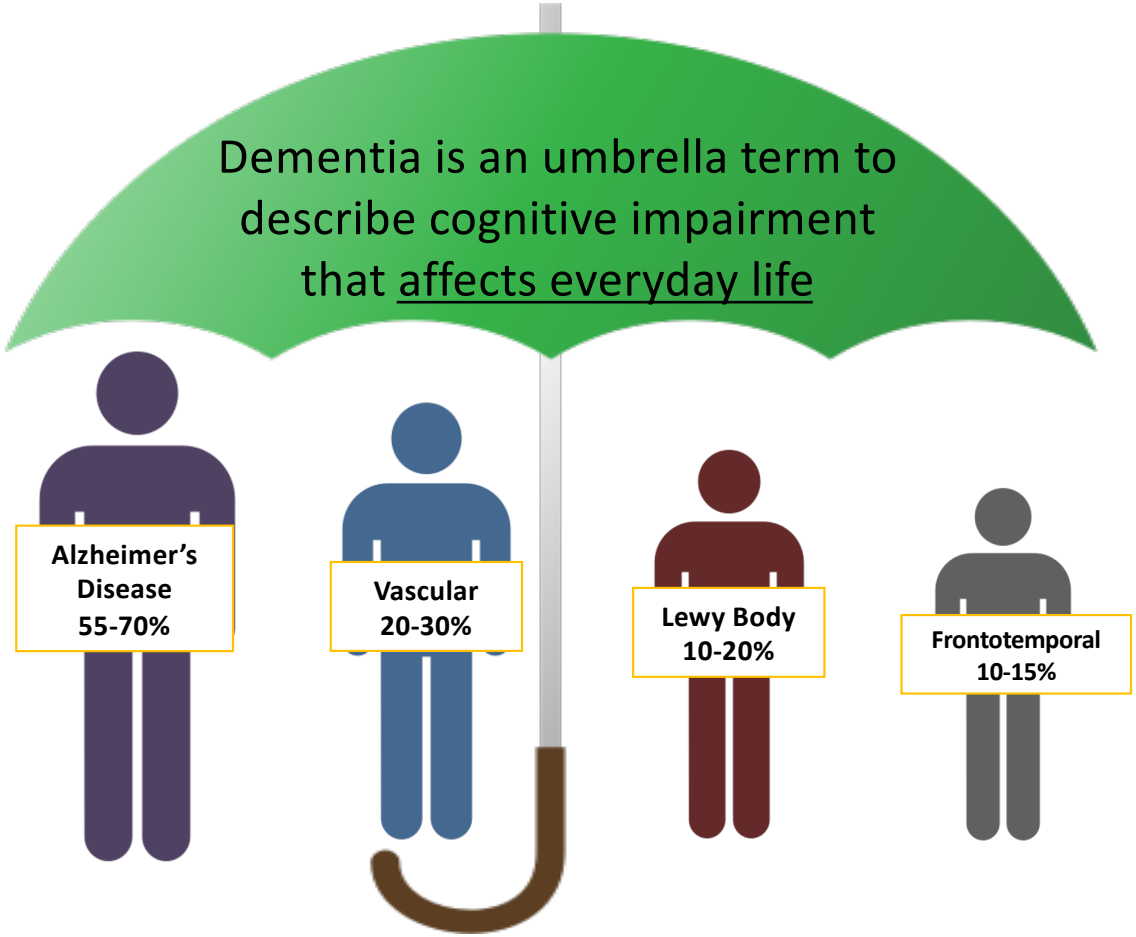
- DSM-5 Mild Neurocognitive Disorder
- Petersen criteria (1999)
  - Only considered memory impairment
- Revised Petersen criteria (2004)
  - Cognitive complaint by patient or family
  - Significant impairment (>1.5sd) in at least one cognitive domain
  - Intact daily functioning (ADLs/IADLs)
  - Single domain vs. Multiple domain
  - Amnestic vs. Non-amnestic



Petersen et al., 2004; Journal of Internal Medicine, Volume: 256, Issue: 3, Pages: 183-194, DOI: (10.1111/j.1365-2796.2004.01388.x)

Dementia

- DSM-5 Major Neurocognitive Disorder
- Evidence of **significant** cognitive decline from the previous level of performance in one or more cognitive domains based on:
  1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function, AND
  2. A **substantial** impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantifiable clinical assessment
- The cognitive deficits interfere with capacity for independence in everyday activities
- Not better explained by delirium, psychosis, mental health dx, other medical problem…
- Specifiers
  - Major NCD due to _____ (Alzheimer's, Lewy Body, TBI, HIV, etc); Probable vs. Possible
  - With/Without behavioral disturbance
  - Severity: Mild (difficulties w/IADLs), Moderate (difficulties w/ADLs), Severe (fully dependent)



Other Causes:

- Mixed Dementia
- Parkinson's disease
- Huntington's disease
- TBI
- Substance Abuse
- HIV/"HAND"

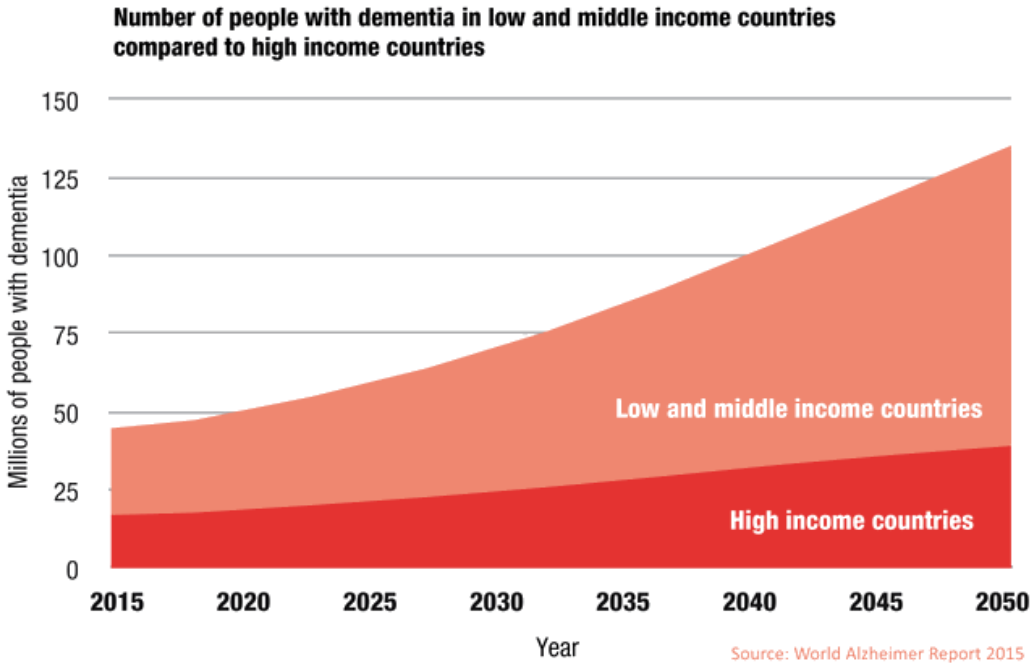
Alzheimer's Disease

- Most common cause of dementia
  - 5.8 million cases in U.S. currently
  - By 2050, U.S. 14 million cases (131 mil. globally)
- Females > Males
- Early onset (<65yo) versus Late onset (>65yo)
- Insidious onset, gradual decline
- Cardinal features: rapid forgetting, repetition, word finding problems, and executive deficits (problem-solving, reasoning)

- Pathology
  - "Tau Tangles" = Tau Protein aggregation
  - Beta Amyloid Plaque build-up
  - CSF studies and PET imaging can help identify Tau and Amyloid presence

Dr. Alois Alzheimer

Frau Auguste Deter, ~1890s

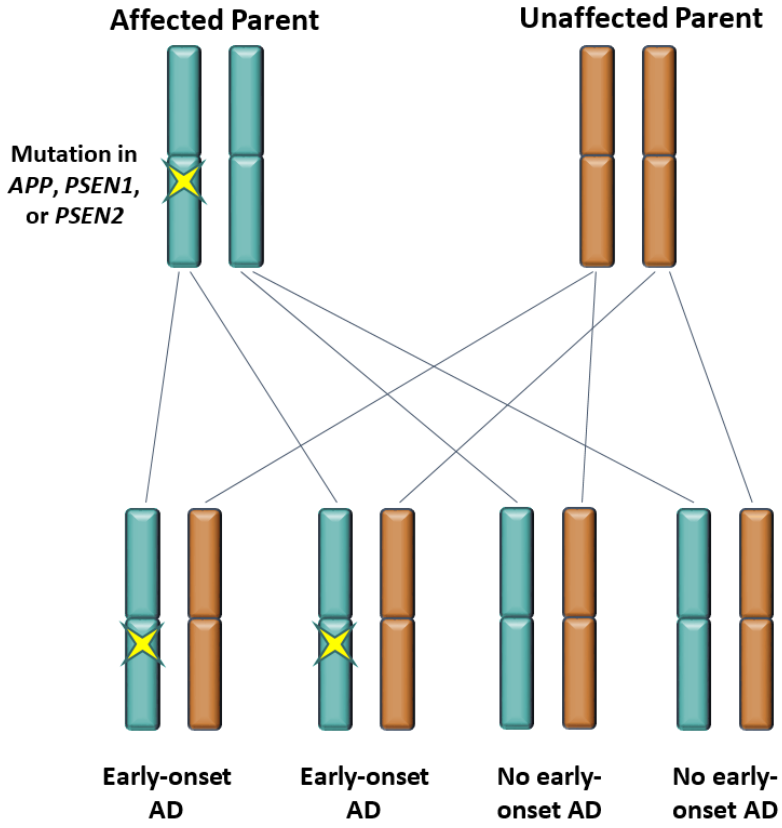


UW Medicine

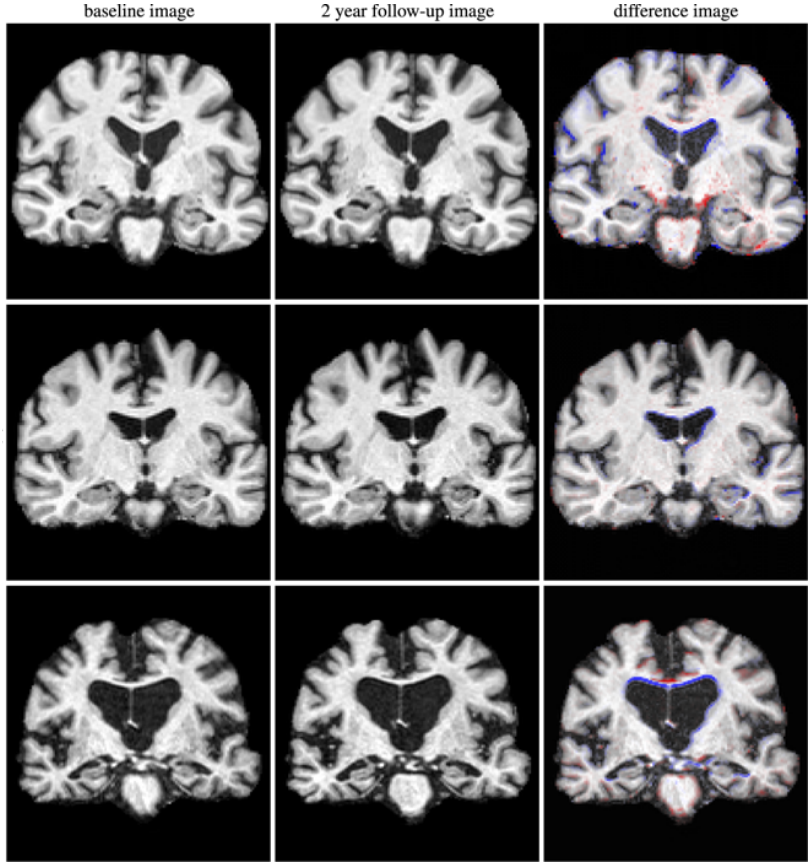
Alzheimer's Disease - Genetics

- Early-onset AD (<10% of AD cases)
  - "Familial" variant, autosomal-dominant
  - APP on Chrom. 21
  - Presenilin (PSEN) 1 on Chrom. 14
  - PSEN 2 on Chrom. 1
  - Single-gene mutations → abnormal protein development

- Late-onset AD (>65yo)
  - Apolipoprotein E (APOE) on Chrom. 19
  - Two alleles = APOE genotype
    - E2 – possibly protective*
    - E3 – neutral
    - E4 – increases risk
      - 1 copy = increases risk 2-3x
      - 2 copies = increases the risk by ~10x
      - NOT guaranteed that will get AD

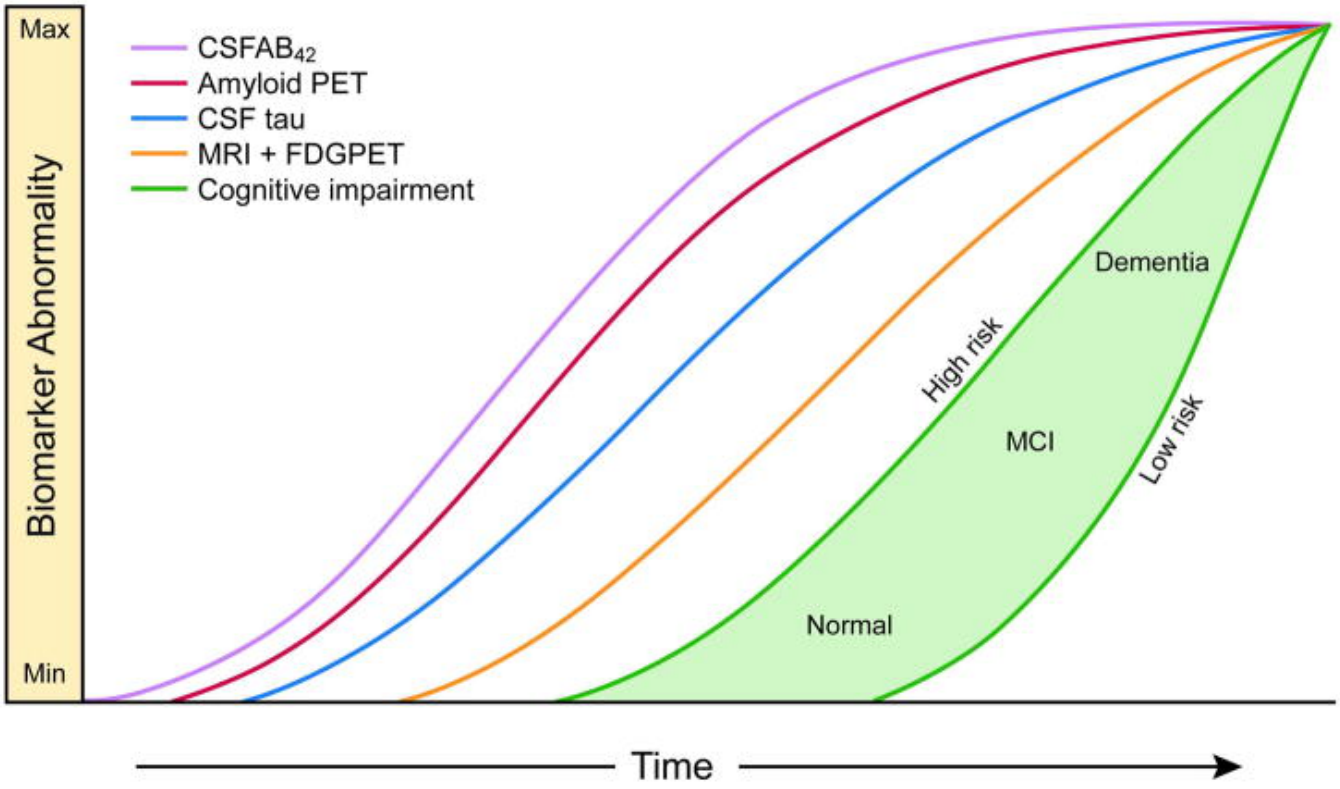


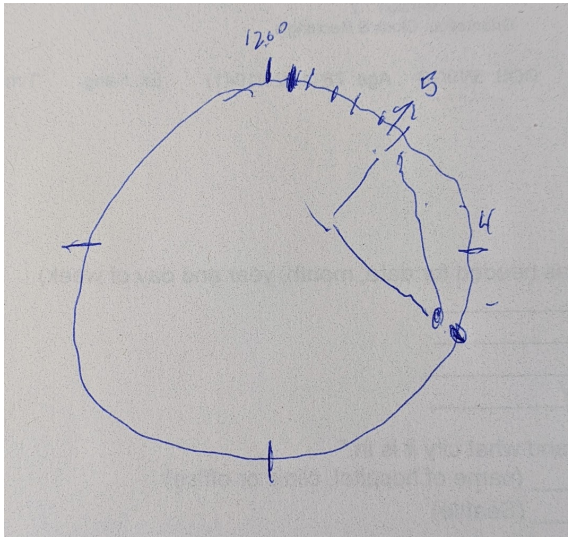
Alzheimer's Disease – Neuroimaging & Pathology

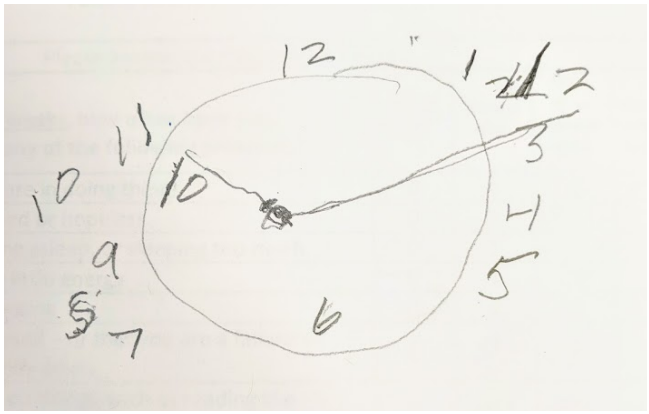


- MRI/Structural: Atrophy
  - Often non-specific/generalized
  - Medial temporal lobe
    - Hippocampus, entorhinal cortex
- PET: Decreased glucose metabolism
  - Posterior temporoparietal
  - Precuneus
  - Poster cingulate

Jack et al. (2013) Model of AD





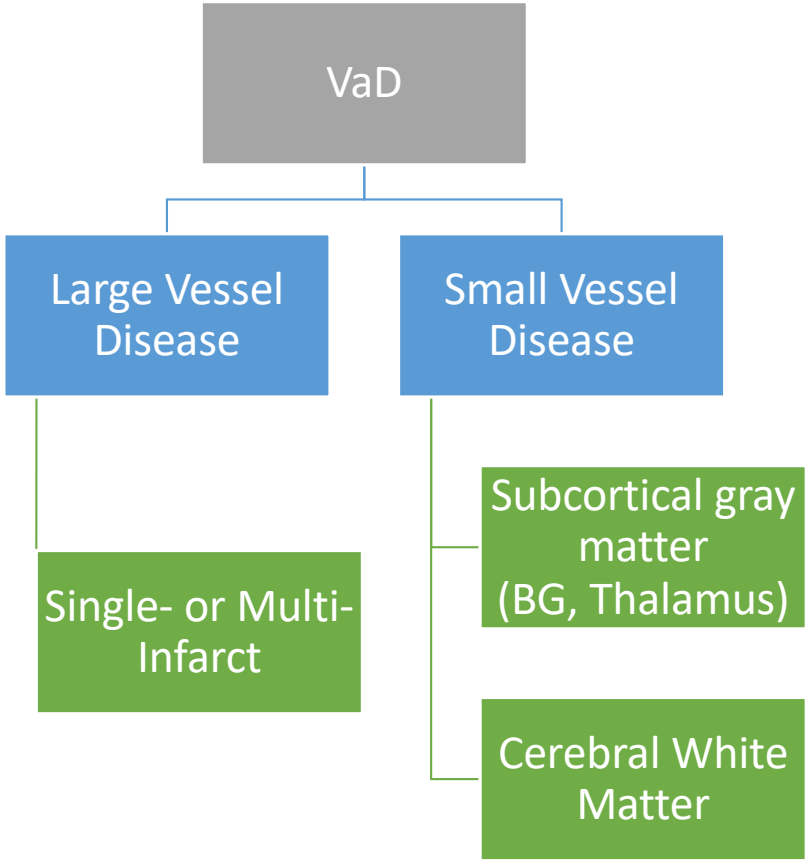


MEMORY	Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	
		1ST TRIAL	✓	✓				NO POINTS
		2ND TRIAL	✓	✓		✓	✓	

DELAYED RECALL	(MIS)	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	0 /5
Memory Index Score (MIS)	X3								
	X2	Category cue	✓					MIS = 3 /15	
	X1	Multiple choice cue					✓		
ORIENTATION	[ ] Date	[ ] Month	[ ] Year	[ ] Day	[ ] Place	[ ] City			/6

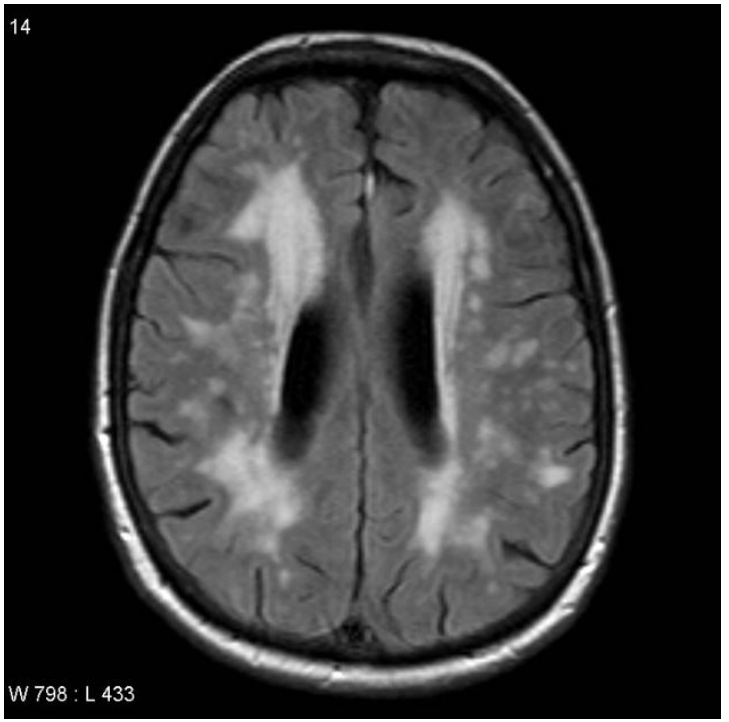
Vascular Dementia (VaD)

- Second most common cause of dementia
- Acute (e.g., stroke) or Chronic
  - Onset: Event-specific onset vs. insidious
  - Course: Step-wise vs. gradual
- Risk Factors: CAD, HTN, hyperlipidemia, DMII, OSA, COPD, afib, etc.
- Clinical Presentation: "Subcortical" pattern
  - Reduced processing speed, executive functioning, working memory
  - Retrieval deficits that can improve with recognition tasks
  - Apathy, depression, emotional blunting, bradyphrenia



Vascular Dementia - Neuroimaging

- Chronic small vessel ischemic changes
- Microhemorrhages
- Leukoaraiosis >25% on imaging*
  - White matter change near lateral ventricles
- “Binswanger’s Disease” = subcortical vascular dementia



MoCA for Amnestic vs. Non-amnestic Differentiation

MEMORY	Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	NO POINTS
		1ST TRIAL						
		2ND TRIAL						
ATTENTION	Read list of digits (1 digit/ sec.).	Subject has to repeat them in the forward order. [ ] 2 1 8 5 4 Subject has to repeat them in the backward order. [ ] 7 4 2						__/2
	Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B							__/1
	Serial 7 subtraction starting at 100. [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65 4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0**							__/3
LANGUAGE	Repeat: I only know that John is the one to help today. [ ] The cat always hid under the couch when dogs were in the room. [ ]							__/2
	Fluency: Name maximum number of words in one minute that begin with the letter F. [ ] _____ (N≥11 words)							__/1
ABSTRACTION	Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ] watch - ruler							__/2
DELAYED RECALL	(MIS)	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	__/5
Memory Index Score (MIS)	X3							
	X2	Category cue						MIS = ____/15
	X1	Multiple choice cue						
ORIENTATION	[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City							__/6

UW Medicine

Vascular Dementia Example:

MEMORY	Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	NO POINTS
		1ST TRIAL	✓	✓				
		2ND TRIAL	✓	✓	✓	✓	✓	

DELAYED RECALL	(MIS)	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only	
Memory Index Score (MIS)	X3		[✓]	[✓]	[ ]	[ ]	[ ]		2 /5
	X2	Category cue					✓	MIS = 10 /15	
	X1	Multiple choice cue			✓	✓			
ORIENTATION	[ ] Date	[ ] Month	[ ] Year	[ ] Day	[ ] Place	[ ] City			/6

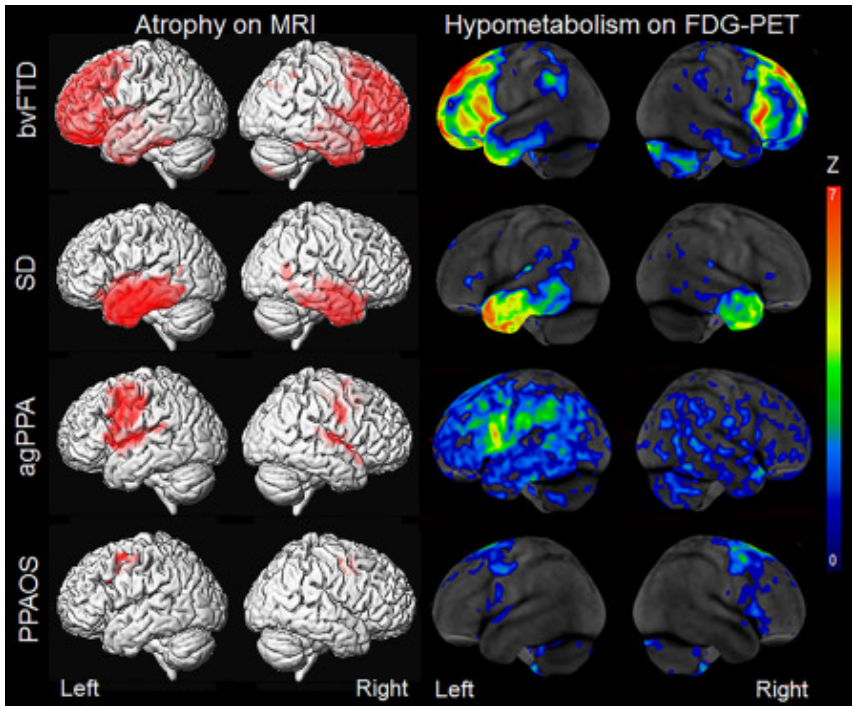
Alzheimer's Disease Example:

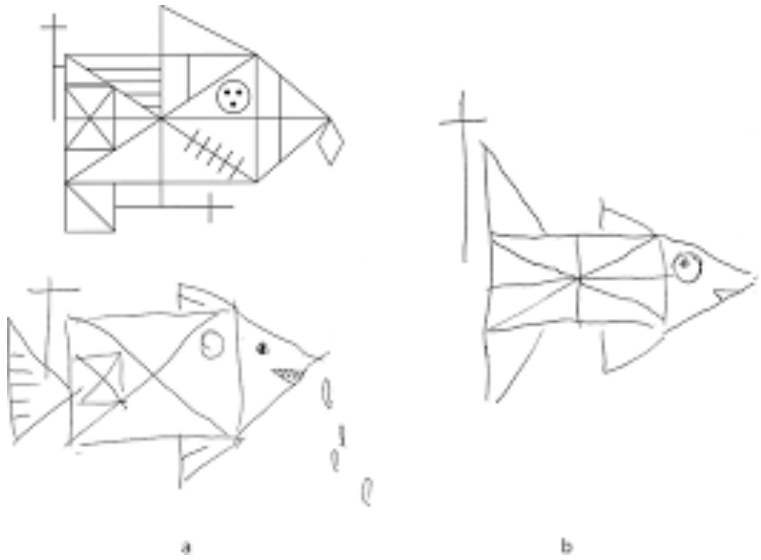
MEMORY	Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	NO POINTS
		1ST TRIAL	✓	✓				
		2ND TRIAL	✓	✓		✓	✓	

DELAYED RECALL	(MIS)	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only	
Memory Index Score (MIS)	X3		[ ]	[ ]	[ ]	[ ]	[ ]		0 /5
	X2	Category cue	✓					MIS = 3 /15	
	X1	Multiple choice cue					✓		
ORIENTATION	[ ] Date	[ ] Month	[ ] Year	[ ] Day	[ ] Place	[ ] City			/6

Frontotemporal Dementia (FTD or FTLD)

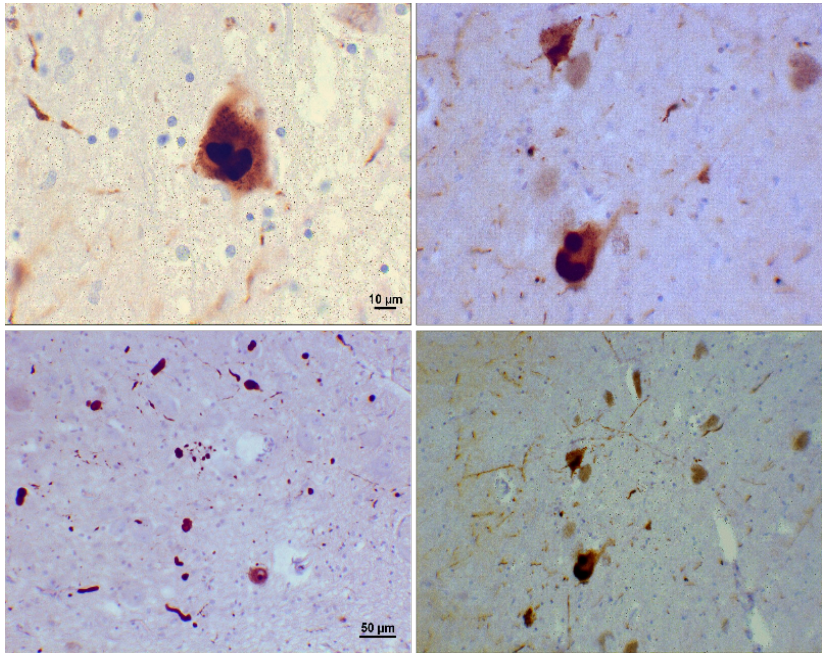
- Typical onset in 50s (40-60), rapid decline
  - Men and women approximately equal; women more likely to have familial variant (C9orf72 mutation)
- Pathology: Tau, TDP-43, and many others
- Several Subtypes
  - Behavioral variant FTD (bvFTD)
    - "Frontal variant"
  - Primary Progressive Aphasia (PPA)
    - Semantic, Logopenic, Nonfluent/Agrammatic
- bvFTD Clinical Presentation
  - Personality/behavioral features often present first
    - Disinhibition, impulsivity, inappropriate social behaviors
    - "Not the person that I used to know"
  - Deficits in executive functioning, language, attention
  - Relatively spared memory and visuospatial skills




a
b

Dementia with Lewy Bodies (DLB)

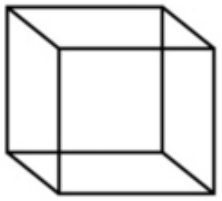
- Cognitive, Psychiatric, and Motor features
- Typical onset 65-75yo, gradual decline
  - Cognitive/psych features first, then motor*
- Pathology: alpha-synuclein
- Males (3-4x) > Females; more rapid decline in men
- Clinical Features
  - Fluctuating cognition with pronounced variation in attention/alertness
  - Recurrent well-formed visual hallucinations
  - REM sleep behaviors and/or fragmented sleep
  - Parkinsonian features – bradykinesia, limb rigidity, postural instability
  - Apathy, depression
  - Deficits in executive functioning, processing speed, and visuospatial skills



Dementia with Lewy Bodies (DLB)

Please draw this figure:

A



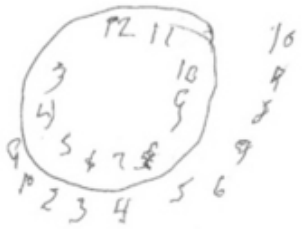
B

C

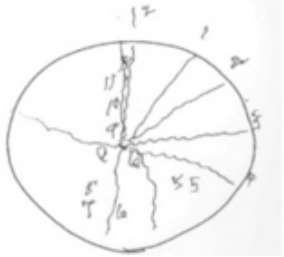
Draw a clock showing the time of 11:10:

D

E

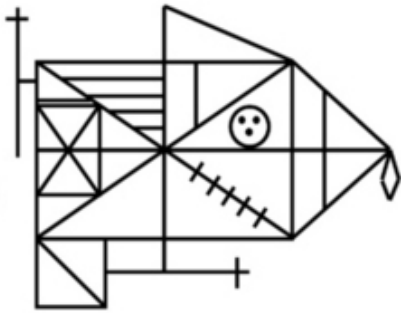


F



Please draw this figure:

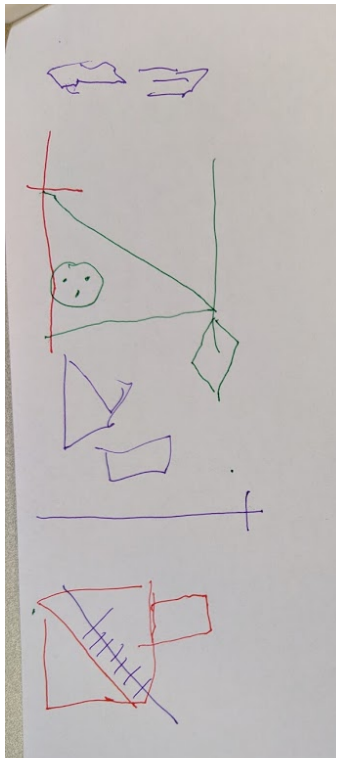
G



H

I

Boeve et al., 2008



“Pseudodementia”

- Subjective cognitive complaints
- Associated with non-neurologic conditions
  - Psychiatric, medical problems (e.g., sleep apnea), substance use, medication side effects
- Clinical Features
  - Subjective complaints, detailed accounts and examples
    - “Great memory for memory problems”
  - Insidious, typically aligns with other conditions (mood, pain, etc)
    - Variability depending on symptoms
  - Improvements on cognitive testing with encouragement, cueing, or additional structure of tests
  - Many cognitive symptoms are reversible when underlying cause is treated

QUESTIONS?

UW Medicine
MEMORY & BRAIN
WELLNESS CENTER

Contact Information
Carolyn Parsey, PhD cmparsey@uw.edu
UW Memory and Brain Wellness Center: www.depts.washington.edu/mbwc