COGNITIVE IMPAIRMENT

Bridget J Keller, MD
Assistant Professor of Neurology
LECOM-Bradenton
bkeller@lecom.edu

Objectives

- Review causes of cognitive impairment
- Understand the risks for, and causes of, cognitive impairment
- Incorporate screening evaluation of patients at risk
- Understand treatment strategies for different types of cognitive impairment

Spectrum of Cognitive Changes

Asymptomatic

▼

Normal Cognitive Aging

▼

Mild Neurocognitive Disorder

▼

Major Neurocognitive Disorder

What is normal aging?

- Most individuals >65 y/o absorb and process information more slowly and less efficiently than younger people.
- Rate of learning, retrieving, analyzing, reacting, and responding to information and actions is slower.
- Preserved semantic knowledge and crystallized intelligence (skills); these can improve until old age

Normal aging (cont'd)

- Older people occasionally and temporarily have difficulty retrieving information (ie. names) but remember later. (the info is not lost and there is no true forgetting).
- Aging should NOT significantly affect:
  - Daily functioning, behavior, personality, or mood.

Normal aging or not?

- 72y/o man states he needs to turn off the radio when driving on an entrance ramp merging on the highway because he can't listen and merge at the same time anymore.

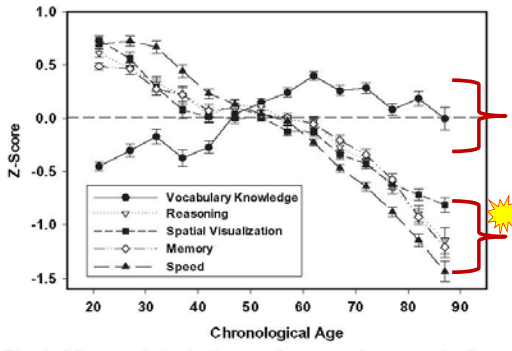
Answer: Normal

- Processing speed diminishes with age
- Rate of learning, retrieving, analyzing, reacting, and responding to information and actions is slower.
- Ability to maintain attention with multiple stimuli coming at us declines with age.

- Supplement to Practical Neurology, The Alzheimer's Disease Spectrum. September 2017

Normal age-related cognitive decline

A finer-grained look



"Crystallized" intelligence [past learning]
- Breadth/depth of general knowledge (e.g., language)
- Accrued over lifetime based on fluid intelligence, education, interests

"Fluid" intelligence [on-the-spot learning & reasoning]
- Aptness in processing information (e.g., learning, reasoning, abstract thinking, problem solving)
- Includes executive function, working memory
- Reflects overall integrity of brain (speed, connectedness, etc.)

*This is the norm, but individuals vary a lot around the norm!

Source: Figure 1 in Salthouse, T. A. (2009). Selective review of cognitive aging. *J of Int Neuropsych Soc, 16*, 754-760.

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Case #1

- 66y/o retired HS teacher reports increasing forgetfulness x 1-2yrs.
- Other cognitive functions (language, attention, executive function, problem solving, visuospatial skills) intact.
- Drives and handles finances without difficulty.
- Wife notes slight increase in forgetfulness but not concerned.
- Patient says he is taking more time to remember previously well-remembered events (doctors appts, scheduled meetings with friends, planned visits with son).
- Patient not particularly disturbed by symptoms but concerned b/c mom had developed dementia late in life and died at 81.

Case #1 (cont'd)

- PMHx: Asthma, seasonal allergies. No surgical history
- Meds: Albuterol inhaler prn. Allergies: NKDA
- Physical exam: unremarkable with normal vital signs.
- Labs: CMP, CBC, TSH, Lipid panel, Vit B12/folate normal. Brain imaging: normal for age.
- MoCA score 25/30 (nl $\geq$26). Missed 4 points on word recall, 1 point on date
- Neuropsychological testing showed profile normal for age/education except delayed recall of lists, paragraphs and nonverbal material.
- Further discussion with patient and wife revealed he was functioning well in all aspects of ADLs. He felt slightly inefficient at some tasks but completed everything correctly.

What is the likely diagnosis?

- A. Dementia with Lewy Body
- B. Alzheimer disease
- C. Mild Cognitive Impairment
- D. Vascular dementia

Answer

- A. Dementia with Lewy Body
- B. Alzheimer's disease
- C. Mild Cognitive Impairment
- D. Vascular dementia

Mild Neurocognitive Disorder (MCD)

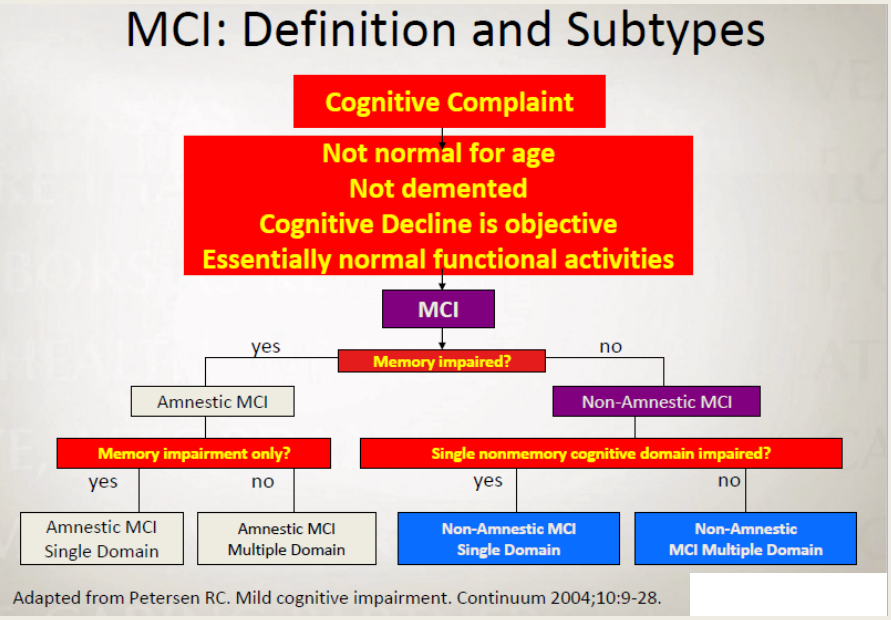
(AKA – MCI)

DSM-5

- Cognitive deficits DO NOT interfere with capacity for independence in everyday activities.
- Complex instrumental ADLs (paying bills, managing meds) preserved, but greater effort, compensatory strategies, or accommodation may be required.
- Heterogeneous category encompassing multiple possible etiologies

American Psychiatric Association: Diagnostic and Statistical Manuel of Mental Disorders, Fifth Edition.

MCI: Definition and Subtypes



Adapted from Petersen RC. Mild cognitive impairment. Continuum 2004;10:9-28.

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MCI Etiologies

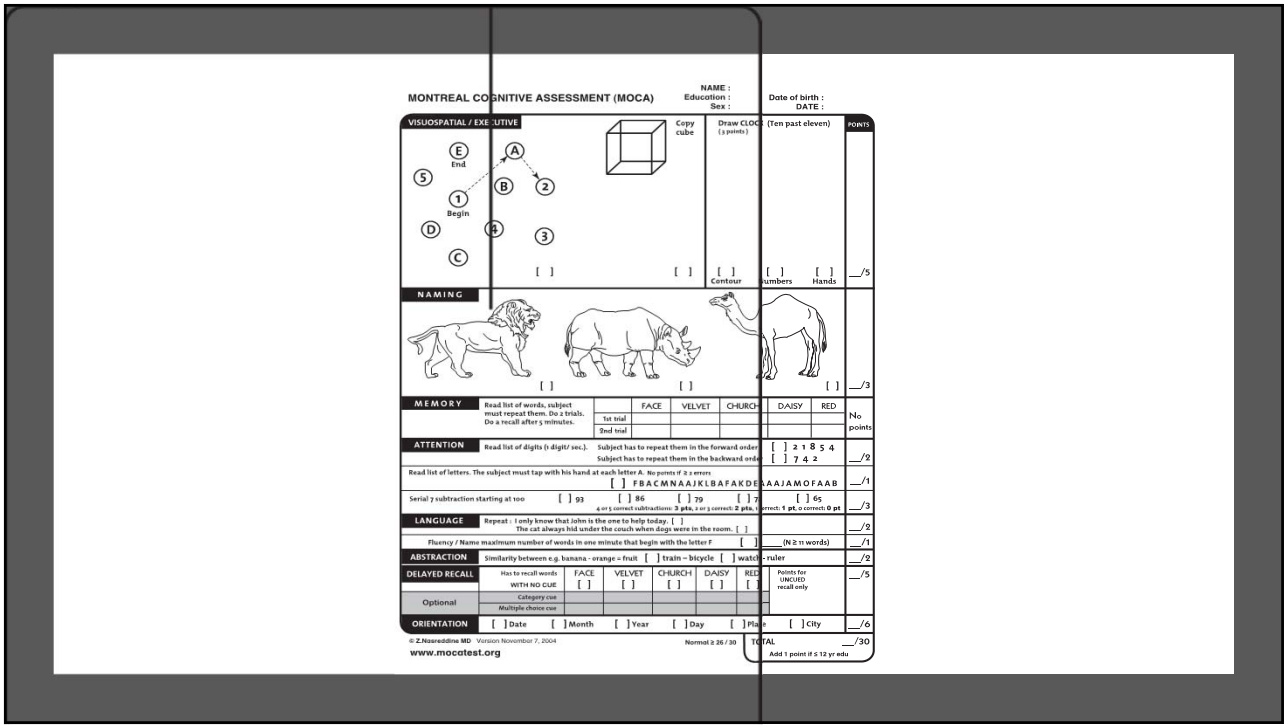
- First cognitive expression of Alzheimer disease (AD)
- Other neurologic, neurodegenerative, systemic or psychiatric disorders
- Other causes (metabolic, vascular, systemic, psychiatric, etc.)

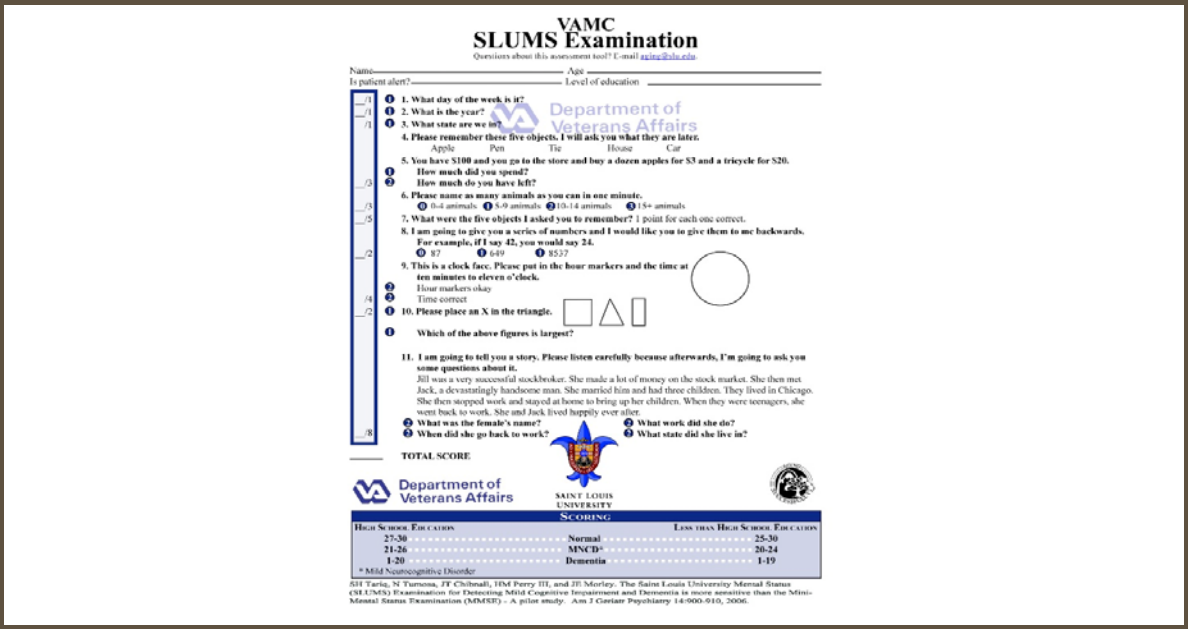
VITAMIN GODS acronym for Diff Dx Mental status changes

- V - vascular
- I - infections
- T - Trauma
- A - Autoimmune
- M – Meds/Migraine/Metabolic
- I - Inflammatory
- N - Neoplastic
- G - Genetic
- O – Oxygen deprivation
- D – Degenerative / Developmental
- S - Seizures

MCI Diagnosis

- Subjective memory loss insufficient for diagnosis
- Use validated tools:
  - *MoCA – Montreal Cognitive Assessment*
  - *ACE-R – Addenbrooke's Cognitive Examination – Revised*
  - *CANS-MCI – Computer –Administered Neuropsychological Screen for MCI*
  - *Others (SLUMS)*
  - *WHY IS MMSE NOT LISITED???*
    - MMSE good for moderate dementia, terrible for MCI





VAMC
SLUMS Examination

Questions about this assessment tool? E-mail aging@slu.edu

Name_____ Age _____
Is patient alert?_____ Level of education _____

1. What day of the week is it?
2. What is the year?
3. What state are we in?
4. Please remember these five objects. I will ask you what they are later.
Apple Pen Tie House Car
5. You have $100 and you go to the store and buy a dozen apples for $3 and a tricycle for $20.
How much did you spend?
How much do you have left?
6. Please name as many animals as you can in one minute.
0-4 animals 5-9 animals 10-14 animals 15+ animals
7. What were the five objects I asked you to remember? 1 point for each one correct.
8. I am going to give you a series of numbers and I would like you to give them to me backwards. For example, if I say 42, you would say 24.
87 649 8537
9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.
Hour markers okay
Time correct
10. Please place an X in the triangle.
Which of the above figures is largest?
11. I am going to tell you a story. Please listen carefully because afterwards, I'm going to ask you some questions about it.
Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They lived in Chicago. She then stopped work and stayed at home to bring up her children. When they were teenagers, she went back to work. She and Jack lived happily ever after.
What was the female's name?
When did she go back to work?
What work did she do?
What state did she live in?

TOTAL SCORE

Department of Veterans Affairs

SAINT LOUIS UNIVERSITY

Scoring		
High School Education		Less than High School Education
27-30	Normal	25-30
21-26	MNCD*	20-24
1-20	Dementia	1-19

* Mild Neurocognitive Disorder

SH Tariq, N Tumosa, JT Chibnall, HM Perry III, and JE Morley. The Saint Louis University Mental Status (SLUMS) Examination for Detecting Mild Cognitive Impairment and Dementia is more sensitive than the Mini-Mental Status Examination (MMSE) - A pilot study. Am J Geriatr Psychiatry 14:900-910, 2006.

MCI Prevalence

- Increased Prevalence with age:
- 6.7 % (60-64)
- 8.4% (65-69)
- 10.1% (70-74)
- 14.8% (75-79)
- 25.2% (80-84)

- Petersen RC et al. Practice guideline update summary: Mild cognitive impairment. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018; 90:125-135

Risk for Dementia

9 class I studies

- 14.9% risk for dementia after 2 years in individuals with MCI >65y/o
- After 2-5years of MCI, relative risk of any type of dementia increased 3.3 x and relative risk of Alzheimer disease was 3 vs controls.

- Petersen RC et al. Practice guideline update summary: Mild cognitive impairment. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018; 90:125-135

Reversion to Normal Cognition

4 Class I studies

- 14.4%-38%
- However, 55-65% ultimately progressed to dementia

- Petersen RC et al. Practice guideline update summary: Mild cognitive impairment. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018; 90:125-135

Pharmacologic Treatment for MCI

- None

- Petersen RC et al. Practice guideline update summary: Mild cognitive impairment. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018; 90:125-135

Pharmacologic Treatment for MCI

1 Class I, 10 Class II, 3 Class III studies

- Donepezil, Rivastigmine, Galantamine (all possibly ineffective)
- Flavonoid-containing drink (insufficient evidence)
- Homocysteine-lowering B vitamins (insufficient evidence)
- Transdermal nicotine patch (uncertain clinical significance)
- Piribedil(insufficient to support or refute data)
- Rofecoxib (possibly increases the risk of progression to AD)
- Tesamorelin injections (possibly ineffective)
- V0191 (insufficient data)
- Vitamin E (possibly ineffective)
- Vitamin E + C (uncertain efficacy)

- Petersen RC et al. Practice guideline update summary: Mild cognitive impairment. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018; 90:125-135

Nonpharmacologic Treatment for MCI

2 Class II (exercise)
1 Class II and 4 Class III (cognitive intervention)

- Exercise training for 6 months: likely to improve cognitive measures
- Cognitive interventions: insufficient evidence to support or refute any individual cognitive intervention strategy

- Petersen RC et al. Practice guideline update summary: Mild cognitive impairment. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018; 90:125-135

MCI Recommendations

- Medicare Annual Wellness Visit requires an assessment to detect cognitive impairment. Use validated tool.
- Reversible causes of cognitive impairment? (ie. Medications, sleep apnea, depression)
- Comorbidity management (behavioral and psychiatric symptoms)
- Prognosis: many but not all progress to dementia
- Counseling: long-term planning
- Follow up reassessment
- No FDA approved medications
- Exercise 2x/week

Dementia

- Dementia- Umbrella term for describing loss of multiple cognitive functions (not confined to memory)
- Variable and different neuropathologies can coexist
- Multiple causes:
  - Degeneration
  - Infection/postinfection(HIV, syphilis, TB, Lyme, Whipple, PML)
  - Nutritional deficiency (thiamine, B12, folate, niacin)
  - Metabolic – uremia, hepatic
  - NPH
  - Trauma (diffuse axonal injury, chronic subdural, dementia pugilistica)
  - Meds: sedatives, anticholinergics, benzos, opioids, diphenhydramine, neuroleptics, occasionally AEDs or dopaminergics
  - Toxins: etoh, drugs of abuse, heavy metals
  - Autoimmune: CNS vasculitis, Lupus, Hashimoto encephalitis, Paraneoplastic, Neurosarcoidosis, Wegener's, Giant cell arteritis

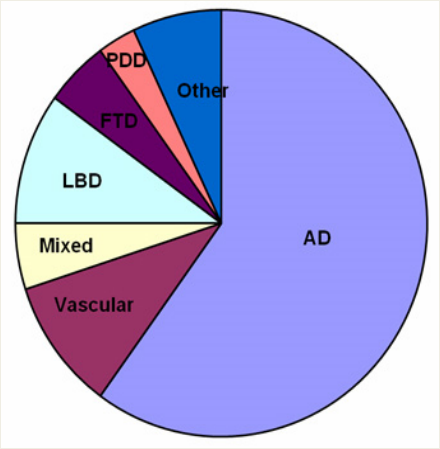
DSM-5 Definition of Dementia

- Dementia = Major Neurocognitive Disorder
- Criteria: 1 or more acquired significant impairments (loss of independence) in cognitive domains such as
  - Memory (amnesia)
  - Language (aphasia)
  - Execution of purposeful movement (apraxia)
  - Recognition/familiarity (agnosia)
  - Visuospatial function (topographical disorientation)
  - Self-control/management (executive functions impairment)
  - Other examples: Math (dyscalculia), emotional expression/comprehension (dysprosody), writing (agraphia)

DSM-5: Definition of Cognitive Deficits

- Cognitive deficits interfere with independence in everyday activities (e.g., at a minimum, requiring assistance with complex instrumental ADLs such as paying bills or managing meds)
- How to determine:
  - Knowledgeable informant or clinician notes significant decline in cognitive function.
  - Substantial impairment in cognitive performance documented by standardized testing (MMSE,MoCA, etc)

"Primary" Dementias: the big ones



- AD= Alzheimer's
- Vascular
- LBD= Lewy Body dementia
- PDD= Parkinson disease dementia
- FTD= Frontotemporal dementia
- Other= Prion disease, Huntington's, HIV dementia, NPH, Wernicke Korsakoff

Case #2

- 72y/o woman with 3 year history of memory impairment
  - HS education
  - Worked in clerical position until retirement at age 68
  - Lives alone and has maintained her own home and financial affairs since husband died 5yrs ago
- Brother has noticed gradual worsening memory impairment and word finding trouble. Also noted decline in housekeeping and financial affairs (wasn't paying bills on time).
- Patient became angry at suggestion she may have progressive cognitive impairment.

Clinical presentation

- Elevated BP documented on several occasions but she never took medication.
- Speech anomic and paraphasic (unintended words or phrase). Tendency to use vague references ("things", "stuff"). Able to provide her name but when asked current age she said, "I don't know, I think 69."
- She incorrectly stated the month and specific date. She did pick month correctly when given 3 choices. Able to give birth year but off by 1 year on current year. She could name current US President but not his predecessor.

Work up

- Well groomed woman, Alert and friendly until began asking memory questions then became a little defensive asking me, “why do you need me to answer that?”
- General and neurological exams were normal and non-focal. Except memory tests: MoCA 21/30
- Formal neuropsychological testing: scored well below average in all cognitive domains.
- Laboratory work-up: CBC, CMP, TSH, Vit B12 level, Urinalysis all normal. (Consider HIV or syphilis testing in at risk patients)
- Brain MRI – minimal PVWM changes, Mild generalized atrophy with slightly greater atrophy in hippocampal area b/l, no acute changes

What is the likely diagnosis?

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- B. Alzheimer dementia
- C. Vascular dementia
- D. Frontotemporal dementia

Answer

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- B. Alzheimer dementia
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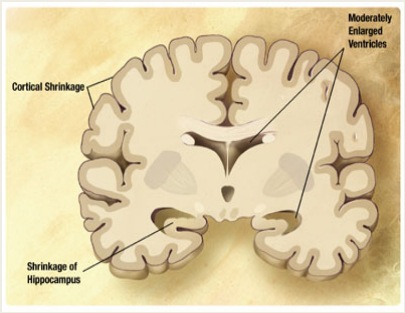
Alzheimer Disease

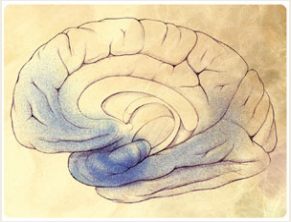
- Most common neurodegenerative and dementing disease
- Prevalence doubles every 5 years after 65; ~50% of those > 85y/o

AD Risk Factors

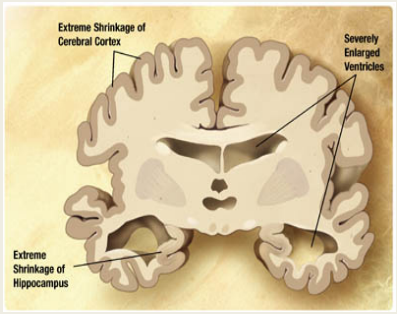
- Age!!
- Mild cognitive impairment (MCI)
- ApoE-e4 positivity (E2 is protective)
- Family hx in first degree relative (especially if younger onset)
- Vascular risk (diabetes, heart disease, etc.)
- Low education and physical/social activity
- Female sex

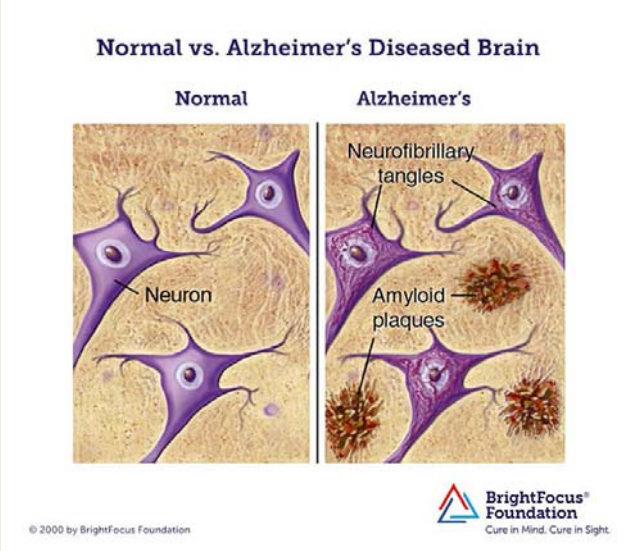
Mild-moderate AD





Severe AD





Neuropathological features of AD

- ℰ-Amyloid Protein aggregation & deposition→ extracellular neuritic plaque formation
- Hyperphosphorylation of Tau → intracellular NFTs
- Brain atrophy with early involvement of MTL, parietal lobe, posterior cingulate
- Primary motor and sensory cortices (including visual) spared until late

MTL –mesial temporal lobe

AD Clinical Features

- Earliest cognitive symptoms are usually poor short term memory; difficulty with finances, loss of orientation
- Smooth, usually slow decline without dramatic short-term fluctuations
- Other domains involved with time

AD: Behavioral/Psych Concerns

- Depression, anxiety
- Irritability, hostility, apathy
- Delusions, hallucinations
- Sleep-wake changes
- Sundowning
- Agitation

Diagnostic Approach

- There is no “dementia test panel”
- For slowly progressive “typical” dementia in adults >65, most essential tests are:
  - Vitamin B12/folate, CBC, CMP, TSH, Brain imaging.
- For younger patients, rapid or atypical course then additional tests depending on presentation.
- Neuropsychological testing can help differentiate types of dementia.

Question

- Which of the following is an unlikely capability of current AD pharmacotherapy?
  - A. Improve repetitiveness
  - B. Slow down progression of disease
  - C. Delay nursing home placement
  - D. Reduce delusional thinking
  - E. Improve daytime alertness

Answer

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  - E. Improve daytime alertness

AD Pharmacotherapy

- Currently no known neuroprotective Rx
- Cholinesterase inhibitors: Aricept (donepezil), Exelon (rivastigmine), Razadyne (galantamine)
  - SEs- nausea, diarrhea
- NMDA antagonist: Namenda (memantine)
  - SEs- dizziness, headache, confusion
- Namzaric (combo Memantine/donepezil 10mg)
- Modest symptomatic and placement effects

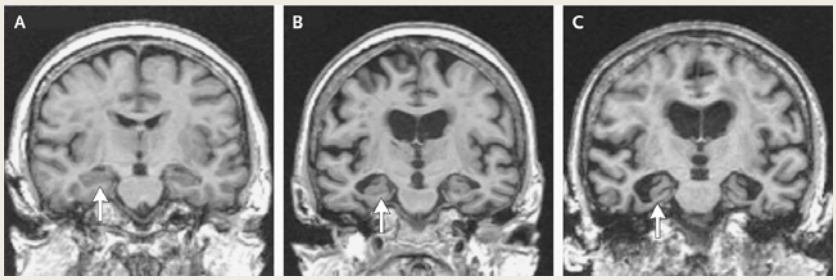
AD Pharmacotherapy (cont'd)

- Treat depression, anxiety (SSRIs)
- Avoid benzos (fall risk)
- Avoid neuroleptics (↑ mortality risk, especially cardiovascular)
  - Neuroleptics Not FDA approved to treat dementia symptoms.
  - Used for hallucinations, delusions, aggression, agitation, hostility and uncooperativeness as last resort

Supportive care

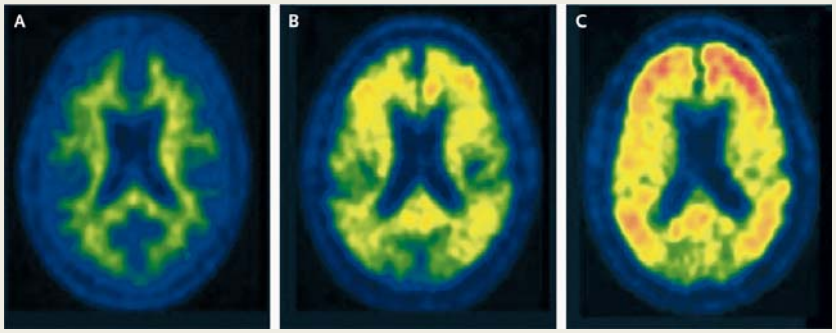
- Encourage physical, mental, social activity
- Safety measures: discuss driving, heights, power tools, weapons, stove, wandering, fall risk, swallow safety
- Dealing with agitation and delusional behavior: redirecting, distracting (playing music/reading to patient)
- Sleep disturbance: enhanced sun exposure, enhanced routine/sleep hygiene, avoid/cautious use of sedatives
- Long-term financial, legal, care issues
- Caregiver stress

Coronal MRI Scans from Patients with Normal Cognition, Mild Cognitive Impairment, and Alzheimer's Disease.



Petersen RC. N Engl J Med 2011;364:2227-2234.

Axial Scans of the Brain Obtained with Positron-Emission Tomography and the Use of Amyloid-Binding Carbon 11–Labeled Pittsburgh Compound B.



Petersen RC. N Engl J Med 2011;364:2227-2234.

Case #3

- 80y/o woman presented with son for evaluation of forgetfulness that became apparent several years earlier but was slowly worsening over time.
  - Son stated mom was easily distracted and repeating same ?s within short time frame. He did not notice any changes in language or behavior.
  - Pt. lived alone, managed household seemingly without difficulty but son had started questioning her ability to drive safely after she recently missed several stop signs. He did not know if she was taking medications as directed. She said she was.
  - Pt. denied getting lost while driving. She did not report any symptoms of anxiety or mood disorders. No complaints of tremor, balance trouble or motor problems.

Case #3 (cont'd)

- PMHx: Hypertension, High Cholesterol, Hypothyroid
- FamHx: Mother died from ovarian CA. Father died after stroke at 85y/o.
- Meds: Lisinopril 20mg, Simvastatin 20mg, Synthroid 25mcg.
- Exam: BP 148/80, HR 80, RR 14, O2Sat 98%
- General physical exam unremarkable
- Neurological exam: Physical exam non-focal but reflexes more brisk in lower extremities vs upper extremities. Plantar response flexor b/l.
- Mental Status testing: Awake, alert and had fluent speech. MoCA 24/30 (nl ≥26). Missed points on attention section, specific date, delayed recall.
- Labs: normal Vit B12, TSH, CMP, CBC. Chol 202, LDL 122, HDL 48, TG 165.
- Brain MRI : Significant PV and subcortical WM changes. Generalized brain atrophy.

Case #3 (cont'd)

- Detailed neuropsychological testing showed:
  - Episodic memory impairment primarily affecting memory retrieval, and to lesser extent, encoding.
  - Fairly pronounced impairment in executive functions
  - Other cognitive domains intact.
- Based on the above information this patient's forgetfulness was suspected to be due to dysfunction of frontal executive network rather than medial temporal lobe/ related structures.

Question

- Combining testing results and neuroimaging, what is the most likely etiology of her cognitive impairment?
  - *A. Alzheimer disease*
  - *B. Vascular disease*
  - *C. Mixed disease*
  - *D. Lewy body disease*

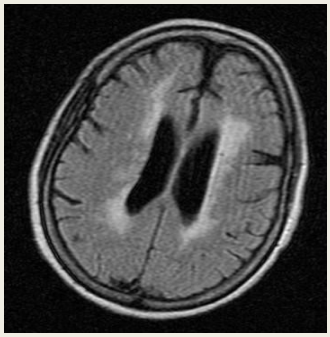
Answer

- Combining testing results and neuroimaging, what is the most likely etiology of her cognitive impairment?
  - *A. Alzheimer disease*
  - *B. Vascular disease*
  - *C. Mixed disease*
  - *D. Lewy body disease*
- Without further evaluation with biomarkers, dual pathology cannot be excluded

Vascular Dementia Summary

- Manage by treating risk factors for vascular disease
- Suspect when:
  - Abrupt onset and/or stepwise decline
  - Fluctuating course
  - History of stroke
  - Focal neurologic symptoms or signs.
- Usually see bilateral infarcts/vascular disease.
- Often associated with executive dysfunction, gait disorder, incontinence.

"…evidence of chronic small vessel ischemic disease involving subcortical white matter"



- This is nondiagnostic and very common with age
- Changes may or may not be symptomatic
- ≠ "Vascular dementia"
- Don't tell patients "Your scan showed strokes."

Case #4

- 72y/o man presented with recent onset short term memory problems and a fine hand tremor.
- Wife reported 8 month history of progressive short term memory problems, disorientation to time and difficulty using household items such as telephone.
  - A few months earlier his cognition worsened when suffering from a UTI. He was dx with delirium at that time.
  - Cognition did not return to baseline after resolution of UTI.
  - Cognition fluctuated between periods of frank confusion and lucidity.
- 3 week history of well formed visual hallucinations, including seeing insects in his home. He had 3 different exterminating companies to his home to 'remove the bugs' that he was seeing.

Case #4 (cont'd)

- Family reported he completed tasks more slowly which affected his ability to perform his ADLs
- No significant PMHx or vascular risk factors. No regular medications. Nonsmoker. Drank alcohol rarely. No past psychiatric history and no family history of cognitive of psychiatric disorder.
- Prior to retirement worked as an accountant. Previously actively played basketball regularly in a league. Last played 1yr earlier after gradually lost interest.
- Still driving and reported no accidents but wife concerned about slow reaction time.

Further assessment

- As well as tremor, he presented with other parkinsonian symptoms – poor mobility & a slow /shuffling gait. Difficulty navigating turns and corners when walking which resulted in recurrent falls.
- Scored 23/30 on MMSE. Lost points on orientation, attention, recall and visuo-spatial construction. Noticeably slow in completing the tasks.
- Brain MRI – generalized atrophy
- F18-FDG PET scan – reduced tracer in frontal, parietal and occipital cortices.

What is the most likely diagnosis?

- A. Alzheimer disease
- B. Progressive Supranuclear Palsy (PSP)
- C. Dementia with Lewy Bodies
- D. Frontotemporal dementia

Answer

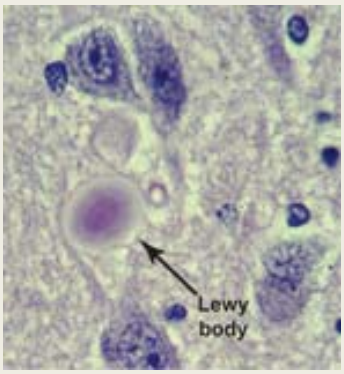
- A. Alzheimer disease
- B. Progressive Supranuclear Palsy (PSP)
- C. Dementia with Lewy Bodies
- D. Frontotemporal dementia

Dementia with Lewy Bodies (DLB)

- Core diagnostic features:
  - Fluctuating cognition with pronounced variations in attention and alertness
  - Recurrent visual hallucinations -typically well formed / detailed
  - Parkinsonism features that begin AFTER the cognitive impairment
- Suggestive diagnostic features:
  - REM sleep behavior disorder
  - Severe neuroleptic sensitivity
  - Low Dopamine transporter uptake in basal ganglia on SPECT or PET imaging (DAT scan).

Dementia with Lewy Bodies (DLB)

- Relatively earlier occipital and basal ganglia degeneration
- Similar to Parkinson disease dementia
- α-synuclein aggregates into Lewy bodies
- α-synucleinopathy – PD, DLB, Also in AD and normal elderly.



Management of DLB

- Cholinesterase inhibitors play role in managing symptoms, possibly slowing rate of progression
- L-Dopa for Parkinsonism – less responsive than PD patients. Watch for orthostatic hypotension
- Avoid Dopamine Agonists – increased risk of hallucinations/confusion
- Behavioral issues - SSRIs, atypical antipsychotics
  - -Neuroleptic sensitivity to typical antipsychotics
  - -Low dose atypical antipsychotics are tolerated.
  - -Nuplazid (Pimavanserin) – FDA approved for PD psychosis. [inverse agonist and antagonist at serotonin 5-HT2A, 5-HT2C receptors]

LAST CASE!

- 51y/o male real estate attorney began embezzling money at work, regularly listing mysterious expenses on travel reimbursement forms. These turned out to be purchases of pornographic materials via the internet.
- Around the same time this behavior was discovered by his partners, a few female law clerks reported he made inappropriate comments about their physique and he stared at them in ways that made them uncomfortable.

Case (cont'd)

- His work dramatically deteriorated, rather than working with clients he spent most of day shuffling papers, reading magazines or downloading pornography onto his computer. He was asked to leave the firm, but made no attempts to find a new job.
- Developed strong desire for cookies and gained 15lbs. His manners deteriorated, and he stuffed his mouth, often choking at the dinner table. Wife said he behaved "like a child" and said, "he is not the man I married." Family history: father and 1st cousin died from "Lou Gehrig's disease"

Exam and assessment

- Exam: Profoundly apathetic and indifferent. Denied any wrong-doing at work. Passively shrugged his shoulders when his tearful wife described the problems.
- When asked about his future – he was very optimistic, stating he could make lots of money as a real estate mogul if he wanted. (grandiose thinking)
- Basic neurological exam revealed pathologically brisk snout and jaw jerk. In his arms and legs he had fasciculations, subtle atrophy and mild weakness. Plantar responses were flexor

Cognitive Evaluation

- Cognitive testing in office: Speech fluent but insisted on telling off-color jokes.
  - MMSE 27/30 (nl $\geq$25) – missed 1 point each for floor of the building, season, and for spelling 'world' backward.
  - MoCA 26/30 (nl $\geq$26)- 1 point on abstraction (watch-ruler), 1 point word generation (only named 6 words that begin with letter 'f'), 1 point on date, 1 point on serial 7s.
  - Trail making Test Part B – frequent perseverative errors.
  - Unable to abstract on proverbs, just repeated the proverb back rather than interpreting.
  - Copied complex designs without error and remembered most of them at 5min
  - Recalled 7 of 9 words at 5 minutes

Studies

- Labs- CMP, CBC, TSH, RPR, Vit B12 all normal
- EMG - normal
- MRI brain – Fronto-insular atrophy, R>L. No evidence vascular disease.
- Brain FDG PET scan – bilateral hypometabolism frontal and temporal lobes.
- Diagnosis???

Fronto-Temporal Dementia (FTD)

- Dementia often seen in younger population (45-65y/o)
- 3 clinical syndromes:
  - Behavioral variant frontotemporal dementia (bvFTD)
  - Semantic dementia (SD)
  - Progressive non-fluent aphasia (PNFA)
- Previously, "FTD" referred only to bvFTD –aka "frontal variant FTD or Picks's disease. The language variants are sometimes grouped together under the term "Primary Progressive Aphasia" (PPA)
- Genetics: 20-50% patients have a positive family history

FTD (cont'd)

- Definitive dx requires postmortem tissue or +gene test
  - *(MAPT, PGRN, CHMP28, VCP, C9orf72)*
- C9orf72 – common mutation linking familial FTD and ALS
- Pathology – Tauopathy (unlike DLB which is synucleinopathy)
  - Other Tauopathies: Corticobasal degeneration, PSP
- Treatment - supportive care with general commonsense measures (as for AD)
  - Pharmacotherapy for psychiatric disease (SSRI for mood, anxiety)
  - Cholinesterase inhibitors can worsen symptoms!
  - Memantine needs further study.

Table 3—Diagnostic Features and Treatment of Dementia Syndromes

Syndrome	Onset	Cognitive Domains, Symptoms	Motor Symptoms	Progression	Imaging	Pharmacologic Treatment of Cognition
Mild cognitive impairment	Gradual	Primarily memory	Rare	Unknown, 12% per year proceed to Alzheimer disease	Possible global atrophy, small hippocampal volumes	Cholinesterase inhibitors (ChIs) possibly protective for 18 months (SOE=A) in subset of high-risk patients
Alzheimer disease	Gradual	Memory, language, visuospatial	Rare early, apraxia later	Gradual (over 8–10 years)	Possible global atrophy, small hippocampal volumes	ChI for mild to severe (SOE=A); memantine for moderate to severe stages
Vascular dementia	May be sudden or stepwise	Depends on location of ischemia	Correlates with ischemia	Gradual or stepwise with further ischemia	Cortical or subcortical changes on MRI	Consider ChI for memory deficit only (SOE=C); risk factor modifiers
Lewy body dementia	Gradual	Memory, visuospatial, hallucinations, fluctuating symptoms	Parkinsonism	Gradual but faster than Alzheimer disease	Possible global atrophy	ChI (SOE=B); ± carbidopa/levodopa for movement
Frontotemporal dementia	Gradual; age <60 years	Executive, disinhibition, apathy, language, ± memory	None	Gradual but faster than Alzheimer disease	Atrophy in frontal and temporal lobes	Not recommended per current evidence

THE END