Dementia

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Dec. 7, 2021

Goals of Presentation

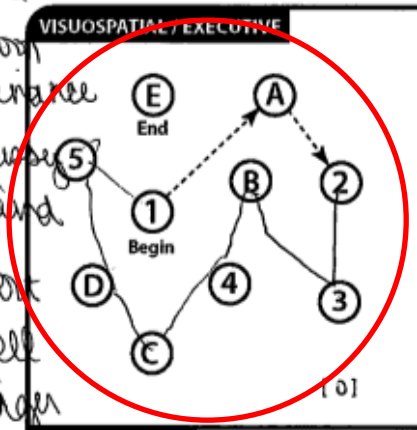
1. Define MCI, 4 criteria
2. Define dementia, diagnostic criteria
3. Review appropriate evaluation of MCI and dementia, with cognitive screening tests, laboratory and imaging tests
4. Compare and contrast AD, LBD, FTD, Vascular dementia and NPH

Case 1

- 77-year-old male, retired physician (practiced for 35 years) and his wife both report cognitive difficulties over about 10 months:
  - Very nervous about updating his own will
  - Can't recall/retain as much; spouse: "a lot slips by"
  - Word finding difficulty more generally; close acquaintances and friends now often called "that person"
  - He knows he's repeating to/for himself, such as looking in his travel bag before a trip, over and over, insecure he's not packed a cell phone charger
  - Drove to a golf course for a game, halfway there forgot the agenda, forgot where he was headed, went home, wife had to notify the other players
  - Has made a wrong turn driving, but can correct quickly, self-limiting driving alone
  - Fears he will lose ability to help manage finances
- Physical and Neurological exam: NORMAL
- Lab work (CMP, CBC, TSH, B12 level normal)

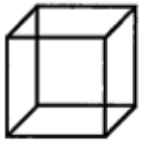
DOB
Evaluation
Clinician Name: Weidman

VISUOSPATIAL / EXECUTIVE



[0]

Copy cube



[1]

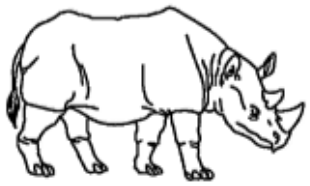
Draw CLOCK (Ten past eleven) (3 points)

[1] Contour [1] Numbers [0] Hands

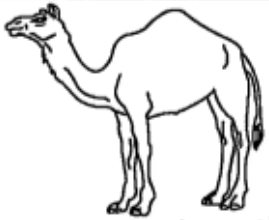
POINTS: 2/5

NAMING

lion [1]



Rhino [1]



camal [1]

3/3

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	√	√	√	√	√
2nd trial	√	√	√	√	√

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [1] 2 1 8 5 4

Subject has to repeat them in the backward order [0] 7 4 2 2 4

1/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[1] 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

1/1

Serial 7 subtraction starting at 100 [1] 93 93 [0] 86 87 [1] 79 80 [0] 72 70 [1] 65 67

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

2/3

LANGUAGE Repeat : I only know that John is the one to help today. [1]

The cat always hid under the couch when dogs were in the room. [1]

2/2

Fluency / Name maximum number of words in one minute that begin with the letter F [1] 20 (N ≥ 11 words)

1/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [1] train – bicycle [0] watch - ruler

1/2

DELAYED RECALL

Has to recall words WITH NO CUE	FACE [0]	VELVET [0]	CHURCH [0]	DAISY [0]	RED [0]
Optional Category cue	X	X	X	X	X
Optional Multiple choice cue	X	X	X	X	X

Points for UNCUED recall only

0/5

NO RECALL

ORIENTATION [1] Date [1] Month [1] Year [0] Day [0] Place [1] City

4/6

© Z.Nasreddine MD Version 7.1 www.mocatest.org Normal ≥ 26 / 30

TOTAL 17/30

Question 1A

- What is the present diagnosis? Assume the patient is still overall independent, knows how to compensate for himself
  - Amnestic MCI, single domain
  - Amnestic MCI, multiple domains
    - Memory, spatial, executive function
  - Non-amnestic MCI, meaning not memory predominant impairment
  - Vascular dementia

Mild Cognitive Impairment (MCI)

Cognitive decline more than expected for normal aging

- Cognitive decline *from a previous level of performance*
- Cognitive impairment **does not** impair everyday activities (work, IADLs, ADLs)
- Does not occur exclusively during the course of delirium
- Not accounted for by another mental disorder (depression, schizophrenia, etc.)

DSM V – Minor Neurocognitive Disorder

Cognitive Changes with Aging

- Mild changes in memory
  - decline in rate of learning new information but not in memory retention (rate of information processing slows, occasional "information overload")
- More difficulty with multi-tasking (divided attention)
- Mild word finding difficulty (especially names)
- "Sometimer's"
- Age "catching up with" longstanding ADD, depression, (longstanding compensatory strategies harder to implement)

Significant declines in cognitive function do not represent normal aging!

Cognitive Impairment:

(Nasreddine et al, 2005)

— A score of 26 or above is considered normal

— For individuals with 12 years or fewer of formal education, one point is added to the score as a correction

Sensitivity and Specificity (%) MoCA and MMSE			
Cut-off	>26	<26	<26
Group (n)	Normal Controls (90)	Mild Cognitive Impairment (94)	Alzheimer's Disease (93)
MoCA	87	90 %	100
MMSE	100	18 %	78

In normal controls, 87% specificity for MoCA, no false positives for MMSE, using >26/30 as cut-off for "normal"

MCI

- No single cause of MCI (syndrome, not a disease)
- Symptoms may remain stable for years, improve over time, or progress to dementia
- No FDA approved treatment at this time

  (my view: cholinergic deficits exists if MCI due to Alzheimer's, rationale to start a cholinesterase-inhibitor)

MCI Etiologies

Reversible, Readily treatable Conditions

- Depression
- Severe stress
  - anxiety
  - Occupational burnout
- Obstructive sleep apnea
- Metabolic disturbance
  - B12 lack; hypothyroid
- Alcohol
- Other toxins
- Infection
- Occ: lacunar infarct, heals

Neurodegenerative disorders

- Alzheimer's disease
- Vascular dementia
- Lewy Body dementia, PD
- Frontotemporal dementias
- Mixes of the above
- PSP/CBD, CJD, NPH, Amyloid angiopathy

PROGNOSIS of MCI

- In a 2008 meta-analysis of 15 studies, for example, the total number of patients who had progressed to a dementia in studies lasting less than 5 years was 27.4%, while the total number of patients who had progressed to dementia by the end of studies lasting up to 10 years was 31.4%.
- Amnestic MCI, ***single domain*** has less chance of progressing, annually, than if other domains are also showing impairment
- Meaning … **development of dementia usually happens within the first 5 years after diagnosis of MCI, the conversion rate drops dramatically subsequently**

Dementia - Definition

- Cognitive decline from a previous level of performance
- Cognitive impairment **does** impair everyday activities (work, IADLs, ADLs)
- Does not occur exclusively during the course of delirium
- Not accounted for by another mental disorder (depression, schizophrenia, etc.)

DSM V – Major Neurocognitive Disorder

Functional Decline – Symptoms

1. Occupational
2. Social
3. Instrumental ADLs (IADLs)

usually affected earlier in the disease process

- Housework
- Shopping
- Using the telephone
- Medications
- Managing money
- Transportation

4. Basic ADLs –

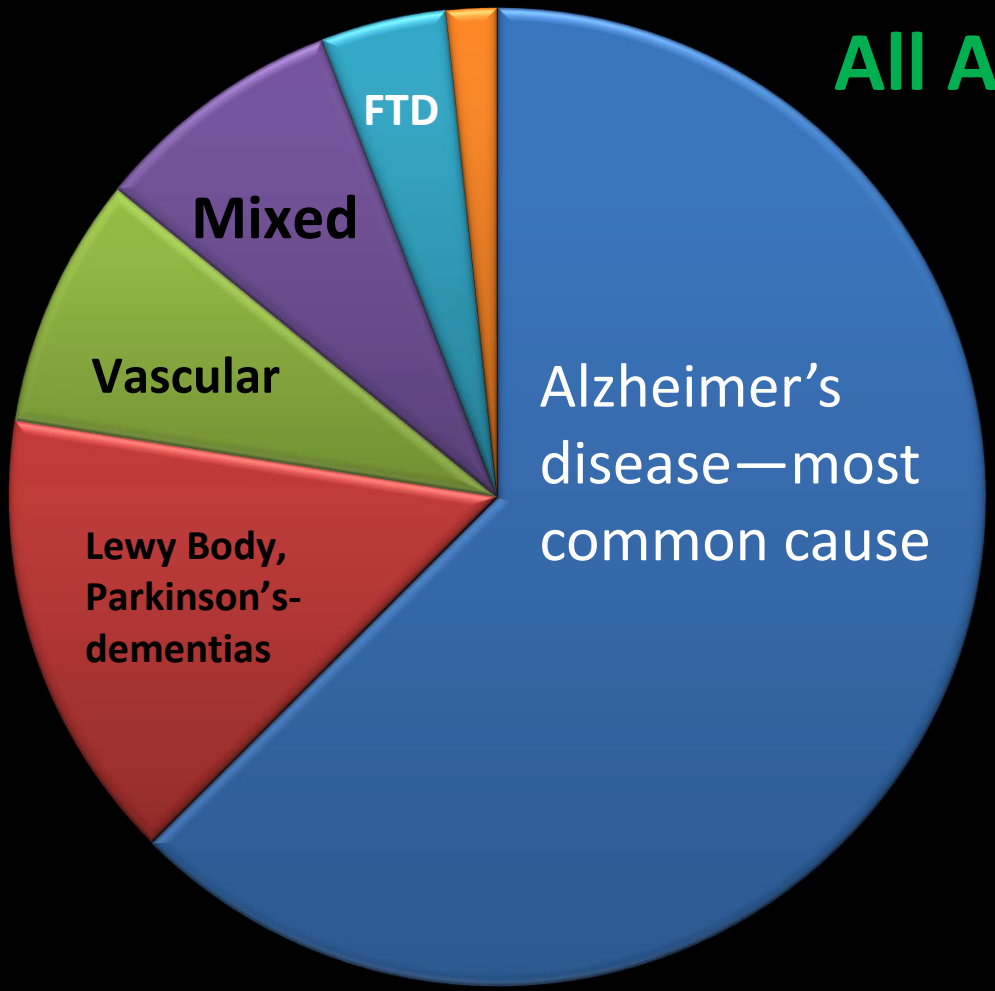
affected later in disease process

- Functional mobility
- Bathing/showering
- Dressing
- Grooming and hygiene
- Toileting

NEURODEGENERATIVE DEMENTIAS

- Alzheimer's disease
- Dementia with Lewy Bodies:
  - Lewy Body Dementia
  - Parkinson's disease- Dementia
- Vascular Dementia
- Mixed Dementia
- Frontotemporal Dementias
- Other (eg, Normal Pressure Hydrocephalus)

DEMENTIA
All Age Groups



- Alzheimer's disease
- Dementia with Lewy Bodies / PDD
- Vascular Dementia
- Mixed Dementia
- Frontotemporal Dementias
- Others — NPH, CJD, PSP, CBD, HC-Sclerosis, **PART, LATE** Amyloid- angiopathy, MS, CTE, HD, HIV, syphilis, MSA, ETOH

Question 1B

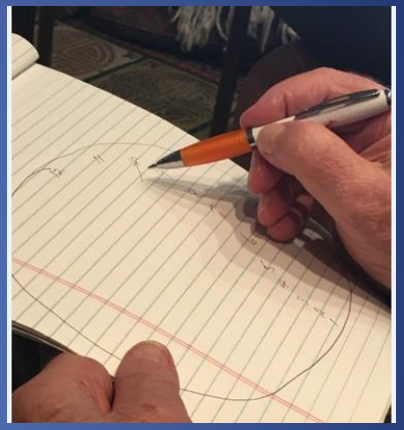
- The 77-year-old retired physician with amnestic mild cognitive impairment multiple domains
  - The most likely etiology for the cognitive impairments in this patient is:
    - Vascular dementia
    - Alzheimer's disease
    - Lewy body dementia
    - Depression

Evaluation of Cognitive Impairment

- Detailed history
  - Should have informant
  - Social and Family histories are important
- Examination
  - Mental status: alert, attentive, engaged, cooperative, etc
  - Non-cognitive (“Elemental”) neurological exam
  - Seeing, hearing, feeling, vital signs
- Laboratory testing
- Cognitive Testing
- Imaging

Appropriate Evaluation of a patient with MCI or dementia

- Screening metrics we use:
  MMSE, Montreal Cognitive Assessment



- Lab work to rule out reversible causes
  - **CBC, CMP**
  - **TSH level, reflex to T4/T3**
  - **Vitamin B12 level**
  - ESR (sedimentation rate), in occasional cases
  - RPR (no longer routinely done, only if at increased risk)
  - Selectively: HIV, MMA if B12 level intermediate, FTA&CSF VDRL/cell count if suspected neurosyphilis
- Brain MRI (CT, if MRI not safe or feasible)

May Need:

- Neuropsychologic evaluation
  - 3-5 hours (simple vs. complex)
  - Provides a baseline (for potential future reference)
  - Assist with making a more specific diagnosis
  - Relative strengths vs. weaknesses helps understand how to compensate, how to rehabilitate
  - May help understand how mood and behavior are contributing to impairments

Case #2

- An 87-year-old woman
- Gradually progressive symptoms 2-3 years ago, began showing difficulty recalling recent information/events, and a tendency to repeat herself is increasing in frequency.
- Son helping more with finances, he has set up a pill organizer for what are only 3 medications, but one needs to be taken before breakfast.
- She recently lost ability to play bridge as well as she used to, friends have told him. She stopped driving 1 year ago after getting lost several times.

QUESTION 2A

- What is the most likely diagnosis?
  - Frontotemporal dementia
  - Alzheimer's disease
  - Lewy body dementia
  - Vascular dementia

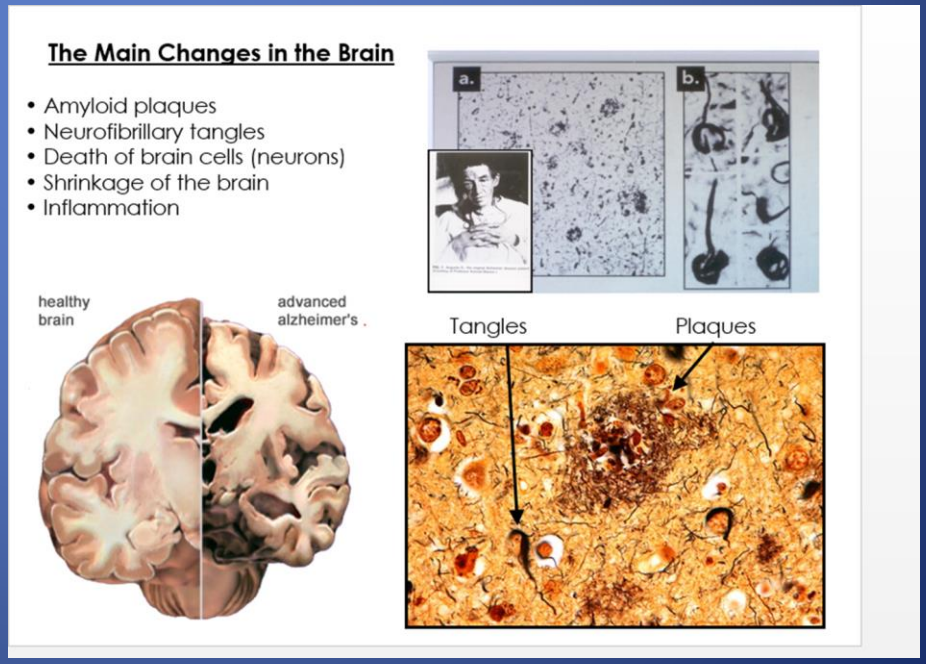
Alzheimer’ s Disease - Symptoms

Insidious onset and progressive decline

- Memory changes
  - Repeating, loss of recall of recent events, information, conversations
  - Misplacing items more often
- Mild confusion
- Difficulty planning, organizing
- Personality and behavior changes
  - Neuropsychiatric Symptoms:
    - Depression, anxiety, withdrawal, irritability, aggression, apathy
- **EARLY ON: Should be no motor symptoms**
  - **“Elemental” non-cognitive neurologic examination expected to be unremarkable**

Alzheimer's Disease

- Most common form of dementia
- Progressive neurodegenerative disorder that damages and eventually destroys brain cells
- Greatest risk factor is age
- 5% of people with the disease are < 65 years
- Microscopic changes in the brain begin long before the first signs of memory loss (preclinical phase)



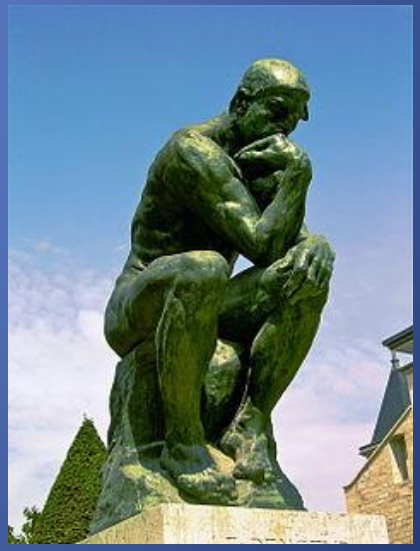
Alzheimer's disease

- Acetylcholine is the main transmitter affected
  - Glutamate, NE, 5-HT, & others are affected
- Apo-E4 allele increases lifetime risk of developing Alzheimer's
- Aβ-42 (Beta-amyloid) is increased in brain but *low* in CSF
- Tau is increased in CSF and cerebral cortex (in particular, phosphorylated Tau)

QUESTION 2B—Back to Case 2

For this 87-yr. old woman with probable Alzheimer's disease

- **Should you order an MRI?**
  - **Yes**
  - **No**
  - **Optional**
  - **Need more information**



QUESTION 2B—Back to Case 2

The 87-yr. old woman with probable Alzheimer's disease

- **Would you order an MRI?**
  - **Yes**

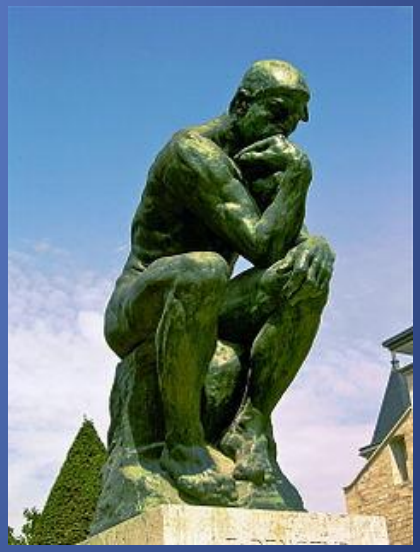


Figure 3. Brain Magnetic Resonance Imaging Showing a Right Frontal Extra-Axial Mass (asterisks) With Extensive Intraparenchymal Inflammatory Reaction (arrows)

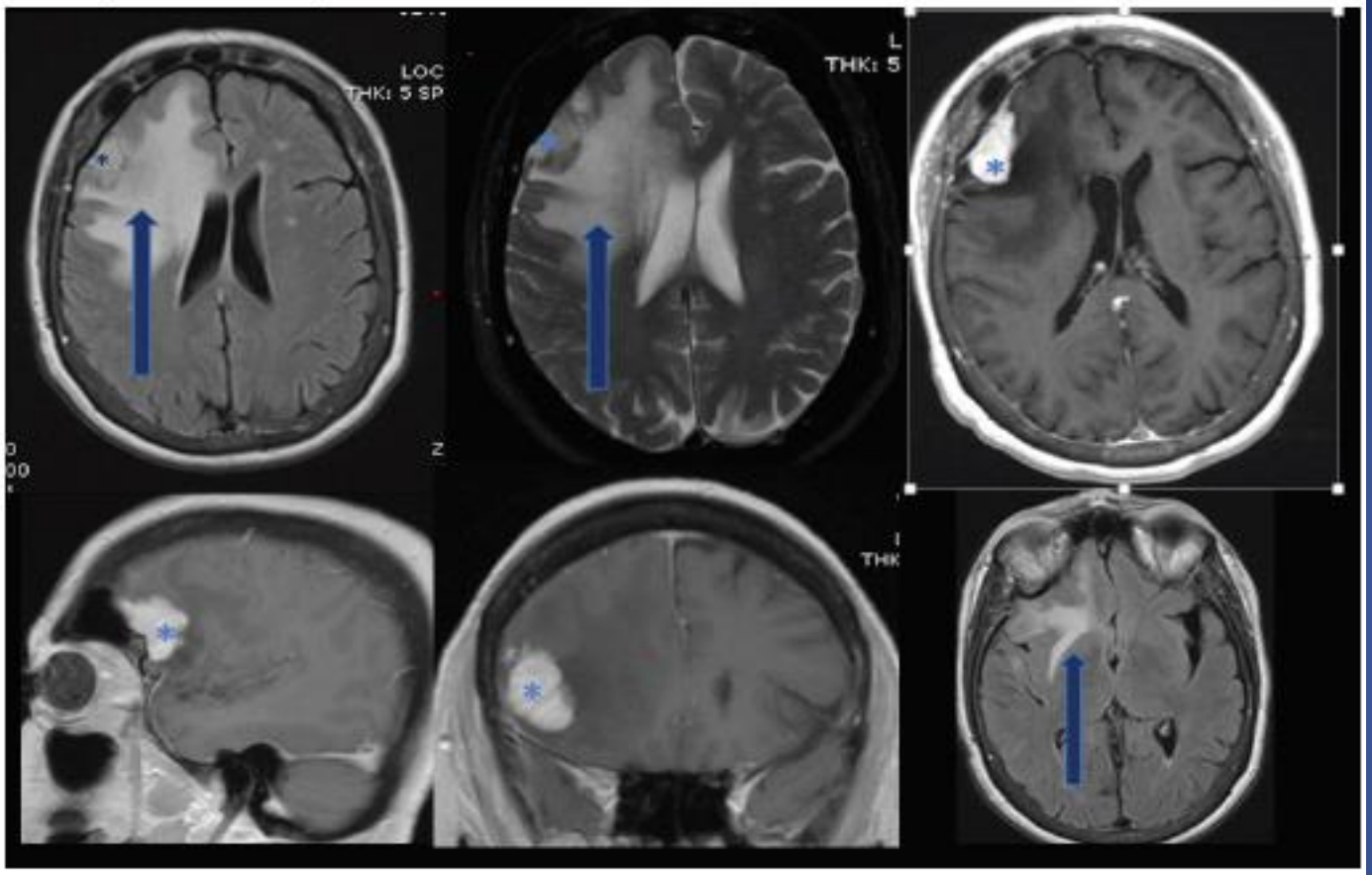
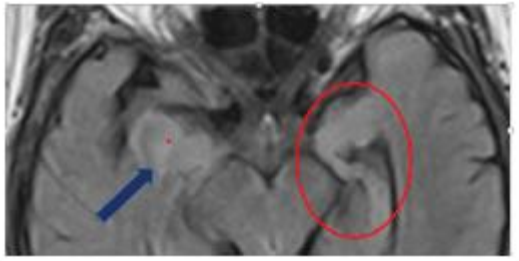
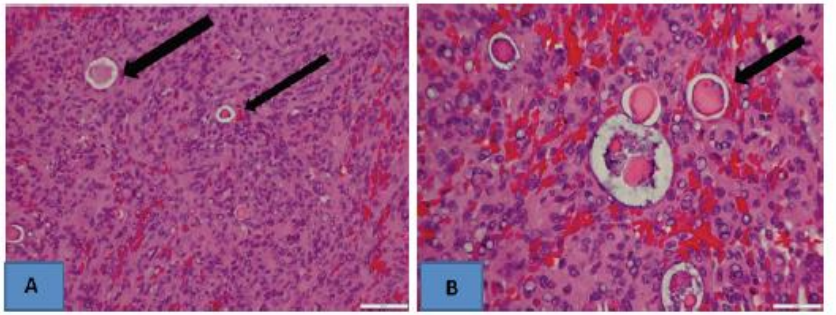


Figure 4. Axial Fluid-Attenuated Inversion Recovery Image at the Midbrain and Medial Temporal Lobes[a]



[a]Edema or inflammation extends down to the right hippocampus (arrow), with effacement of the temporal horn, right lateral ventricle. Compare to the normal left hippocampus (red oval).

Figure 5. Brain Biopsy Histology, Right Frontal Head Region[a]



Low power view (A) and high power view (B) show a secretory meningioma with scattered intracellular lumina containing eosinophilic secretory material (arrows).

Alzheimer's treatments - Medications

Acetylcholinesterase Inhibitors

Donepezil (Aricept™)

Rivastigmine (Exelon™)

Galantamine (Razadyne™)

NMDA Antagonist

Memantine (Namenda™)

2021: aducanumab (anti-amyloid monoclonal antibody)

memantine

- NMDA antagonist
- Moderate to severe AD (little help in mild disease)
- Modest benefits
  - Cognition
  - Activities of daily living
  - Behavior
- Immediate release (twice daily) and XR (once daily) forms
  - IR generic in summer of 2015
- Dose needs to be slowly titrated for the first month
- Well tolerated
  - Headache, dizziness, confusion

Case 3

- 62 y/o male battling several years of anxiety and depression
- 4-5 years of episodes of violent dream enactment, usually dreaming that escaping from jail, wife would witness, he wouldn't always sleep though this
- 2-3 years ago began losing balance, when walking, without vertigo, and falls have increased in frequency this year, occasional rest tremor observed
- Shows worse days and better days of focus/concentration
- Intact behavior, acts appropriately

Case 3

- Occasional tremor at rest seen in the left hand, like “I’m flipping the bird”
- Misplacing items more often, mild difficulty recalling comes back later
- Stopped driving, could no longer navigate well enough, lost depth perception for cars in front him
- Lab work and brain MRI are normal

Case 3

- **EXAMINATION:**
- **Some psychomotor slowing, fluctuation in attention**
- **Cognitive:**
  - **MMSE score is 20/30**
  - **MoCA score is 13/30, with relatively spared language and orientation**
- **Cranial Nerves:**
  - **Mildly reduced upgaze**
  - **Saccadic substitution**
  - **Mild loss of prosody in speech**

Case 3

- **EXAMINATION:**
- **Mild motor perseveration**
- **Minimal to mild bradykinesia in natural movements**
- **Loss of amplitude and rhythm in rapid alternating movements**
- **Gait: Minimally reduced speed, with increased cadence compensating for slightly reduced stride length**

QUESTION 3A

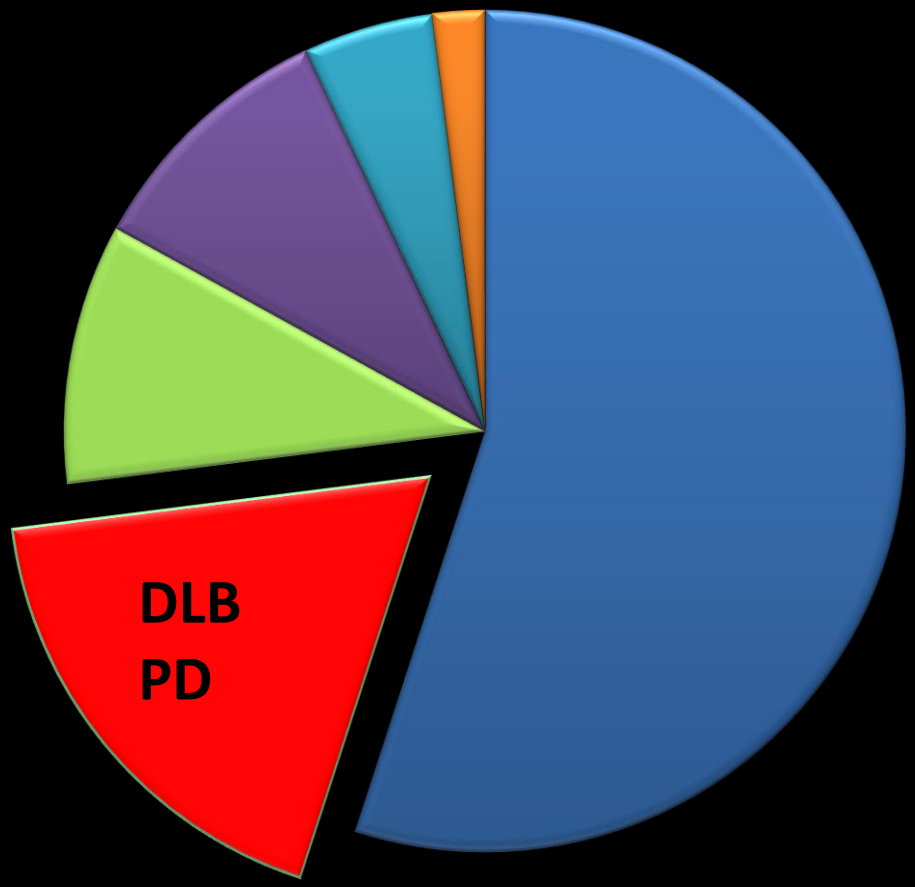
- Assuming a degenerative dementia is present, the most likely etiology of this presentation is:
  - Alzheimer's disease, atypical
  - PD-dementia
  - Dementia with Lewy bodies (Lewy body dementia)
  - Frontotemporal dementia

QUESTION 3A

- Assuming a degenerative dementia is present, the most likely etiology of this presentation is:

  - Dementia with Lewy bodies (Lewy body dementia)

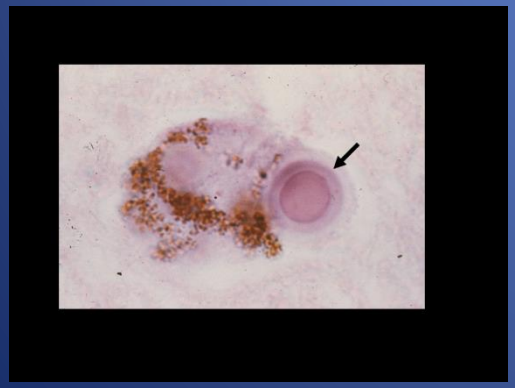
All Age Groups

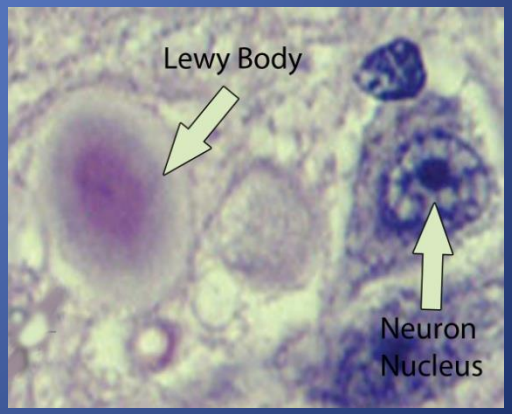


- Alzheimer's disease
- Dementia with Lewy Bodies / PDD
- Vascular Dementia
- Mixed Dementia
- Frontotemporal Dementia
- Others

Dementia with Lewy Bodies

- Progressive neurodegenerative disease
- Proteins called Lewy Bodies (alpha synuclein) are deposited in nerve cells
- Prominent memory impairment may not be evident in early stages





Dementia with Lewy bodies

Early impairment of visual-spatial skills and attention, "Pure" cases tend to spare memory/language early on

4 Core Clinical Features

- Fluctuations in
  - Cognition and levels of alertness
  - Subtle or dramatic
- Visual Hallucinations
  - Occur early in the disease (occurs later in other forms of dementia)
- Parkinsonism
  - Bradykinesia, gait disorder, limb rigidity
  - Usually more symmetric than PD and often without tremor
- RBD (REM-sleep Behavioral Disorder)
  - Dream enactment and vocalizations
  - Usually occurs early in the course of the disease

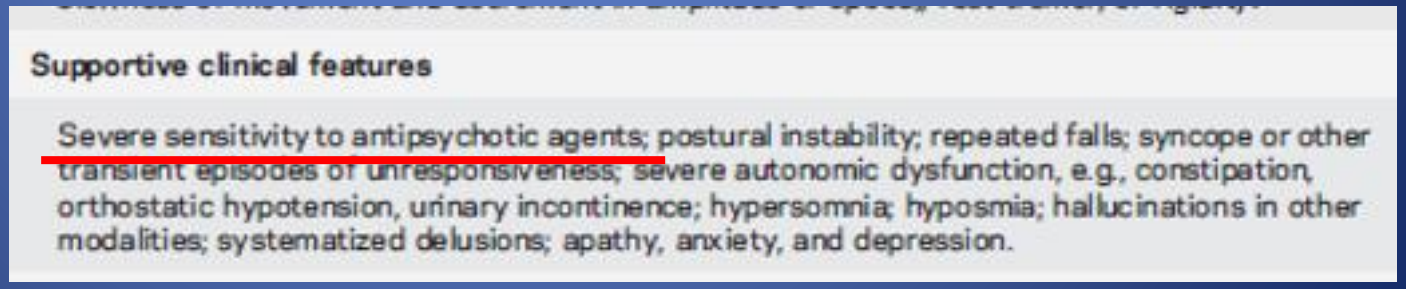
QUESTION 3B

- The same 62 yr. old man with DLB develops urosepsis, admitted to a hospital, and becomes agitated on day #2, with aggressive behavior, despite non-Rx strategies such as reorienting by staff, familiar home objects/clocks around, quieter/darkened room overnight, and a 1:1 sitter
- Which of the following medications is not an agent of choice in this particular patient?
  - **Ativan**
  - **Haldol**
  - **Trazodone**
  - **Valproic acid, IV**

QUESTION 3B

- The same 62 yr. old man with DLB develops urosepsis, admitted to a hospital, and becomes agitated on day #2, with aggressive behavior, despite non-Rx strategies such as reorienting by staff, familiar home objects/clocks around, quieter/darkened room overnight, and a 1:1 sitter
- Which of the following medications is not an agent of choice in this particular patient?

– **Haldol**



Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.

Dementia with Lewy Bodies

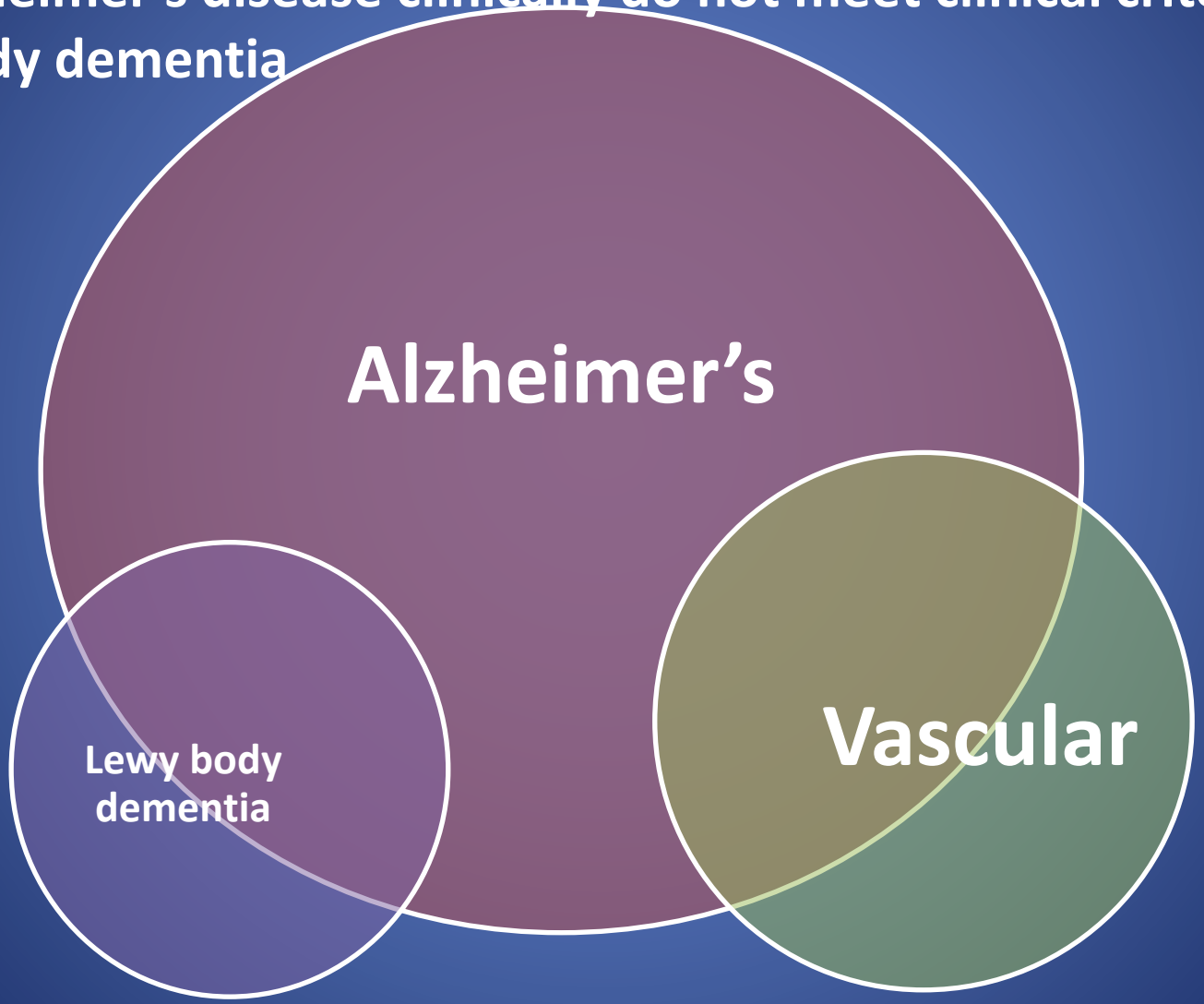
- Supportive features
  - **Severe sensitivity to anti-psychotic agents**
  - Autonomic dysfunction
  - Repeated falls & postural instability
  - Syncopal episodes or transient unresponsiveness
  - Hallucinations in other modalities
  - Systematized delusions
  - Apathy, anxiety, depression

Parkinson's Disease Dementia (PDD)

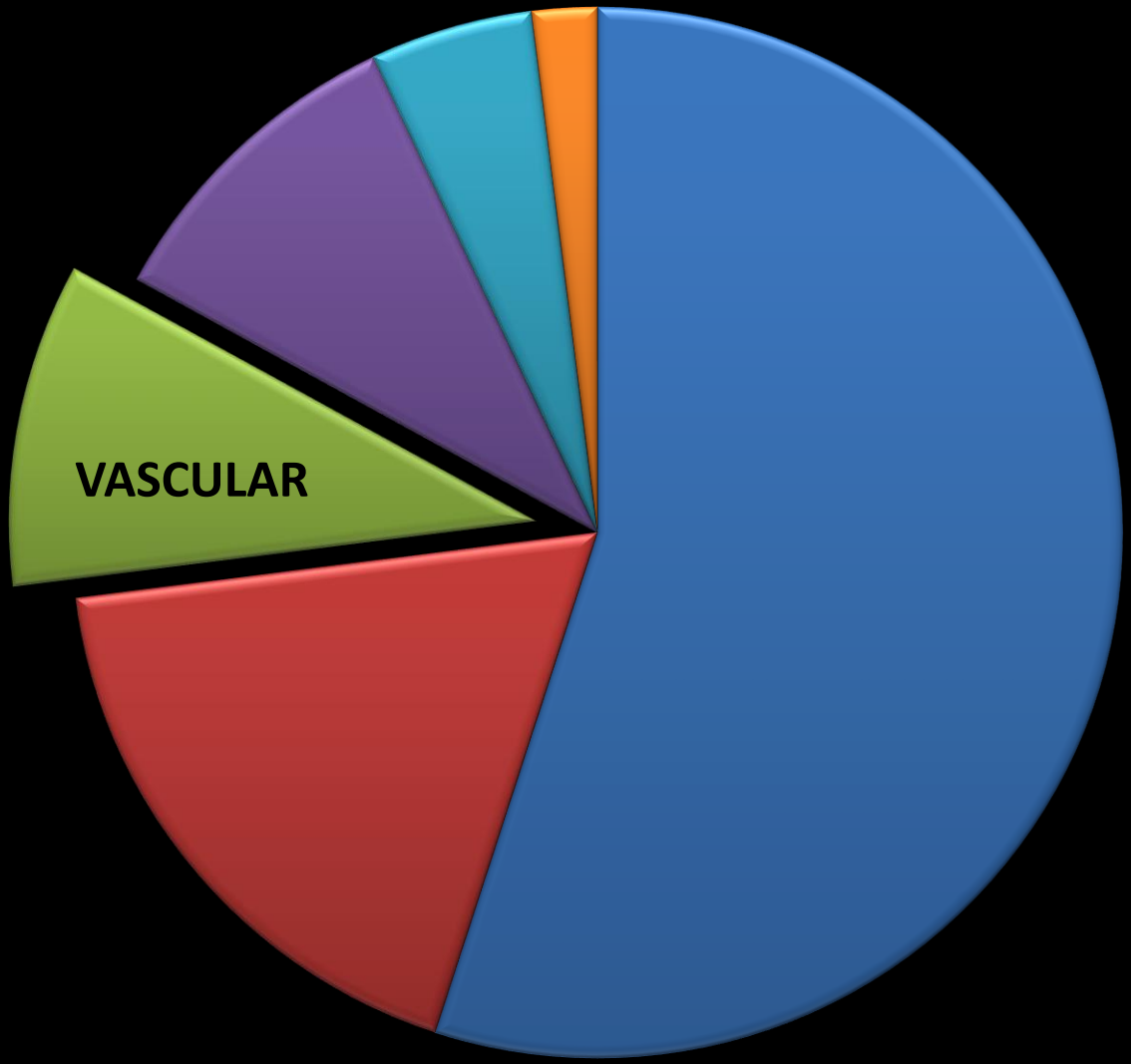
- Dementia occurs in the setting of established parkinsonism
- "1 year rule"
  - parkinsonian motor features are present for more than 1 year before the onset of cognitive decline
- Symptoms similar to DLB

- Parkinson’s medications can help reduce motor symptoms but can also cause increased confusion and hallucinations
- Usually a good response to cholinesterase inhibitors

Many individuals with Lewy body dementia also have Alzheimer's pathology, and overlap of symptoms as well, whereas most patients with Alzheimer's disease clinically do not meet clinical criteria for Lewy body dementia



All Age Groups

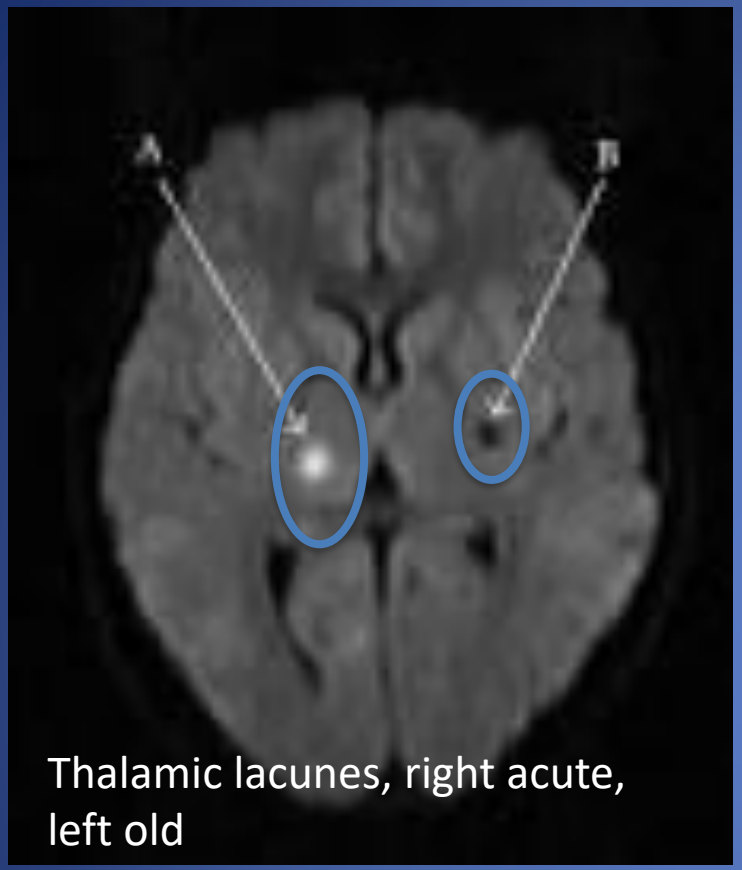


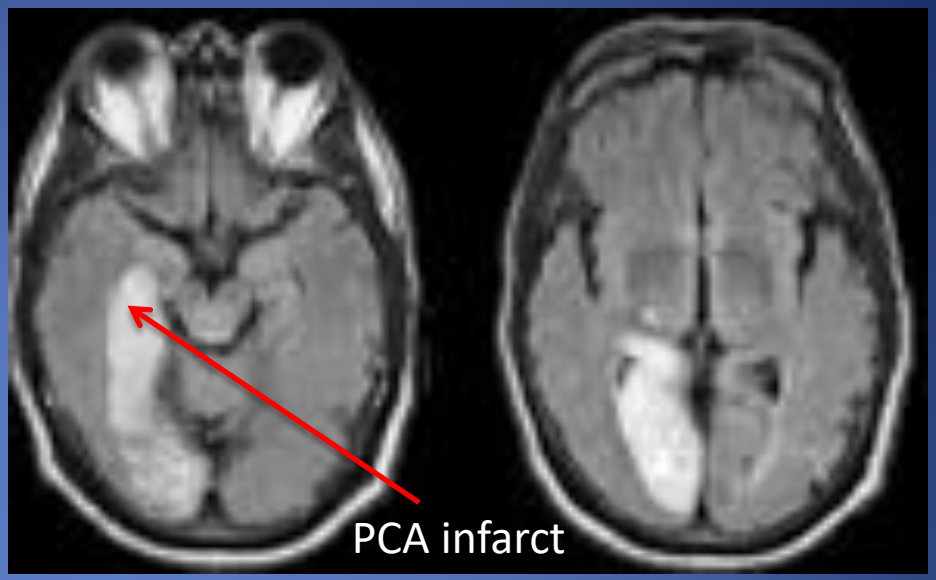
- Alzheimer's disease
- Dementia with Lewy Bodies
- Vascular Dementia
- Mixed Dementia
- Frontotemporal Dementia
- Others

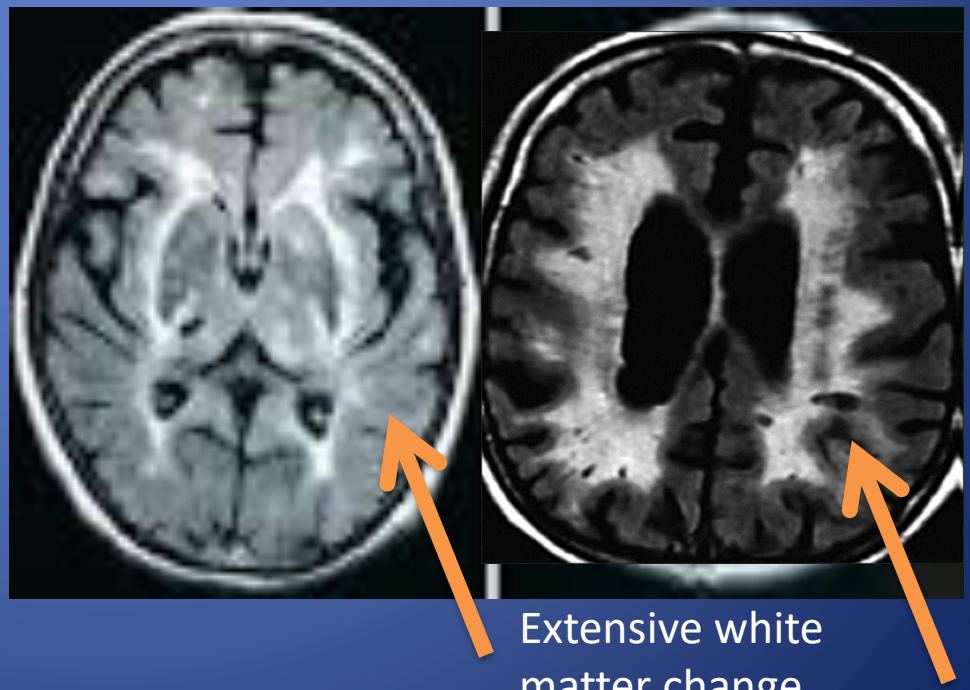
Vascular Dementia (VaD)

- May be overdiagnosed
- Not a single disease but a group of syndromes
  - Underlying cause is cerebrovascular disease in some form
  - Different pathophysiologic mechanisms
    - Chronic uncontrolled HTN/DM
    - PCA infarct
    - Thalamic lacune
    - Cerebral amyloid angiopathy
  - Variety of clinical manifestations
- Classified in many different ways

Cerebral Infarcts



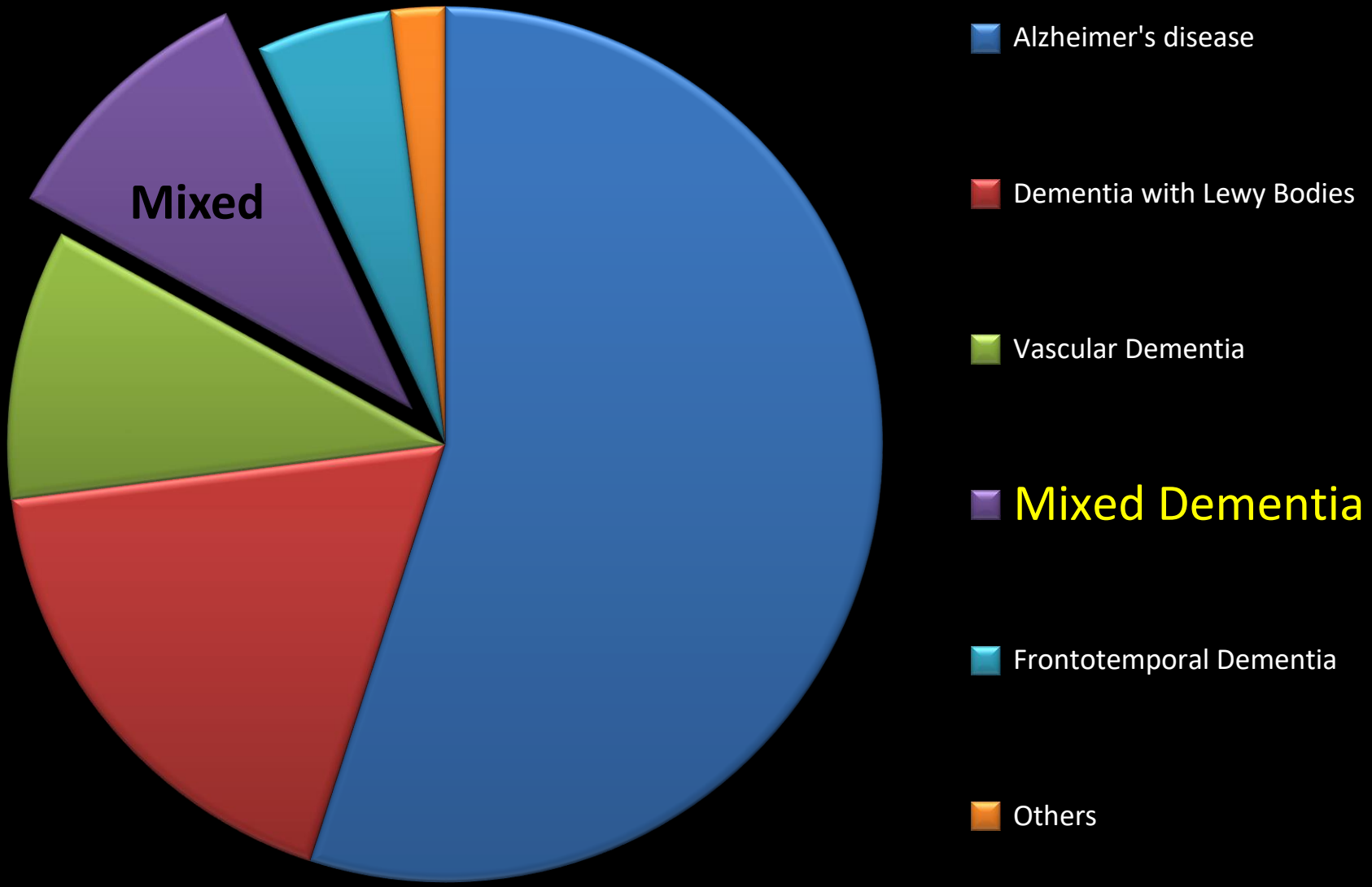




Clinical Features Consistent with a diagnosis of VaD

- Abnormal executive functioning (planning, sequencing, etc)
- Personality and mood changes
- Pseudobulbar palsy
- Psychomotor retardation
- Possible gait disturbance
- Possible urinary symptoms not explained by urologic disease

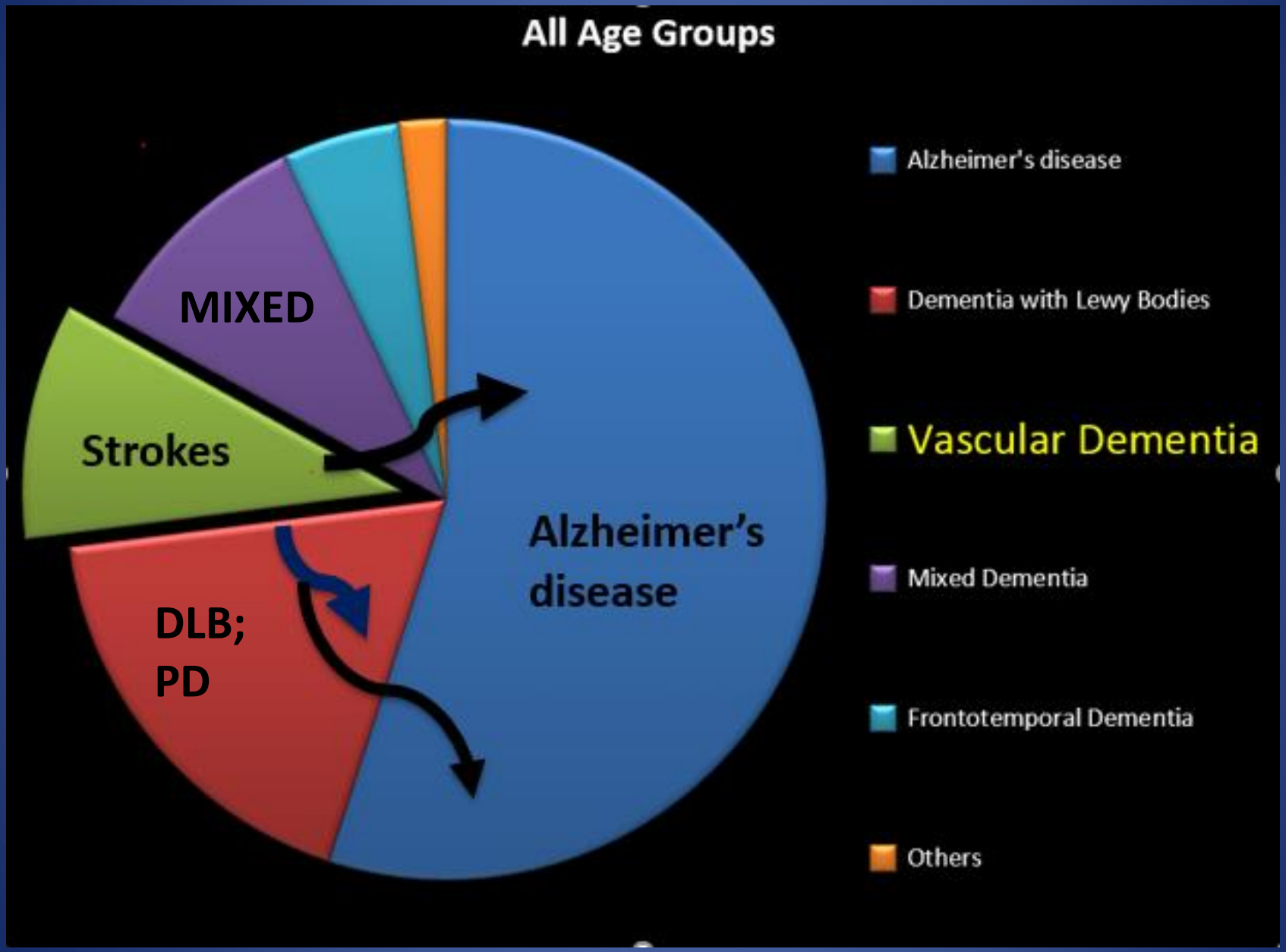
All Age Groups



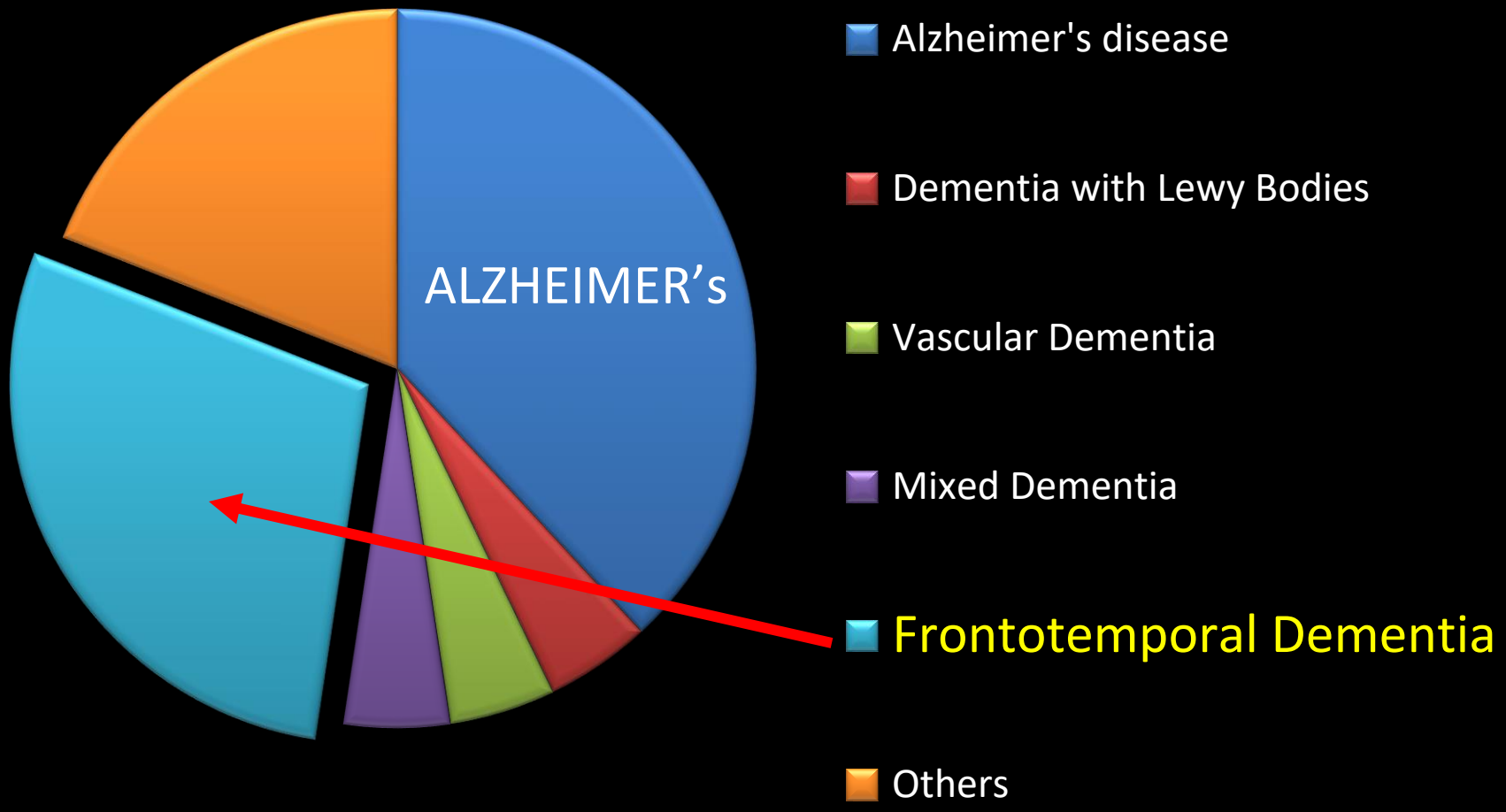
Mixed Dementia

- Refers to the co-occurence of 2 diseases (usually AD and VaD pathology; many with DLB have mixed pathology with AD)
- Can be difficult to distinguish which process is "more important"
- 1/3 of patients diagnosed with VaD will have AD pathology (meet the path definition of AD) at autopsy

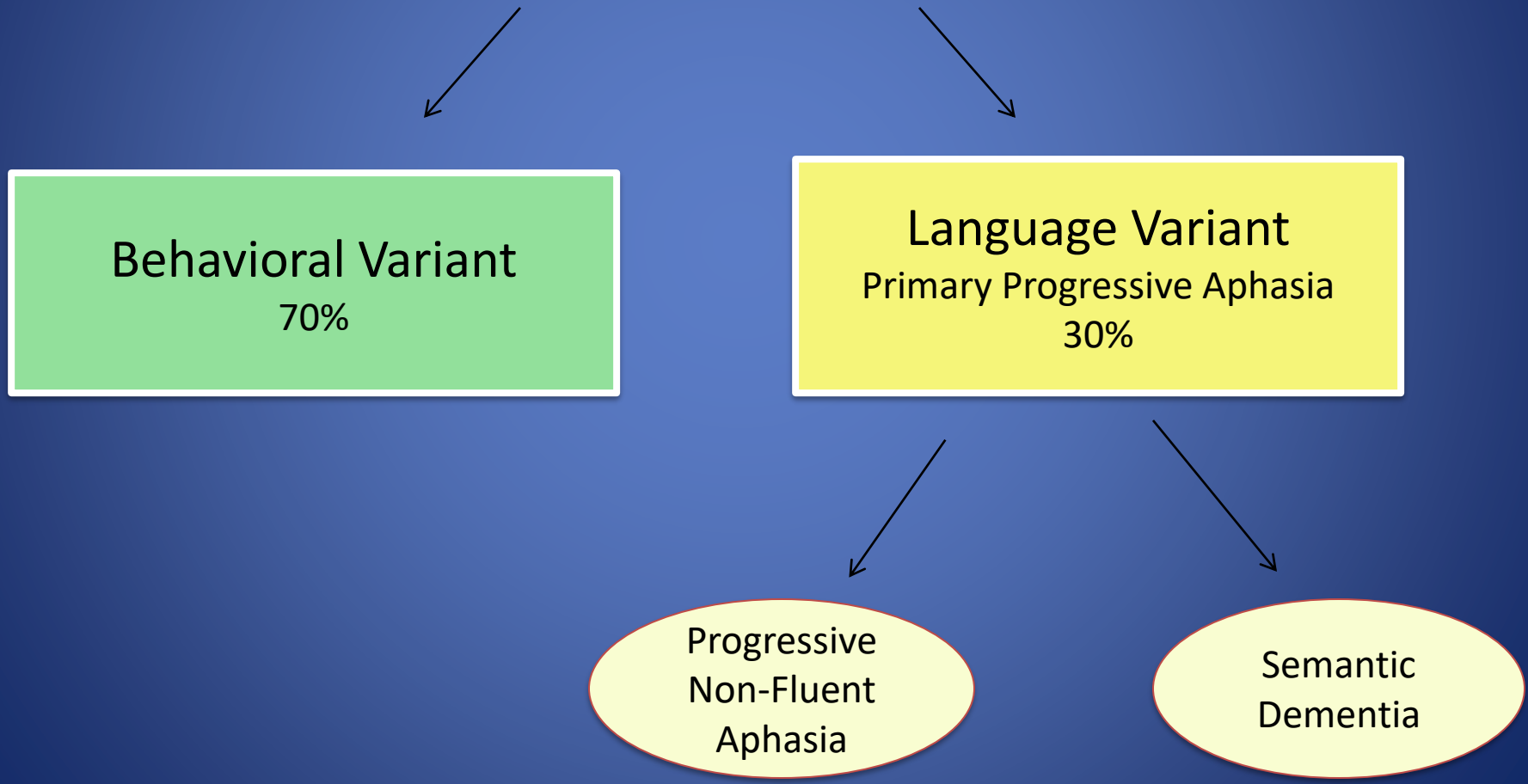
(Alzheimer Dis Assoc Disord. 1999)


All Age Groups
MIXED
Strokes
DLB;
PD
Alzheimer's disease
Alzheimer's disease
Dementia with Lewy Bodies
Vascular Dementia
Mixed Dementia
Frontotemporal Dementia
Others

Dementia, under Age 65

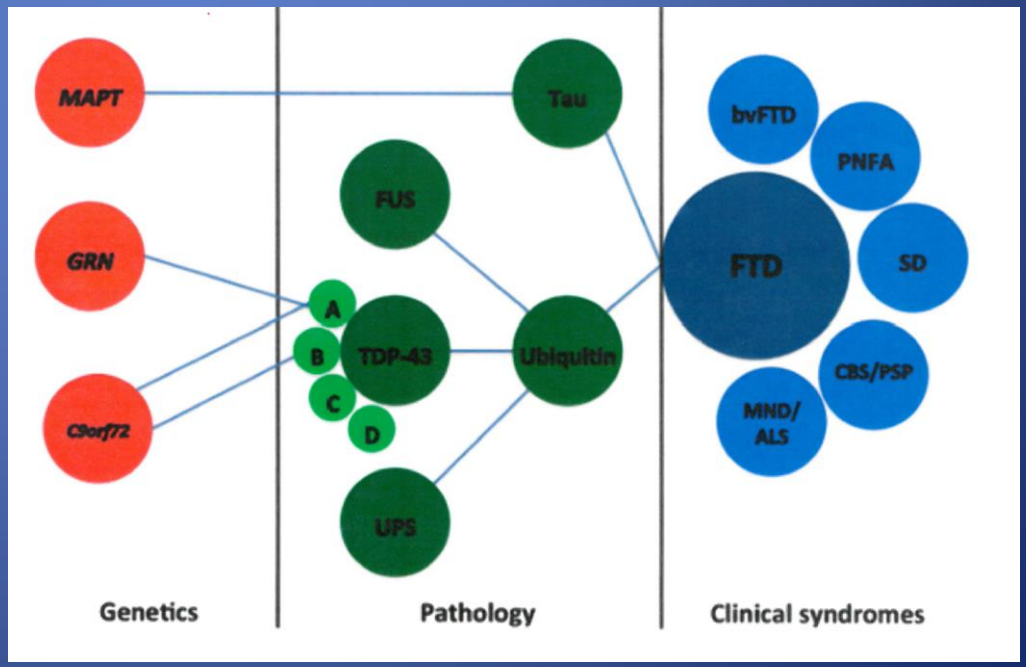


Frontotemporal Dementia (FTD)



Frontotemporal Dementias (FTD)

- Typical onset is < 65 years
- More commonly a reason for dementia in those younger than 65
- 3 main clinical syndromes
- Diverse pathology



Behavioral Variant FTD

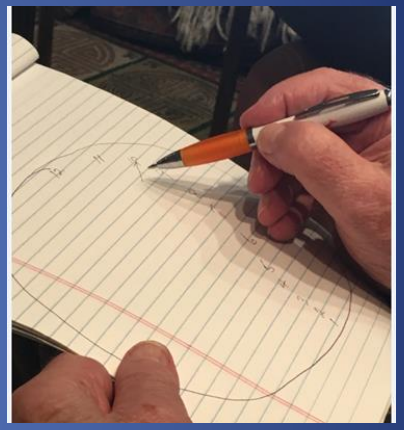
- Insidious onset and slow progression
- Personality change and disordered social conduct may be the dominant features at onset
- Memory intact initially
- Lack of insight and empathy
- Decline in personal hygiene

Behavioral Variant FTD

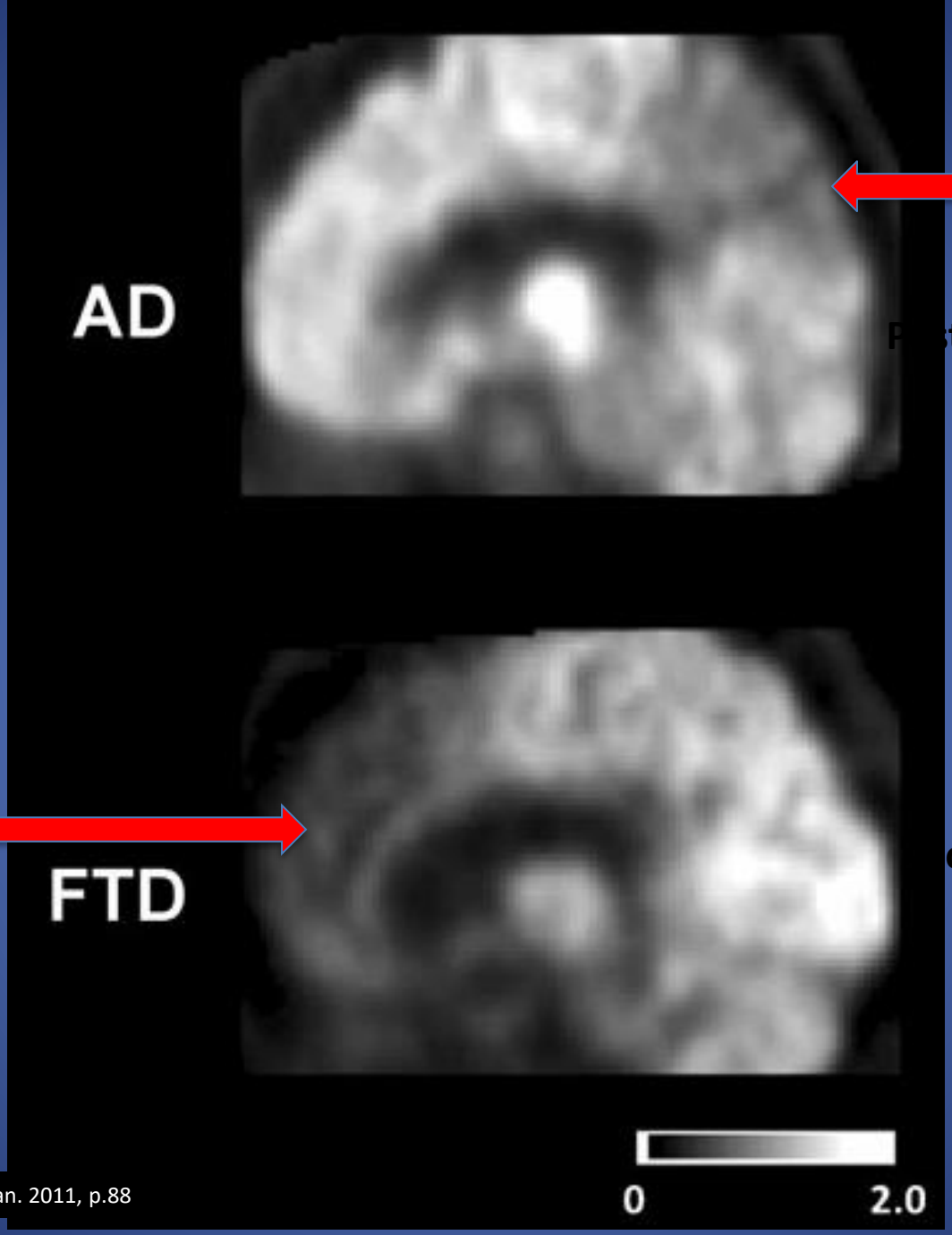
- Mental rigidity and inflexibility
- Hyperorality
- Executive dysfunction OR
- Disinhibition
  - Antisocial and Compulsive behaviors
  - Hoarding
  - Food compulsions

Appropriate Evaluation of a patient with dementia

- Screening metrics: MMSE, MoCA, Clock drawing



- Lab work to rule out reversible causes
  - **CBC, CMP**
  - **TSH level, reflex to TFT's**
  - **Vitamin B12 level**
  - ESR (sedimentation rate), in occasional cases
  - RPR (no longer routinely done, only if at increased risk)
  - Selectively: HIV, MMA if B12 level intermediate, FTA&CSF VDRL/cell count if suspected neurosyphilis
- Brain MRI (CT, if MRI not safe or feasible)
- **FDG-PET, selectively: differentiate between Alzheimer's and a frontotemporal dementia**



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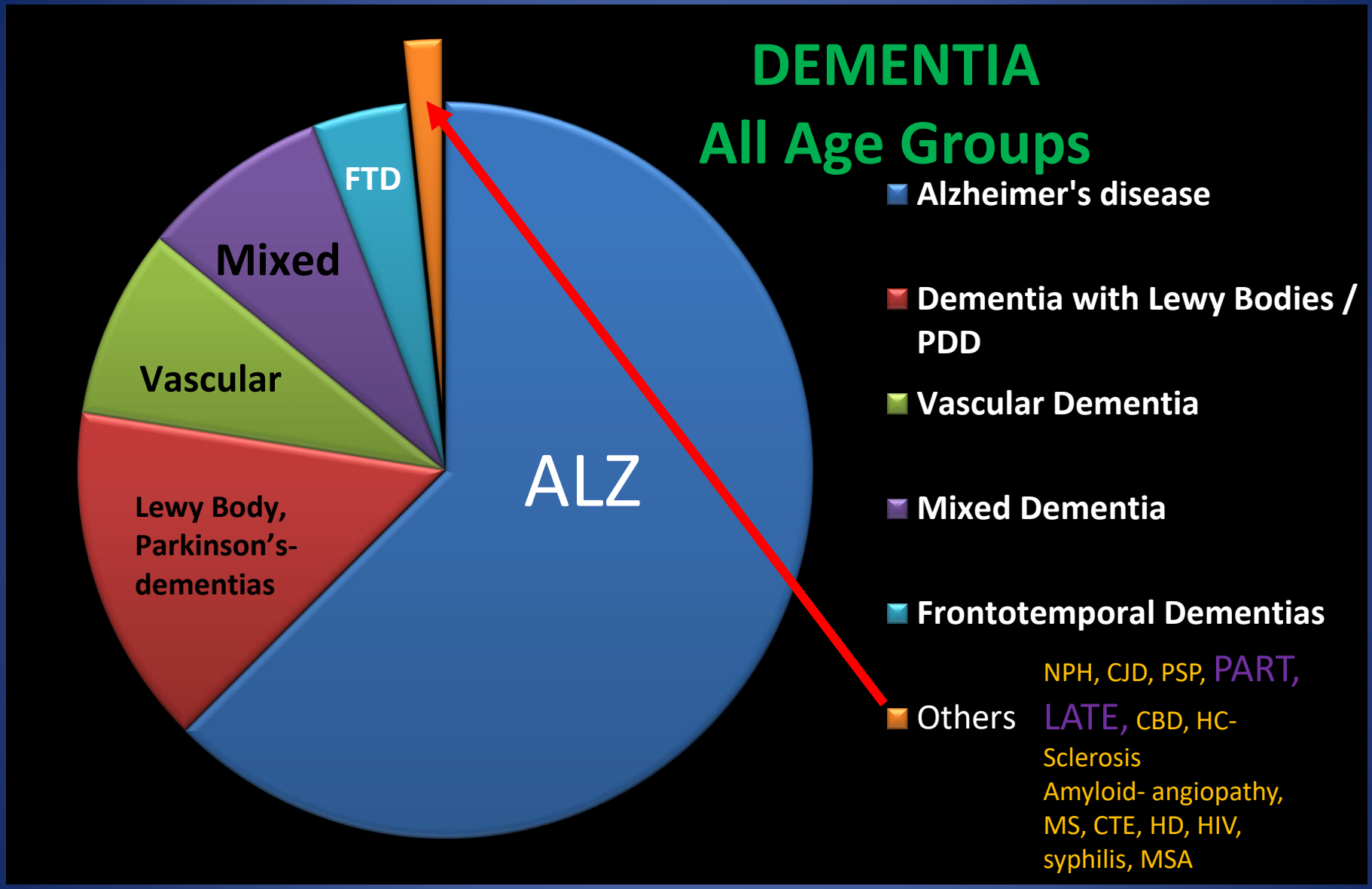
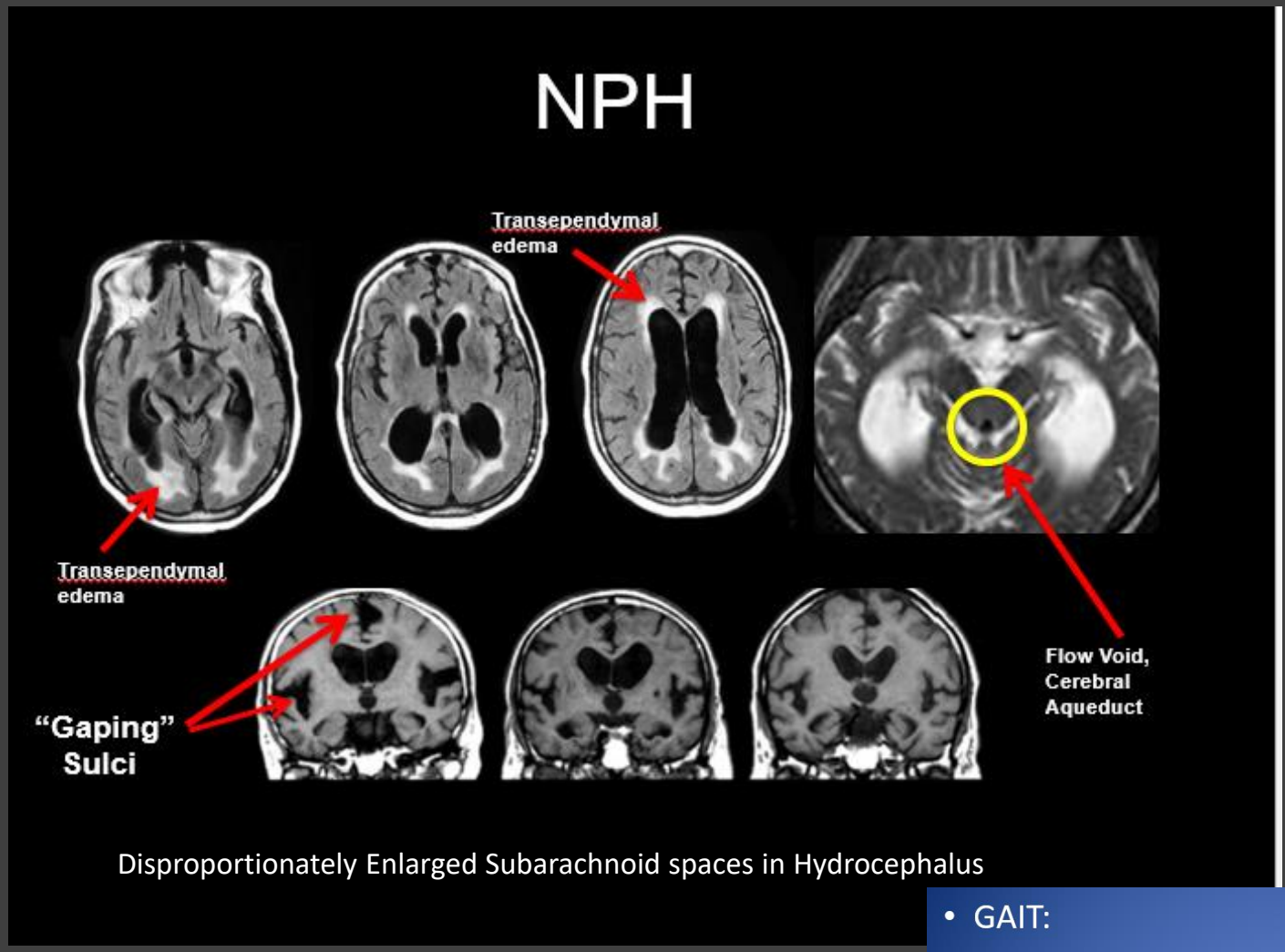
FTD - Language Variant
Primary Progressive Aphasia

- Progressive non-fluent aphasia
  - Expressive aphasia, word finding difficulty
  - Understand but cannot speak
  - Loss of grammar, speech apraxia
- Semantic Dementia
  - Speak fluently but cannot understand meaning of individual words, significant anomia, cannot follow commands adequately


DEMENTIA
All Age Groups
FTD
Mixed
Vascular
Lewy Body, Parkinson's-dementias
ALZ
Alzheimer's disease
Dementia with Lewy Bodies / PDD
Vascular Dementia
Mixed Dementia
Frontotemporal Dementias
Others
NPH, CJD, PSP, PART, LATE, CBD, HC-Sclerosis
Amyloid- angiopathy, MS, CTE, HD, HIV, syphilis, MSA

“Other” Dementias

- Reversible causes
- Cortical Basal Degeneration
- Progressive Supranuclear Palsy
- **Normal Pressure Hydrocephalus**
- Chronic Traumatic Encephalopathy
- Creutzfeldt-Jacob disease
- Huntington’s disease
- Alcohol
- HIV
- Anoxia



Disproportionately Enlarged Subarachnoid spaces in Hydrocephalus

NPH:

Triad of
1) Gait disturbance
2) urinary incontinence and
3) mild dementia (attention, executive function impairments)

With good memory

- GAIT:
  - Magnetic; robotic, "glue-footed", sliding feet along the floor
- BLADDER:
  - Large volumes voided without control or warning
    - ? Less urgency than usual overactive bladder
- Dementia
  - is usually LATER

QUESTION 4

- The following feature on an early/mild dementia is a red flag the primary cause is unlikely to be Alzheimer's disease:
  - Executive dysfunction worse than memory
  - Visual hallucinations
  - Prominent gait disturbance
  - Moderately severe word finding difficulty

QUESTION 4

- The following feature in an early/mild dementia is a red flag the primary cause is unlikely to be Alzheimer's disease:

  - **Prominent gait disturbance**

Disease	Age (y) at diagnosis	Progression	Earlier cognitive symptoms	Visual hallucinations	Parkinsonism	REM sleep behavior disorder	Autonomic insufficiency	Dominant presenting symptoms
Alzheimer dementia	Late (> 65) Early (< 65)	Gradual	Early impairment of memory and attention	Rare	Late stages	Rare	Rare	Memory loss, cognitive impairment
Vascular dementia	≥ 60	Sudden, stepwise	Executive dysfunction, deficits depend on location of stroke or lesion	Rare	Depends upon location of stroke	None	None	Sudden onset of cognitive deficits and impairment
Dementia with Lewy bodies	70s [6]	Gradual with fluctuation in cognition	Early Impairment of visual spatial skills and attention Delayed recall is relatively preserved in the beginning	Typical	Within first year	Common	Occasional	Parkinsonism or cognitive impairment
Frontotemporal dementia	Mostly < 65	Gradual	Difficulty with language and executive function or behavioral change	Rare	Sometimes	Occasional	Infrequent	Behavioral changes
Primary progressive aphasia	Around 60	Gradual	Expressive language impairment	Rare	In late stages	None	None	Expressive language impairment
Normal-pressure hydrocephalus	50s–60s	Gradual	Impairment of attention, working memory, verbal fluency and executive function; recognition memory is preserved	Rare	May present as parkinsonism	None	None	Gait impairment with urinary frequency and/or cognitive impairment

Progression can be gradual

	Clinical Syndromes	Pathophysiology, Pathogenesis	Management, treatment
Alzheimer's Disease—75% of all dementias and 75% of all MCI	Typical: Early impairment of memory and attention, gradual decline; "early" <65; "later" >65 Atypical/variants: Logopenic/language first Posterior cortical atrophy (visual variant) Behavioral/dysexecutive Apo-E4 allele risk for earlier amyloid and symptoms during life	Amyloid plaques, from toxic soluble amyloid polypeptides, between nerve cells Neurofibrillary tangles (Tau) builds up within neurons Hippocampal/medial temporal lobe degeneration and neocortical CSF can confirm diagnosis in younger patients	• Cholinesterase-inhibitors • Memantine—moderate stage • In select cases, early, aducanumab (Aduhelm), an anti-amyloid monoclonal antibody • SSRI's for depression/anxiety • Trazodone or suvorexant for sleep, melatonin • Avoid antipsychotics unless a safety issue
Dementia with Lewy bodies	Parkinsonism Visual hallucinations Fluctuations in cognitions (within a day, day to day) REM-sleep behavior disorder More symmetric parkinsonism than in idiopathic PD Very sensitive psychotroic medications, eg, anticholinergics	Lewy bodies (accumulations of alpha-synuclein) Sometimes see occipital lobe hypometabolism on FDG-PET	• Cholinesterase-inhibitors—greater cholinergic deficit than in a "pure" AD case; Exelon FDA approved • Avoid all neuroleptics except quetiapine or clozapine • Consider levodopa • Consider anti-psychotics ONLY if aggressive/agitated • Pimavanserin can help for psychosis but only approved for PD-dementia
Frontotemporal Dementias	Behavioral variant Loss of social comportment Loss of initiative/drive Progressive non-fluent aphasia Semantic dementia	TDP-43 proteinopathy most common Tauopathy most common TDP-43 proteinopathy most common	Supportive, symptomatic
Normal pressure hydrocephalus	Gait "Apraxia"; magnetic Overactive bladder/incontinence Frontal/subcortical dysfunction	Reduced resorption of CSF, from ventricles	Only gait may respond to a VP shunt
Vascular dementia **Small vessel ischemic** **Multi-infarct** **Strategic infarct** **Cerebral amyloid angiopathy**	Frontal subcortical dysfunction impaired free recall, improves with cues or choices Diminished attention, executive dysfunction Reduced processing speed	Need imaging (usually MRI) to diagnose	Can respond to donepezil Supportive Symptomatic, eg, Nuedexta for PBA

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THE END