LOUISIANA DEPARTMENT OF HEALTH

Diagnosing Dementia Subtypes

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Project ECHO

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Objectives

1. **To understand cognitive profiles specific to dementia subtypes.**
    - Alzheimer's disease
    - Frontotemporal dementia – Behavioral Variant
    - Vascular Cognitive Impairment – Vascular Dementia
    - Dementia of Lewy Body

2. **To understand how screening assessments, including digital exams, can enhance early diagnosis & treatment.**

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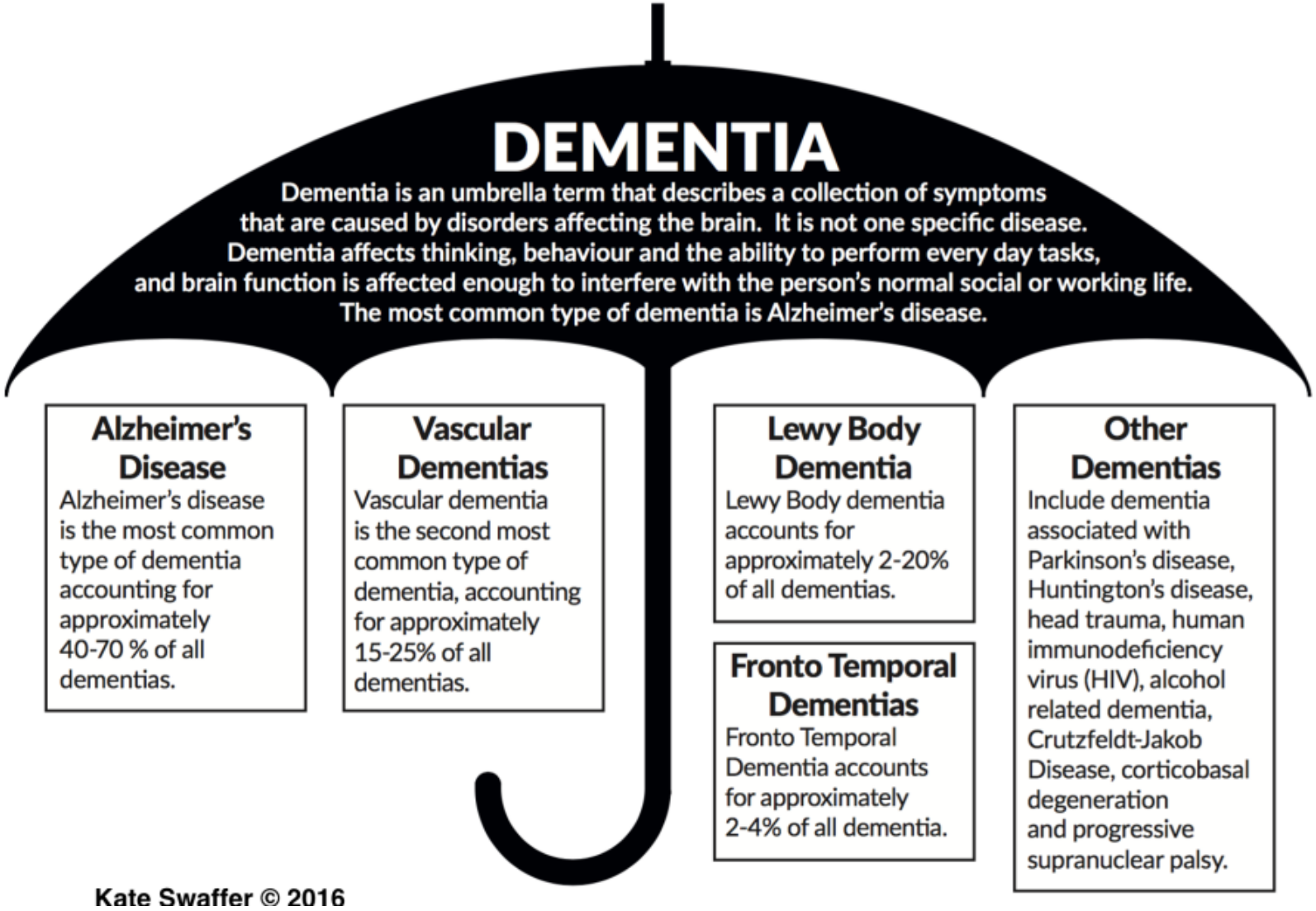
Dr. Foundas has nothing to disclose. All figures included are referenced/source material acknowledged.

Statement of the Problem

- **Lifetime risk estimates indicate that about 42% of adults aged >55 will develop dementia**
- **One study showed that about 39.5% of adults >65 years meeting dementia criteria were undiagnosed**
  - Amjad H, Roth D, Sheehan O, et. al. (2018) Underdiagnosis of dementia: an observational study of patterns in diagnosis and awareness in US older adults. *J Gen Intern Med*. 2018:33
- **Louisiana citizens are at increased risk of developing cognitive decline with about 1 in 5 citizens >45 years currently meeting the criteria of subjective cognitive decline (SCD).**
  - This rate is one of the highest in the United States with 20.9% of Louisiana citizens reporting SCD compared to the national average of about 10.8%.



- Cognitive
- Behavioral
- Motor
- Autonomic
- Sleep

Clinical Case 1

Chief Complaint: memory complaint

History of Present Illness: Mrs. Roberts is a 79-year-old woman with slowly progressive memory loss over the past 3-4 years. She has word finding difficulty and gets lost in unfamiliar places. She lives independently but is having trouble paying bills and assembling taxes.

Past Medical – unremarkable, no hearing or visual loss, no depression or other psychiatric history, no known sleep disorder, no prior TIA/stroke or TBI Social History: No history of smoking; Past alcohol use

Family history: no known history of dementia

Examination – Recall 0 of 3 words at 5 minutes, Difficulty naming parts of objects, Impaired ability to copy complex geometric figures (intersecting pentagons)

Cranial nerves, Sensorimotor, Cerebellar, Gait & Station, DTRs intact, No Babinski responses present & no pathological reflexes.

Clinical Case 2

Chief Complaint: progressive change in behavior

History of Present Illness: Mr. Jones is a 70-year-old man with a progressive change in behavior. He has become sloppier in his appearance; he has difficulty completing tasks. He has developed some repetitive behaviors. He can manage ADLs but is showing poor judgement in managing finances.

Past Medical & Social History – Unremarkable Past history of cigarette and alcohol use

Family history: Father with a dementia diagnosis (unknown type)

Examination – Recall 2/3 words at 5 minutes, 2/3 with a longer delay. He has difficulty with verbal fluency and with response inhibition & difficulty on Go-No-Go. He is perseverative.

Cranial nerves, Sensorimotor with faciliatory paratonia, Cerebellar, Gait & Station, DTRs intact, No Babinski response nor pathological reflexes

Clinical Case 3

Chief Complaint: stepwise decline in cognitive function

History of Present Illness: Mrs. Moore is a 72-year-old woman with a stepwise decline in memory. She also has some word finding difficulty and she has had several falls. No known history of TIA or stroke. No history of TBI/concussion.

Past Medical & Social History – Atrial fibrillation; History of Heart disease, S/P MI with stents in 1995; HTN & HLD treated with medication

Social history: past smoking history; no alcohol Family History: mother with dementia in 80s; sister died with probable vascular dementia

Examination – Recall 1 of 3 words at 5 minutes, Difficulty naming parts of objects, difficulty with shifting mental set and reduced Letter fluency

Cranial nerves, Sensorimotor, Cerebellar, Gait & Station with right facial asymmetry, right pronator drift, wide based gait and circumduction on right, DTRs with increased RUE>LUE, No Babinski response on left; equivocal on the right.

Clinical Case 4

Chief Complaint: hallucinations and gait disturbance

History of Present Illness: Mr. Groom is a 72-year-old man with a history of new onset visual hallucinations and a gait disturbance. He has had several recent falls but no head injury/concussion. He has difficulty with sleep and is light-headed with positional changes. There is no history of TIA/stroke or TBI/concussion. He minimizes memory loss. His wife is concerned.

Past Medical & Social History – no prior psychiatric history, no pre-existing chronic medical conditions ; He lives with his wife, he can manage ADLs

Examination – Recall 1 of 3 words at 5 minutes, Difficulty naming parts of objects, difficulty with shifting mental set, difficulty copying complex figure

Cranial nerves, Sensorimotor, Cerebellar, Gait & Station with masked-like facial expression, petit-pas gait with reduced arm swing and UE rigidity, DTRs symmetric, No Babinski responses present.

	CASE 1 Alzheimer's disease	CASE 2 FTD-behavioral variant	CASE 3 Vascular dementia	CASE 4 Lewy Body Dementia
Cognitive	▪ **Profound amnesia** ▪ **Anomia** ▪ **Visuospatial function deficits**	▪ Memory loss late ▪ **Executive function deficits**	▪ Memory loss +/- ▪ Executive function deficits ▪ **Others lesion based**	▪ **Memory loss** ▪ **Executive dysfunction** ▪ **Visuospatial function deficits [language]**
Behavioral	▪ Late stages ▪ Early – possible depression	▪ **Prominent feature early** ▪ Impulsive, Perseverative	▪ Variable not uncommon	▪ **Prominent feature early - Hallucinations**
Motor – Focal deficits	▪ **No focal deficits at diagnosis** (unless mixed type)	▪ **Uncommon-** Minor motor deficits	▪ **Variable deficits** ▪ Lesion based	▪ **Atypical Parkinson's Early gait changes**
Autonomic	▪ *Not typical*	▪ *Not typical*	▪ *Not typical*	▪ **Dysautonomia common**
Sleep	▪ **+/- before onset**	**+/- before onset**	▪ **Not uncommon with vascular risks**	▪ ***REM behavior disorder can precede diagnosis***

Alzheimer's disease – typical presentation

Chief complaint: Slowly progressive memory loss & cognitive decline

Cognitive profile:

- Early & Clinically significant episodic memory loss
- Language deficits including word-Finding difficulty with anomia
- Visuospatial function deficits

Social comportment: preserved in the early – mild/moderate phases

Functional changes: changes in higher order **Behavioral changes:** later

No focal deficits on elemental neurological exam.

Case 2

Executive function (Frontal Lobe) deficits

- Poor judgment & impaired insight
- Reduced concentration, planning & multi-tasking
- Lack of inhibition (disinhibition) & impulsive

Behavioral Changes & Social Comportment

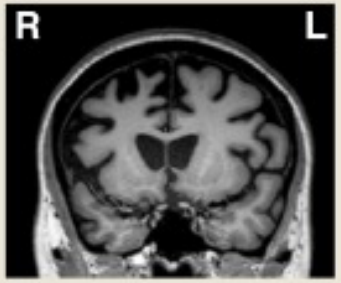
- Socially inappropriate, Bathing – changes in eating
  - *Neglect of personal hygiene & behavior*
- Personality changes, Mood changes
- Repetitive behaviors (OCD-like)

Minor Motor & Speech problems

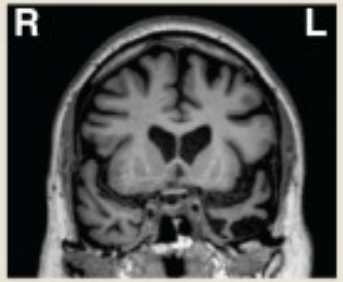
Frontotemporal Dementia

Primary Progressive Aphasia
Progressive disorder of language

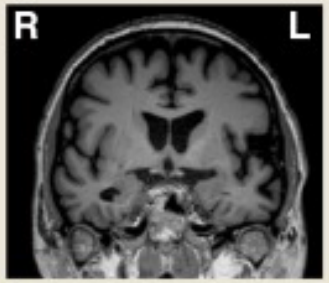
Behavioural-variant frontotemporal dementia (bvFTD)
- Changes in social conduct and behaviour
- Loss of empathy
- Apathy
- Disinhibition
- Lack of insight



Semantic dementia (SD)
- Loss of semantic knowledge, impaired word comprehension and object naming
- Fluent speech with spared repetition



Progressive nonfluent aphasia (PNFA)
- Apraxia and effortful speech
- Spared object knowledge and word comprehension



Current Opinion in Behavioral Sciences

Johnson, E. & Kumfor, F. (2018) Current Opinion in Behavioral Sciences, 22: 82-89.

Alzheimer's versus Frontotemporal

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Alzheimer's Disease *Frontotemporal Dementia*

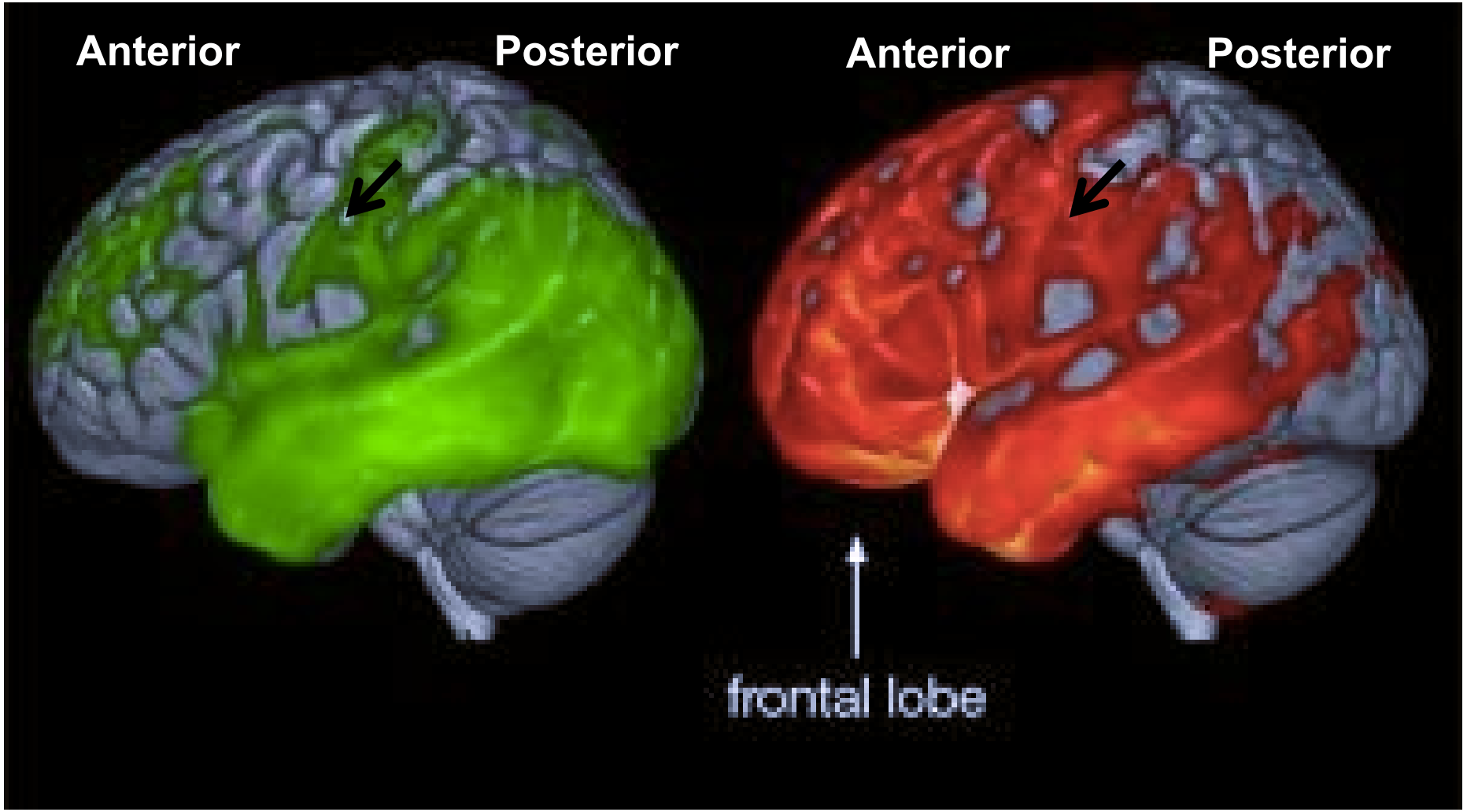

Image from medschool.ucsf.edu

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Vascular Cognitive Impairment

Cognitive decline

- Less memory loss early compared to AD
- More Executive function deficits

Onset – can vary

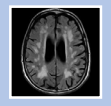
- - Abrupt
- - Stepwise
- - Slowly progressive

Vascular risks

- Predispose to Vascular cognitive impairment with or without history of stroke
- Patients can have focal elemental neurological deficits & focal cognitive deficits

Vascular Dementia Subtypes

Multi-infarct dementia (Large-vessel stroke)



Small-vessel disease (Chronic microvascular disease)

Mixed Large & Small Vessel disease

- **Different lesion locations = different symptoms**
- **Different burden of disease = different clinical decline**
- **Different clinical history & onset = potentially treatable**

Vascular Dementia

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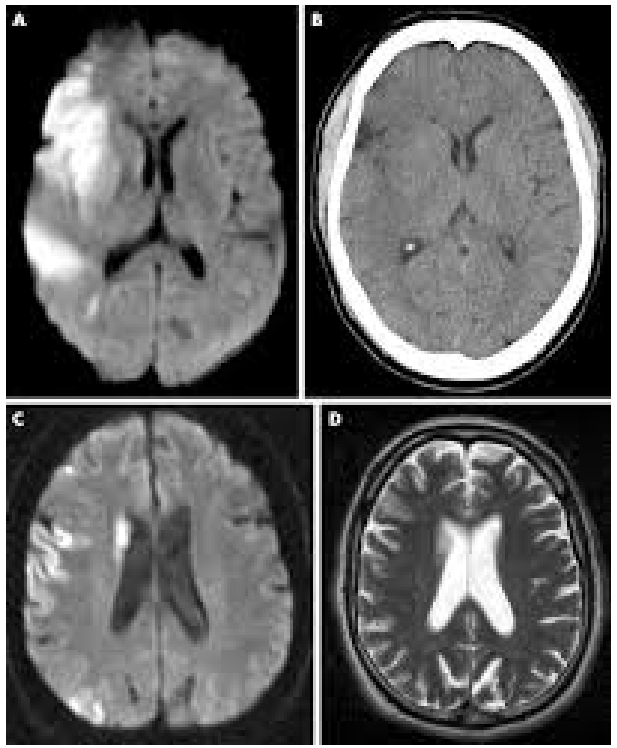
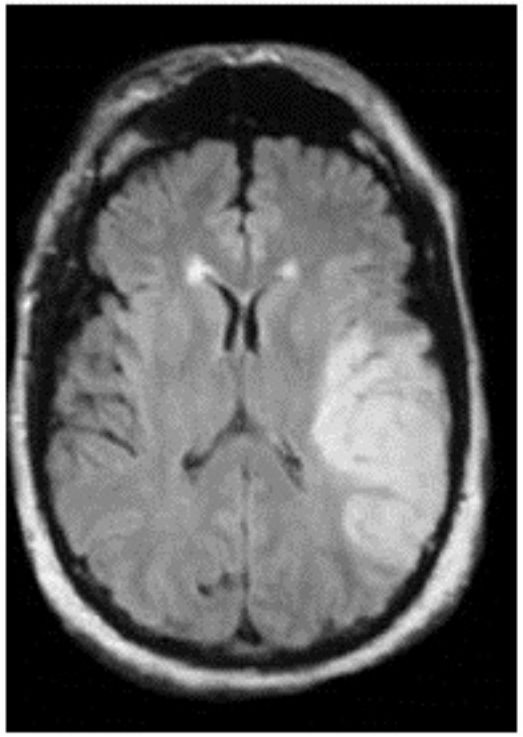
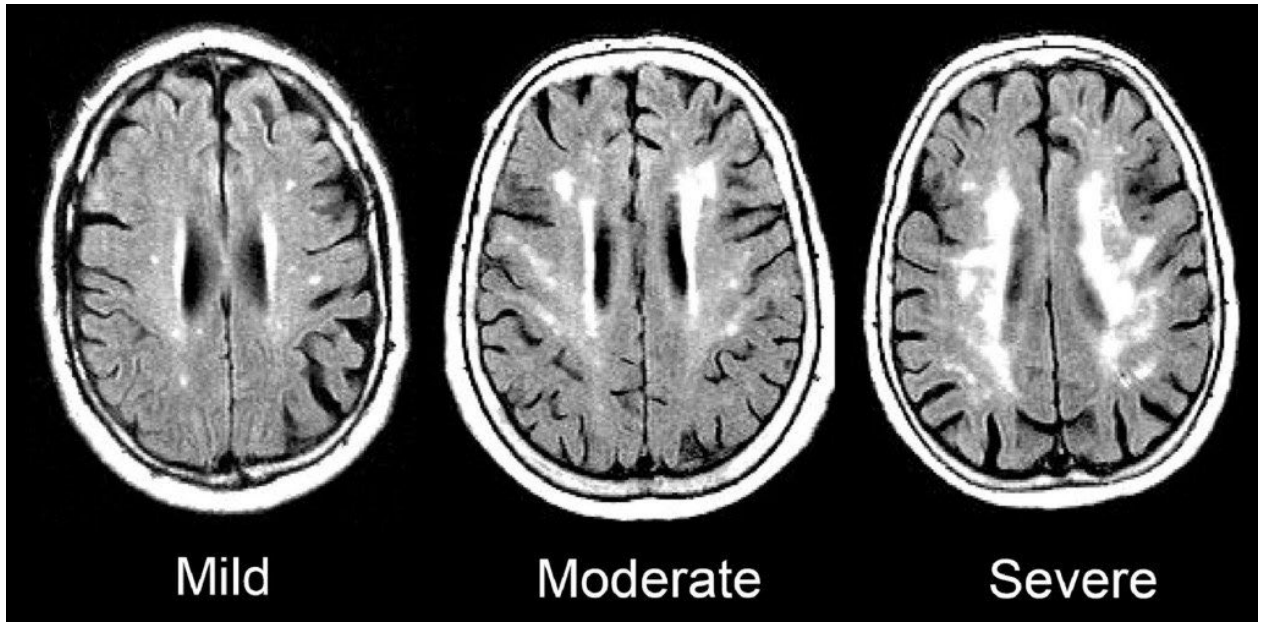
- **Strategic unilateral lesions**
- **Chronic Microvascular disease**



Unilateral Right Hemispheric Lesion



Unilateral Left Hemispheric Lesion



Chronic Microvascular Disease
Bilateral Periventricular White Matter (PVWM) disease

Case 4 - Lewy Body Dementia

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- Cognitive
- Behavioral
- Motor
- Autonomic
- Sleep

Table 2. Clinical Characteristics of Early-Onset DLB Compared With Early-Onset AD and Late-Onset DLB[a]

Characteristic	No. (%) Early-onset AD (n = 363)	Early-onset DLB (n = 32)	*P* value, early-onset AD/early-onset DLB	*P* value[b]	Late-onset DLB (n = 147), No. (%)
Memory impairment					
Present	351 (96.7)	28 (87.5)	.02[c]	.30	142 (96.6)
As predominant presentation	229 (63.1)	15 (46.9)	.15	.20	101 (68.7)
Cognitive fluctuations	27 (7.4)	3 (9.4)	.66	.80	25 (17.0)
Psychosis					
Visual hallucinations	42 (11.6)	15 (46.9)	<.001[c]	<.001[c]	60 (40.8)
Auditory hallucinations	19 (5.2)	4 (12.5)	.11	.002[c]	24 (16.3)
Delusional beliefs	54 (15.0)	6 (18.8)	.58	.03[c]	45 (30.6)
As predominant presentation	14 (3.9)	5 (15.6)	.005[c]	<.001[c]	31 (21.1)
REM sleep behavioral disorder					
Present	9 (6.6)	5 (15.6)	<.001[c]	.002[c]	19 (12.9)
As predominant presentation	12 (3.3)	0 (0)	.99	.98	12 (8.2)
Gait disorder					
Present	80 (22.0)	20 (62.5)	<.001[c]	<.001[c]	104 (70.7)
As predominant presentation	44 (12.1)	8 (25.0)	.04[c]	.007[c]	44 (29.9)
Falls					
Present	29 (8.0)	6 (18.8)	.04[c]	.004[c]	52 (35.4)
As predominant presentation	5 (1.4)	1 (3.1)	.45	.21	9 (6.1)
Tremors					
Present	40 (11.0)	17 (53.1)	<.001[c]	<.001[c]	60 (40.8)
As predominant presentation	24 (6.6)	5 (15.6)	.07	.04[c]	18 (12.2)
Motor slowing					
Present	95 (26.2)	23 (71.9)	<.001[c]	<.001[c]	105 (71.4)
As predominant presentation	54 (14.9)	10 (31.3)	.02[c]	.004[c]	45 (30.6)
Change first observed in					
Cognition	335 (92.3)	22 (68.8)	<.001[c]	.001[c]	116 (78.9)
Behavior	19 (5.2)	3 (9.4)	.33	.91	8 (5.4)
Motor function	6 (1.7)	7 (21.9)	<.001[c]	<.001[c]	19 (12.9)
NPI-Q					
Hallucinations present	54 (14.9)	9 (28.1)	.05	.001[c]	45 (30.6)
Apathy present	189 (52.1)	23 (71.9)	.03[c]	.02[c]	80 (54.4)
Nighttime behavior	102 (28.1)	17 (53.1)	.004[c]	<.001[c]	71 (48.3)
Depressed mood					
Present	189 (52.1)	19 (59.4)	.45	.22	54 (36.7)
As predominant presentation	101 (27.8)	11 (34.4)	.34	.59	19 (12.9)
Geriatric Depression Scale, mean (SD)	2.87 (2.66)	4.96 (3.7)	<.001[c]	.02[c]	3.25 (2.73)
Neuropsychological battery, mean (SD)					
Logical memory, units recalled					
IA	3.21 (3.47)	7.74 (4.49)	<.001[c]	<.001[c]	5.70 (3.93)
IIA	2.13 (3.37)	6.65 (5.10)	<.001[c]	.001[c]	4.19 (3.84)
Time to complete, s					
Trail making test A	95 (48.2)	87 (44.8)	.42	.62	105 (40.0)
Trail making test B	242 (76.8)	227 (84.4)	.47	.64	261 (67.4)
Boston naming test score	20.6 (8.4)	24.6 (4.2)	.02[c]	.29	21.8 (6.3)

Abbreviations: AD, Alzheimer disease; DLB, dementia with Lewy bodies; NPI-Q, Neuropsychiatric Inventory Questionnaire; REM, rapid eye movement.

[a] Psychosis, REM sleep behavior disorder, motor symptoms, and falls were more commonly seen with early-onset DLB, whereas cognitive decline was the predominant complaint in early-onset AD. Neuropsychological testing battery scores and Geriatric Depression Scale values are provided. NPI-Q variables where *P* > .05 in univariate are excluded here.

[b] *P* value is adjusted by age at onset and Mini-Mental State Examination scores.

[c] *P* value has been adjusted for use of mood medication.

Sim J, Li H, Hameed S, Ting SKS. Clinical Manifestations of Early-Onset Dementia With Lewy Bodies Compared With Late-Onset Dementia With Lewy Bodies and Early-Onset Alzheimer Disease. JAMA Neurol. 2022 79:702-709.

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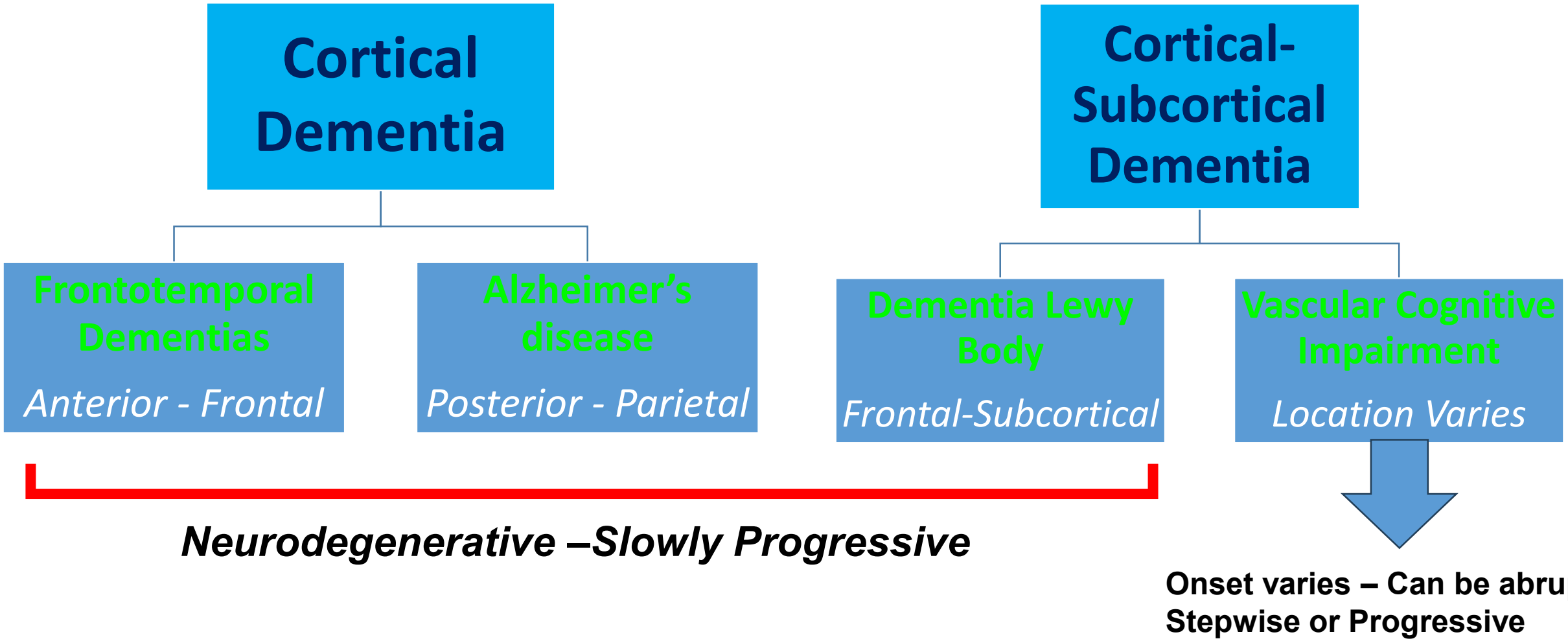
Cortical Dementia
Frontotemporal Dementias
Anterior - Frontal
Alzheimer's disease
Posterior - Parietal
Cortical-Subcortical Dementia
Dementia Lewy Body
Frontal-Subcortical
Vascular Cognitive Impairment
Location Varies
Neurodegenerative –Slowly Progressive
Onset varies – Can be abrupt, Stepwise or Progressive

DEGENERATIVE DEMENTIA SUBTYPES

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Dementia type	%	Symptoms	Pathology-Biomarkers
Alzheimer's disease • *Early-onset* <65yrs • *Late-onset* >65yrs	**40**	• Profound memory loss • Cognitive decline • Slowly Progressive	• Amyloid (αβ lipoprotein) plaques • Neurofibrillary (*tau*) tangles
Frontal Dementias • *Behavioral variant* • *Pick's disease* • *Primary Progressive Aphasia* • *Semantic Dementia*	**10**	• Variable • Less amnesia • Executive function deficits more common	• Heterogeneous • *Tau versus Non-tau*
Mixed Dementia types • *AD plus VaD* • *Lewy Body Dementia (LBD)* • *Corticobasal degeneration (CBD)*	**15**	• Variable • Executive function deficits more common	• Heterogeneous • Synucleinopathies

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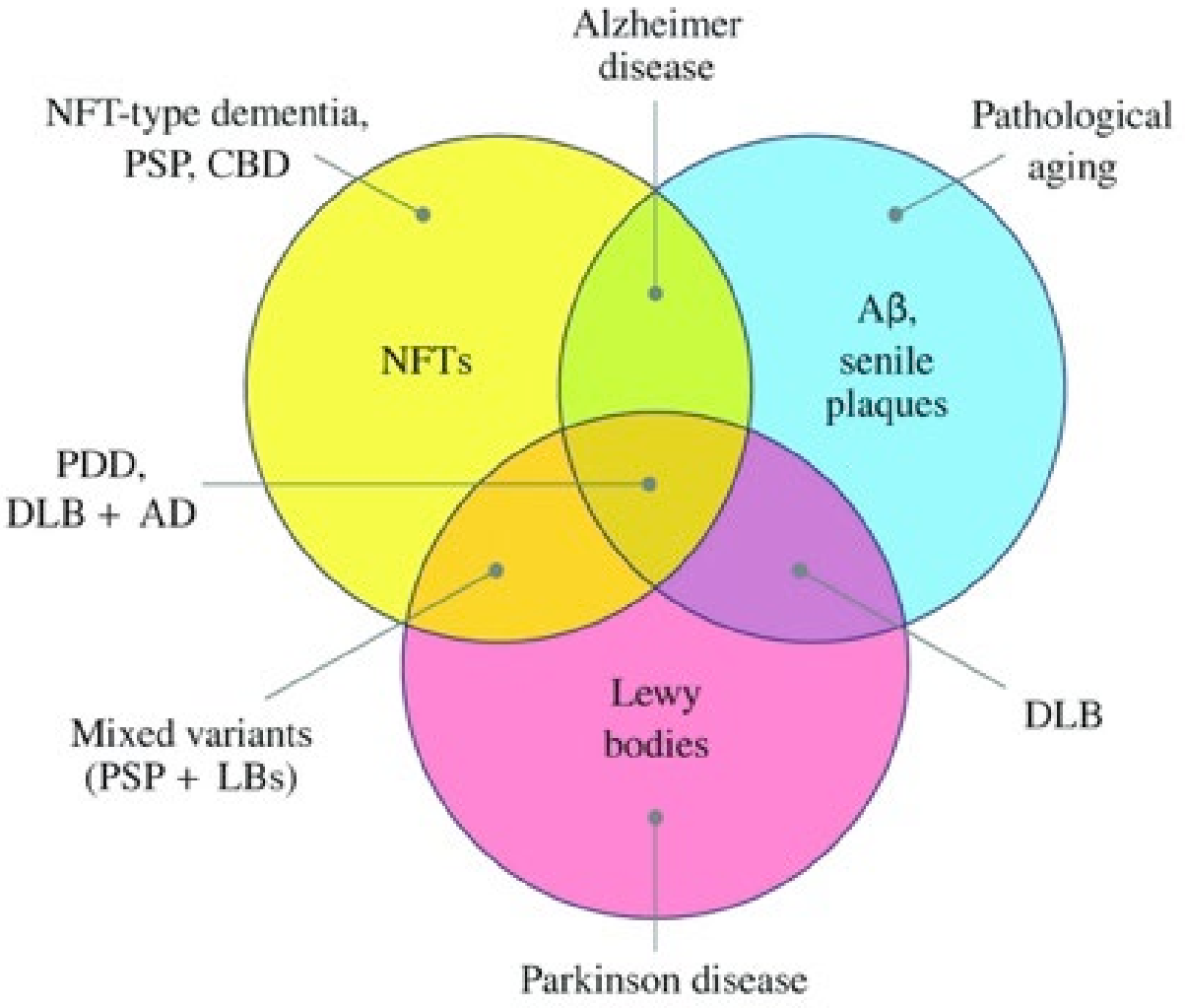
Pathology of Neurodegeneration



Synucleinopathies, Tauopathies, & Amyloidopathies

- NFTs: neurofibrillary tangles
- PSP: progressive supranuclear palsy
- CBD: corticobasal degeneration
- PDD: Parkinson disease dementia
- DLB: dementia with Lewy bodies
- AD: Alzheimer disease
- LBs: Lewy bodies

Jellinger, K. (2011) Interaction between α-Synuclein and Other Proteins in Neurodegenerative Disorders, The Scientific World Journal, 11: 1893-1907.

Questions?

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Additional Materials

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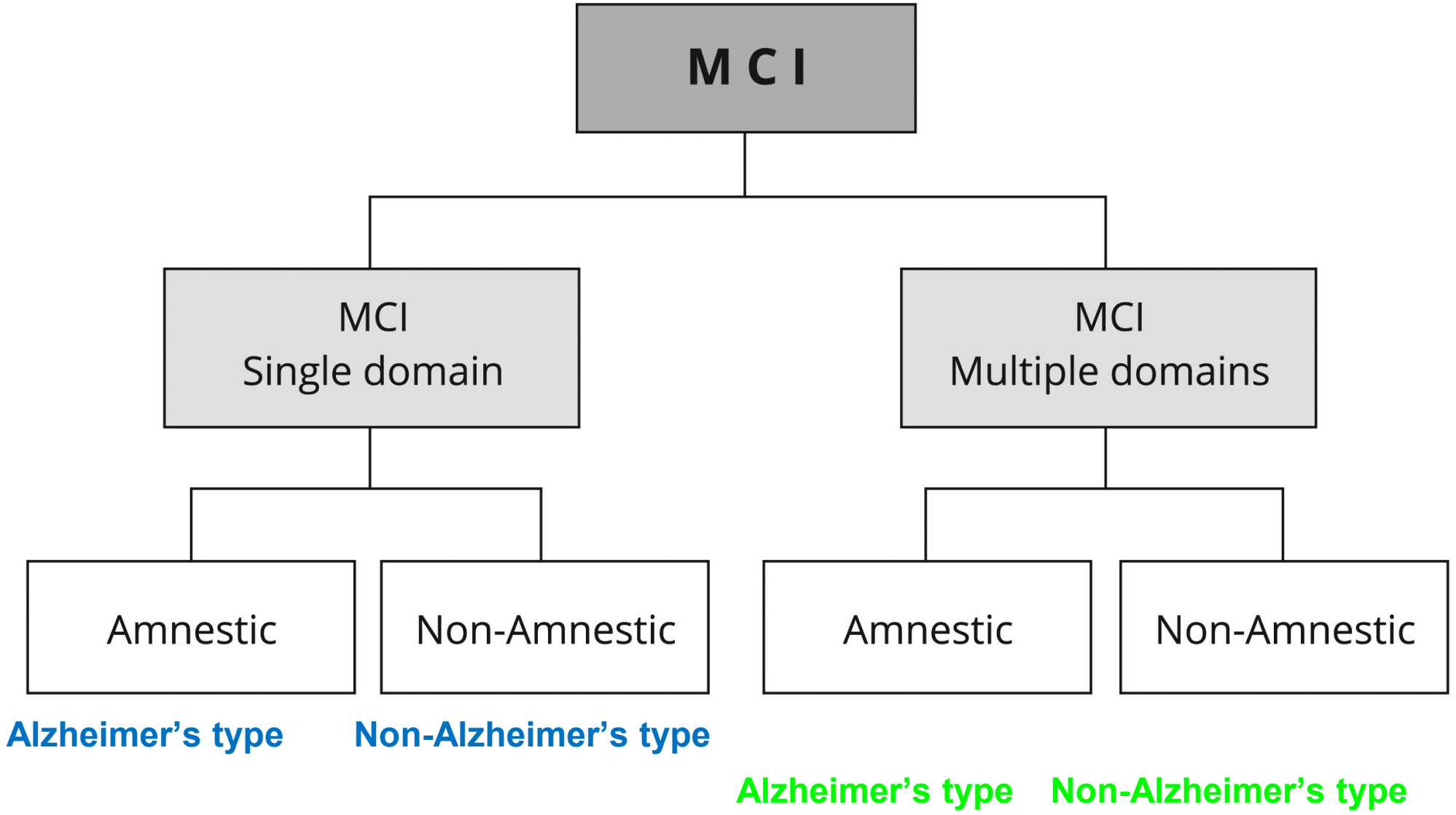
Taxonomy to Classify Patients with Mild Cognitive Impairment



Peterson, Mayo Clinic; Forlenza et al., 2013

How to evaluate and diagnose?

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History of Present Illness & Medical History

Cognitive Assessment

- Orientation
- Attention & Concentration
- Memory testing
- Executive function tests
- Speech, Language & Praxis testing
- Tests of Spatial Attention [R/O neglect]
- Visuospatial processing & Reproduction

Elemental Neurological Exam

- CN, Sensory, Motor, Cerebellar, Gait-Station, Reflexes

Laboratory Studies

- B12/folate, Vitamin D, Thyroid panel, Syphilis Serology [VDRL]

Structural Brain Imaging

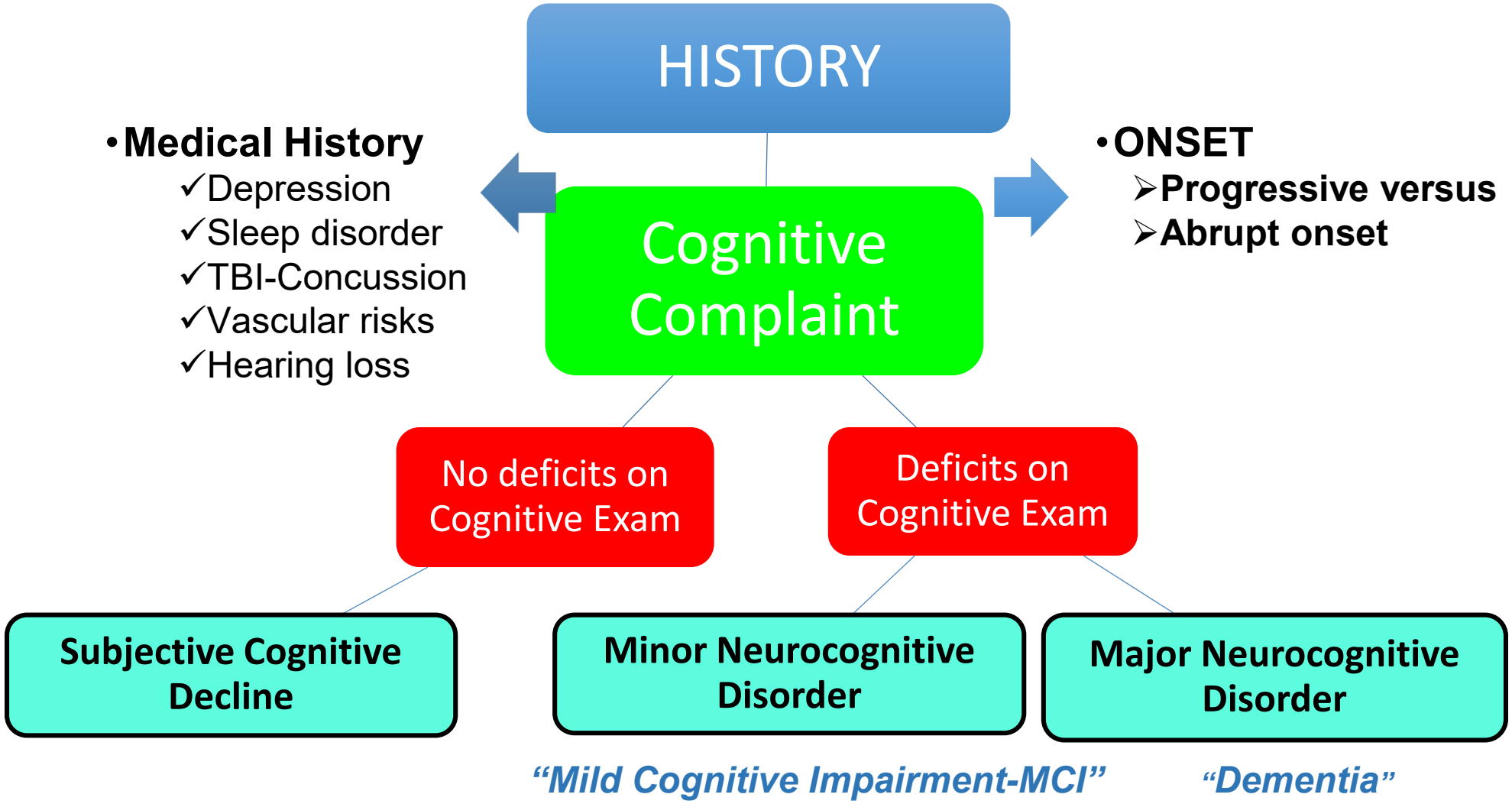
- MRI Brain scan or CT brain [if contraindicated]

Electroencephalography [EEG]

Other imaging studies & Biomarkers

- Resting state MRI or functional MRI
- PET imaging – Amyloid, Tau, Dopamine
- CSF & Blood Biomarker testing

How to approach a patient with Cognitive Decline?



Cognitive Screening tools

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- **Commonly used Clinical Exams**
  - MMSE https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cogimp-smmse.pdf
  - MoCA www.mocacognition.com
  - Mini-Cog www.mini-cog.com

- Self-Administered
  - SAGE [Self-Administered Geriatric Exam] https://wexnermedical.osu.edu/brain-spine-neuro/memory-disorders/sage

- **Digital Cognitive Assessments**
  - Creyos www.creyos.com
  - Linus Health www.linushealth.com
  - Brain Check www.braincheck.com

Advantages/Disadvantages

Billing, Reporting, & Patient Data

Comparison of Commonly Used Cognitive Tests

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	MMSE	MoCa	Mini-Cog	SAGE
Orientation	+	-	-	+
Attention-Concentration	+	+		+
Memory	+	+	+	+
Executive function	-	+	+	+
Language function	+	+		+
Visuospatial function	+	+	+	+
Spatial Neglect	-	-	-	-

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Please also feel free to visit the Well-Ahead website at:

http://wellaheadla.com

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