Dementia with Lewy Bodies

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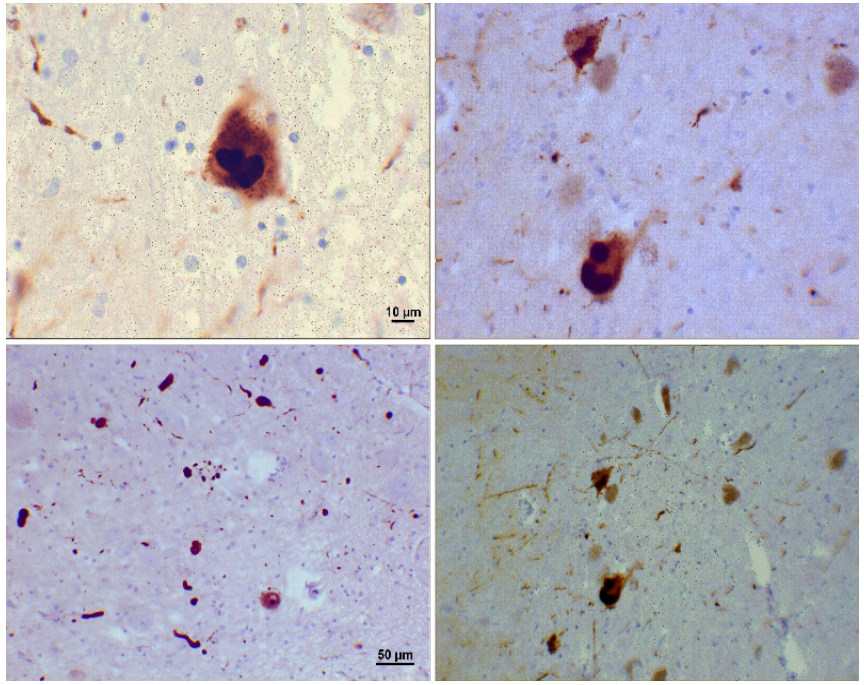
Overview of DLB

- 2nd most common neurodegenerative cause of dementia, after AD
  - Estimated 1.4 million Americans; ~30% of dementia cases
- Slightly higher risk for Males > Females
- Typical onset in 60s
- Average time from diagnosis to death: 5-8 years (range 2-20 years)
- Temporal order of symptoms can help distinguish DLB from PDD – “1 Year Rule”
  - DLB: cognitive and neuropsychiatric sx occur at same time or at least 1-year before motor sx
  - PDD: cognitive sx present at least 1-year after motor symptoms

Neuropathology

- Alpha-synuclein pathology (same as PD and MSA)
- **Lewy bodies (LB):** abnormal aggregation and deposits of *α*-synuclein protein in nerve cells
- LB appear first in limbic and cortical regions in DLB → cognitive/psychiatric sx first
    - In PD, usually first seen in brainstem → extrapyramidal sx first



Diagnostic Criteria – DLB Consortium 2017

- Core Features
  - Fluctuating cognition with pronounced variations in attention and awareness
  - Recurrent visual hallucinations that are typically well-formed and detailed
  - REM sleep behavior disorder, which may precede cognitive decline
- One or more spontaneous cardinal features of parkinsonism
  - Bradykinesia, resting tremor, rigidity
- Supportive Features
  - Severe sensitivity to antipsychotic agents, postural instability, repeated falls, syncope or transient unresponsiveness, orthostatic hypotension, urinary incontinence, mood (apathy, anxiety, depression)

Diagnostic Criteria – DLB Consortium 2017 (Biomarkers)

- Indicative biomarkers
  - Reduced dopamine transporter uptake in basal ganglia (SPECT or PET findings)
  - Abnormal/low uptake of iodine-MIBG myocardial scintigraphy
  - Polysomnography confirmation of REM sleep without atonia
- Supportive biomarkers
  - Relative preservation of medical temporal lobe on MRI/CT
  - Generalized low uptake on SPECT/PET
  - Prominent posterior slow-wave activity on EEG with periodic fluctuations in pre alpha/theta range

COMPREHENSIVE LBD SYMPTOM CHECKLIST

Add a check mark next to any new or concerning LBD symptoms. Write your comments or questions for the doctor in the comment field. Bring this form with you to your next appointment or send it to the doctor in advance.

COGNITIVE SYMPTOMS	
	Forgetfulness
	Trouble with problem solving or analytical thinking
	Difficulty planning or keeping track of sequences (poor multi-tasking)
	Fluctuating levels of concentration and attention
	Disorganized speech and conversation
	Unexplained episodes of confusion
	Difficulty with sense of direction or spatial relationships between objects
PARKINSON'S-LIKE SYMPTOMS	
	Rigidity or stiffness
	Shuffling walk
	Balance problems or repeated falls
	Tremor
	Slowness of movement
	Weak voice
	Change in handwriting
	Decrease or change in facial expression
	Drooling
	Loss of or decreased ability to smell
	Change in posture
BEHAVIOR AND MOOD CHANGES	
	Hallucinations - Seeing or hearing things that are not really present
	Other hallucinations (touch, smell)
	Depression
	Apathy (loss of interest and drive)
	Delusions (false beliefs)
	Anxiety

SLEEP CONCERNS	
	Acting out dreams during sleep (sometimes violently), falling out of bed
	Excessive daytime sleepiness
	Insomnia
	Restless leg syndrome
AUTONOMIC SYSTEM DYSFUNCTION	
	Dizziness, lightheadedness or fainting – or changes in blood pressure
	Sensitivity to heat and cold
	Sexual dysfunction
	Urinary incontinence
	Constipation
	Unexplained blackouts or transient loss of consciousness
REACTIONS TO RECENT MEDICATION CHANGES	
	Significant improvement
	Minimal improvement
	No change
	Increased parkinsonism (stiffness, rigidity, etc.)
	Increased confusion
	Increased hallucinations
	Increased sleepiness
	Increased dizziness or fainting
COMMENTS/OTHER CONCERNS	

LBDA
LEWY BODY DEMENTIA ASSOCIATION

Fluctuations in Arousal and Attention

Episodes of staring and perturbed flow of ideas

Daytime drowsiness and needing naps

Possible Questions:

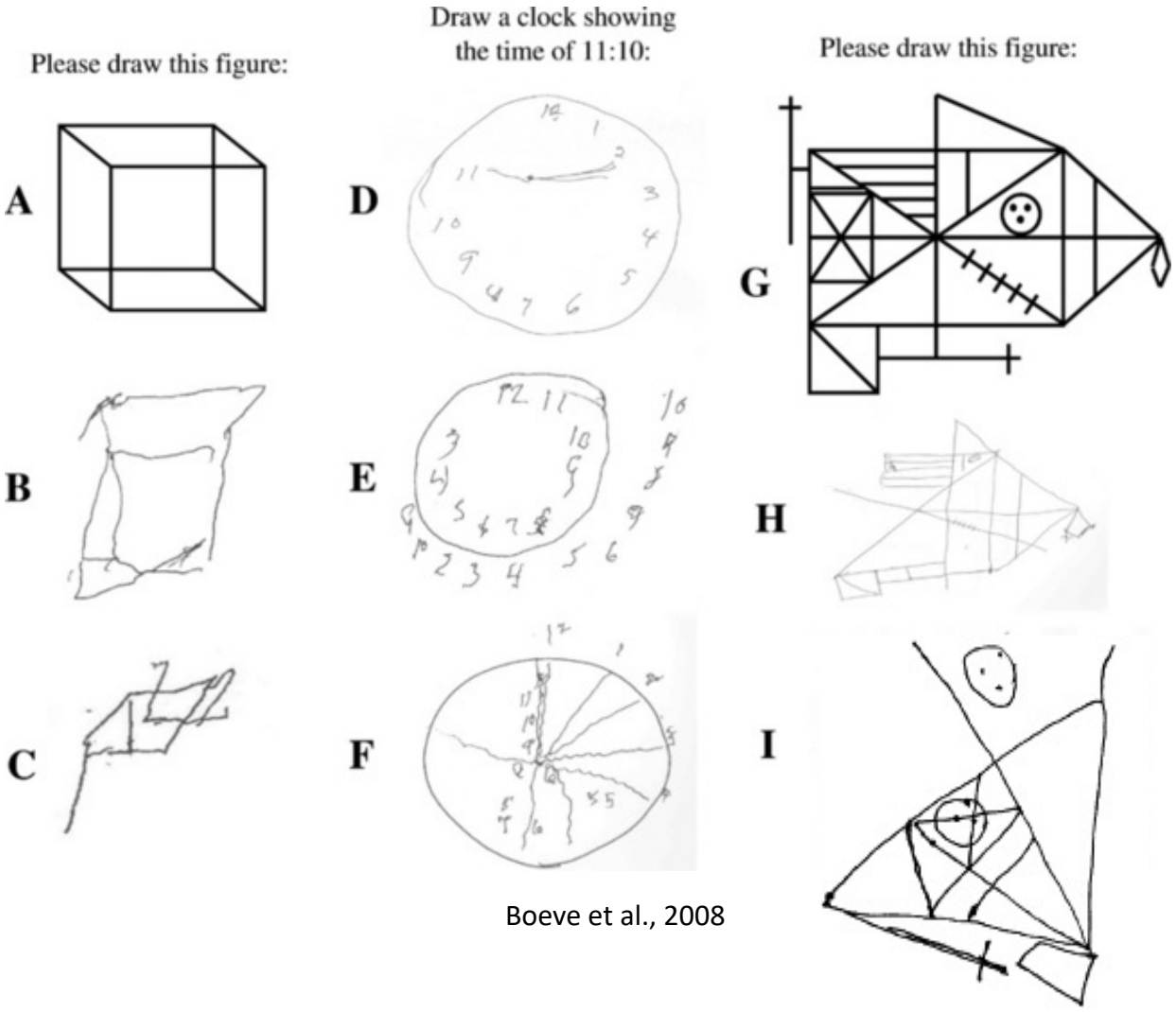
- Any recurring episodes of staring off into space?
- Are they drowsy or lethargic for more than 1 hour during the daytime, despite getting normal sleep?
- Do they have episodes of disorganized speech?
- Are they difficult to rouse on a typical day?

Dementia Cognitive Fluctuations Scale (Lee et al., 2014)

Mayo Fluctuations Scale (from NACC UDS – LBD module)

Cognitive Symptoms

- Attention
- Processing Speed
- Executive Functioning
- Visuospatial Skills
- Memory: reduced encoding and retrieval; recall improves with cueing



Boeve et al., 2008

Neuropsychiatric Symptoms (NPS)

Visual Hallucinations

- Recurrent, complex visual hallucinations
- Well-formed, often animated --- people, children, small animals
  - Usually unimodal, without sound/smell/touch
- Generally well-tolerated and emotionally-neutral
- Illusions too -- mistaking objects for people (e.g., in dimly lit rooms)

Delusions: Infidelity, house intruders, theft, Capgras syndrome

Other: Apathy, anxiety, depression

Can screen with questionnaire like Neuropsychiatric Inventory (NPI)

REM Sleep Behavior Disorder

- Syndrome of impaired paralysis during REM sleep
- Acting out dreams, thrashing, kicking, yelling
- Can begin years prior to onset of other symptoms in DLB or PDD
- Mayo Sleep Questionnaire

Motor Symptoms & Parkinsonism

- Motor signs tend to be more symmetric than in PD
- Bradykinesia and gait impairment are more common than resting tremor
  - High variability in motor sx in DLB
- Extrapyramidal motor symptoms: TRAP
  - **T**remor (typically resting/pill-rolling in PD)
  - **R**igidity
  - **A**kinesia/Bradykinesia
  - **P**ostural Instability
- DLB has variable response to carbidopa/levodopa

Neuroleptic Sensitivity (Supportive Feature)

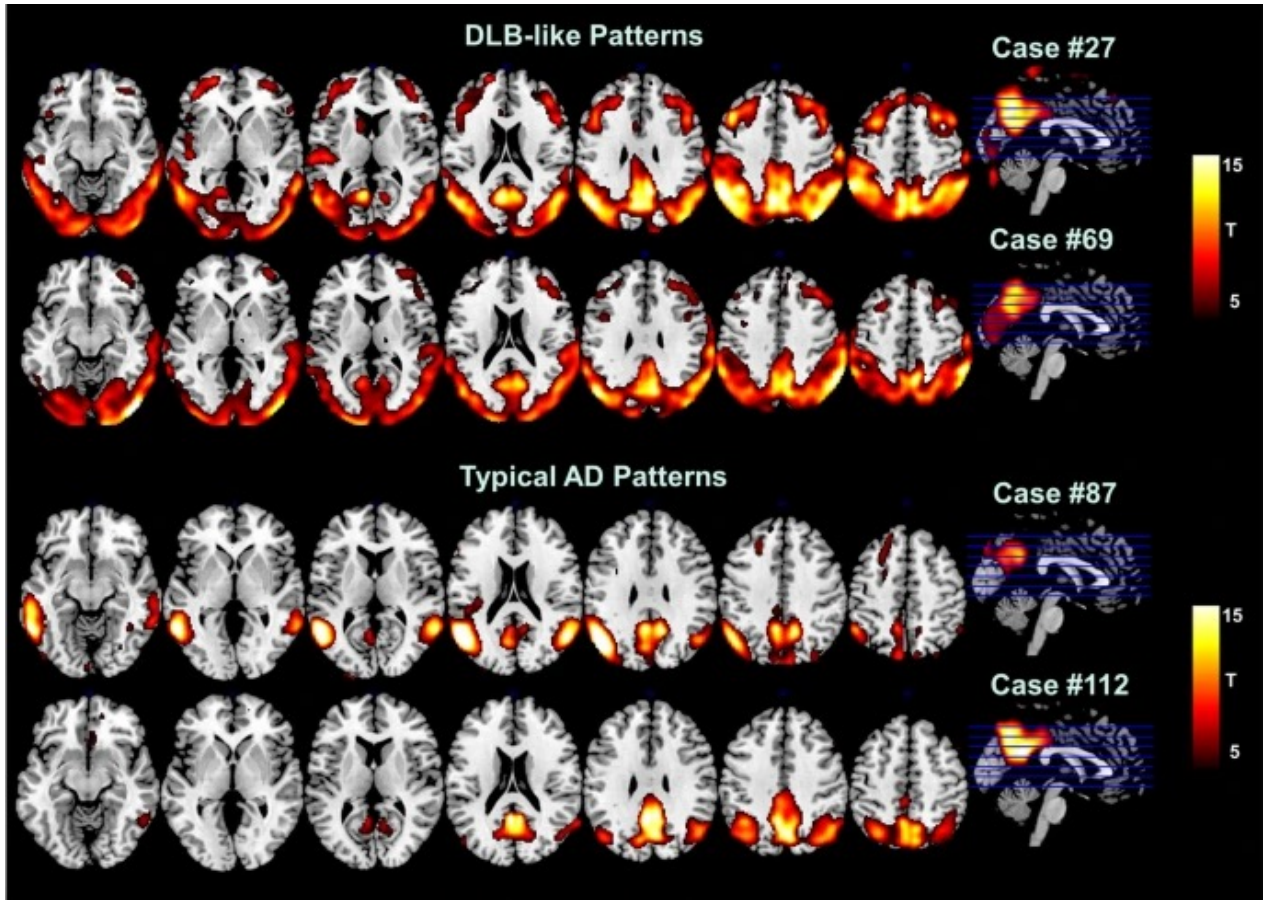
- Neuroleptics can trigger or exacerbate parkinsonism
- Increase risk of mortality and NMS (neuroleptic malignant syndrome)
- Neuroleptics can affect cognition – impaired alertness and attention
- Important for ED: Patients may be evaluated for psychosis or confusion and given Haldol which will make symptoms worse in DLB
- D2 receptor antagonists should be avoided if possible
  - Consider atypical antipsychotics if necessary (quetiapine, clozapine)

Autonomic Dysfunction (Supportive Feature)

- Orthostatic hypotension
- Syncope and falls (more common later in disease)
- Neurogenic bladder, urinary urgency, incontinence
- More common in MSA but can occur in DLB

Neuroimaging & Related Studies

- MRI
  - Often appear normal until late stages
  - Can differentiate from AD if normal MTL volume
- FDG-PET or SPECT
  - Posterior and/or generalized hypometabolism
    - Helpful to distinguish from AD if preservation of medial temporal metabolism
  - "Cingulate Island Sign" = preserved mid-cingulate metabolism
- DaT
  - Reduced DaT levels in BG (can differentiate DLB from AD, but not from PD/PSP/CBS)



Caminiti et al., 2019

Symptom Management

- First line medication = Cholinesterase inhibitor
  - Cognitive symptoms, hallucinations, apathy
- Psych/Mood: SSRI for depression or anxiety
- Sleep: Melatonin for sleep difficulty, sleep study/Sleep Medicine consult
- Motor Symptoms
  - Carbidopa/Levodopa* if motor sx are significant (not always beneficial and can worsen NPS)
  - PT, OT for gait and balance; Home safety evaluation
  - SLP for swallow and speech issues

Symptom Management

Non-Pharmacological Interventions

- Environment management for NPS and safety
  - Maintain daytime structure and a good nighttime routine
  - Good lighting in rooms
  - Padding corners of nightstands, floor lighting/nightlights
  - Driving evaluations may be indicated
- Exercise, social engagement, cognitive stimulation
- Caregiver education, training, and support
  - Online support groups through LDBA.org
  - Local clinics and community trainings

Treatments to Avoid

- Antipsychotics
  - Typical antipsychotics d/t neuroleptic sensitivity
  - Atypical antipsychotics (D2 receptor antagonists) – olanzapine, risperidone
  - Quetiapine and clozapine have demonstrated better safety/efficacy than others
  - Nuplazid (pimavanserin) has been studied in PD only
- *Dopamine agonists – can worsen hallucinations
- *Benzodiazepines – can be helpful for REM/agitation at night
- Diphenhydramine and most sleep aids
- Anticholinergics, including tricyclic antidepressants

Resources for Patients and Providers

- Lewy Body Dementia Association (LBDA): www.lbda.org
- Michael J. Fox Foundation: https://www.michaeljfox.org/news/atypical-parkinsonism#lewy-body-dementia
- Questionnaires Mentioned
  - Mayo Sleep Questionnaire
  - Dementia Cognitive Fluctuation Scale (Lee et al., 2014)
  - Mayo Fluctuations Scale (NACC)
  - Neuropsychiatric Inventory
  - Comprehensive LBD Symptom Checklist
- DLB Clinical Criteria: McKeith et al., 2017 – Consensus Report of DLB Consortium
- Research/Clinical Trials
  - Stanford LDB Research Center of Excellence
  - UW ADRC (LBDA Center of Excellence) – some LDB trials

QUESTIONS?

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