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Understanding Lewy Body Dementia

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PRESENTED BY

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Dementia

- Dementia, or what is called Neurocognitive Disorder in DSM-5, refers to a decline in cognitive functioning that is greater than expected by aging alone.
- Major Neurocognitive Disorder (specify "due to" the underlying pathology)
  - A. Evidence of significant cognitive decline from prior level of performance in one or more cognitive domains, including complex attention, executive function, learning & memory, language, perceptual-motor, or social cognition) based on
    1. Concern of the individual, a knowledgeable informant, or clinician
    2. Substantial impairment in cognitive performance, pref doc by NP testing or another quantified clinical assessment
  - B. Cognitive deficits interfere w/independence in everyday activities
  - C. Cognitive deficits do not occur exclusively in context of a delirium

Dementia / Major Neurocognitive Disorder

- Neurodegenerative disorders result in a progressive and irreversible loss of neurons & brain functioning.
- Various diagnoses causing dementia:
  - Alzheimer's disease
  - Frontotemporal disorders
  - Lewy Body disease
- Other types of progressive brain disease include:
  - Vascular contributions to cognitive impairment & dementia
  - Mixed dementia, combination of 2 or more types of dementia

Dementia / Major Neurocognitive Disorder

- Other conditions that can cause dementia or dementia-like symptoms include:
  - Argyrophilic grain disease, a common, late-onset degenerative disease (Lewy bodies are frequent in the amygdala)
  - Creutzfeldt-Jakob disease or Prion disease
  - Huntington's disease, an inherited, progressive brain disease
  - Chronic traumatic encephalopathy (CTE), caused by repeated traumatic brain injury
  - HIV-associated cognitive / AIDS dementia
  - Wernicke-Korsakoff syndrome / Alcohol Dementia
  - Lyme disease infection-case study, man developed LBD years after, difficult to determine if there was a causal connection

Dementia / Major Neurocognitive Disorder

- DSM-5-TR: Major (or Mild) Neurocognitive Disorder with Lewy Bodies (distinguished from "due to PD")

A. Criteria are met for major or mild neurocognitive disorder
B. Disorder has an insidious onset & gradual progression
C. Disorder meets a combination of core diagnostic features & suggestive diagnostic features of either probable or possible Neurocognitive Disorder with Lewy Bodies
D. Disorder not better explained by cerebrovascular disease, other neurodegen disorder, substance or other neurological disorder

- Probable Major or Mild: requires two core features, or one suggestive feature w/one or more core features
- Possible Major or Mild: requires one core feature, or one or more suggestive features

Dementia / Major Neurocognitive Disorder

- DSM-5-TR: Major (or Mild) Neurocognitive Disorder with Lewy Bodies
  1. Core diagnostic features include:
     a. Fluctuating cognition with pronounced variations in attention & alertness
     b. Recurrent visual hallucinations that are well formed & detailed
     c. Spontaneous features of parkinsonism, with onset subsequent to the development of cognitive decline

Dementia / Major Neurocognitive Disorder

- DSM-5-TR: Major (or Mild) Neurocognitive Disorder with Lewy Bodies
  2. Suggestive diagnostic features include:
     a. Meets criteria for rapid eye movement sleep behavior disorder
     b. Severe neuroleptic sensitivity

  (Code with behavioral disturbance, if present)

Dementia / Major Neurocognitive Disorder

- DSM-5: Major (or Mild) Neurocognitive Disorder with Lewy Bodies
  A. Associated features supporting diagnosis
     1. Frequently experience repeated falls, syncope [fainting, assoc hypotension], & transient episodes of unexplained loss of consciousness / episodes of unresponsiveness
     2. Autonomic dysfunction, such as orthostatic hypotension, urinary incontinence, and constipation
     3. Hypersomnia and hyposmia may also be observed
     4. Auditory & non-visual hallucinations may be experienced
     5. May experience systematized delusions, delusional misidentification, apathy and depression

Lewy Body Dementia

TABLE 1: Panel Consensus Guidelines for the Clinical Diagnosis of Probable and Possible Dementia with Lewy Bodies

(1st pub 1996, 2005, 2017, addl info 2020)

Central, or required, features for diagnosis:

- ✔Dementia: Progressive cognitive decline of sufficient magnitude to interfere with normal social and occupational function.
- ✔Prominent or persistent memory impairment does not necessarily occur in the early stages but is evident with progression in most cases.
- ✔Deficits on tests of attention, executive function, & visuoperceptual ability; impaired frontal-subcortical skills and visuospatial ability can be especially prominent.

Lewy Body Dementia

TABLE 1: Panel Consensus Guidelines for the Clinical Diagnosis of Probable and Possible Dementia with Lewy Bodies

Core clinical features: 2 required for probable & 1 for possible dx.

(or one core clinical + ≥ one indicative biomarker):

- ✔Fluctuating cognition with pronounced variations in attention and alertness.
- ✔Recurrent visual hallucinations that are typically well formed and detailed.
- ✔Rapid eye movement (REM) sleep behavior disorder, which may precede cognitive decline
- ✔One or more spontaneous motor features of parkinsonism: bradykinesia, resting tremor, or rigidity.

Lewy Body Dementia

Panel Consensus Guidelines for the Clinical Diagnosis of Probable and Possible Dementia with Lewy Bodies

Supportive Clinical Features of a diagnosis of LBD:

- ✔Repeated falls / postural instability
- ✔Syncope
- ✔Transient loss of consciousness / unresponsiveness
- ✔Neuroleptic sensitivity (sensitive to antipsychotic agents)
- ✔Severe autonomic dysfunction
- ✔Systematized delusions
- ✔Hallucinations in other modalities
- ✔REM sleep behavior disorder (REM = rapid eye movement) [RBD]
- ✔Depression / apathy

Lewy Body Dementia

Panel Consensus Guidelines for the Clinical Diagnosis of Probable and Possible Dementia with Lewy Bodies

Indicative Biomarkers of a diagnosis of LBD:

- ✔Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT / PET imaging
- ✔Abnormal (low uptake) ^{123} I-MIBG myocardial scintigraphy
- ✔Polysomnographic confirmation of REM sleep without atonia

(increased diagnostic weighting given to RBD & MIBG; research demonstrated high sensitivity & specificity in differential diagnosis of LBD & AD & other dementias)

Lewy Body Dementia

Panel Consensus Guidelines for the Clinical Diagnosis of Probable and Possible Dementia with Lewy Bodies

Supportive Biomarkers of a diagnosis of LBD:

- ✔A relative preservation of medial temporal lobe structures on CT/MRI scans
- ✔Generalized low uptake on SPECT/PET perfusion/ metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging
- ✔FDG-PET imaging shows low energy usage in brain, esp in areas assoc w/vision (assoc w/rate of change of sxs experienced)
- ✔Prominent posterior slow-wave activity on EEG w/periodic fluctuations in the pre-alpha/theta range
- ✔Possible skin test for phosphorylated alpha-synuclein in nerve fibers in small skin samples for PD & DLB (not in normal)

Lewy Body Dementia

TABLE 1: Panel Consensus Guidelines for the Clinical Diagnosis of Probable and Possible Dementia with Lewy Bodies

Negative Features or those less likely to be present in DLB:

- ✔History of stroke, cerebrovascular disease sufficient to account for the clinical picture (these do not exclude dx, may indicate mixed or multiple pathologies contributing to clinical presentation)
- ✔Any other physical illness or brain disorder sufficient to interfere with cognitive performance.
- ✔If parkinsonian features are the only core clinical feature & appear first at a stage of severe dementia

Adapted from McKeith IG, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology 1996;47:1114.

Lewy Body Dementia: Symptom Descriptions

Fluctuations:

- ✔ Typically delirium-like
- ✔ Variability, can be significant, across hours and days, in ability to maintain alertness and wakefulness
- ✔ Spontaneous alterations in cognition, attention, & arousal

Lewy Body Dementia: Symptom Descriptions

Visual Hallucinations:

- ✔ Typically well-formed, Featuring people, children, animals; often moving; not auditory
- ✔ Sometimes accompanied by related phenomena, referred to as minor hallucinations:
  - passage hallucinations (brief appearance of a person, an indefinite shadow or animal passing through periphery of the visual field, moving forward from behind & close to patient's shoulders; described as poorly defined vision passing or walking person or running animals or undefined moving objects; often turn to look),
  - a sense of presence (sensation that someone uninvited is living in their home, but the feeling of that presence is not present nearby (phantom boarder syndrome)
  - visual illusions (transient misperceptions of objects or living beings that differ from objective reality—pile of laundry or tall lamp in corner seen as a person; pareidolias—perception of faces or animals from irrelevant visual stimuli; kineptosia—stationary objects perceived as being in motion; object misidentification illusions—objects misperceived as different objects
  - These often precede onset of well-structured visual hallucinations & are associated with other nonmotor symptoms such as REM sleep behavior disorder & depression

Lewy Body Dementia: Symptom Descriptions

Parkinsonism:

- ✔ Typically less severe than in Parkinson's disease
- ✔ Combinations of bradykinesia, resting tremor, rigidity

REM sleep behavior disorder (RBD):

- ✔ Recurrent dream enactment behavior that includes movements mimicking dream content, with an absence of normal REM sleep atonia (finding significantly improves diagnostic accuracy-moved from supportive to core clinical feature; may occur many years prior & may become quiescent over time)

Terminology

- Dementia with Lewy Bodies (DLB)
- Lewy Body Dementia (used as general term to include both DLB & PD)
- Diffuse Lewy Body disease
- incidental Lewy Body disease
- Parkinson's disease dementia (PDD)
- Cognitive-impairment in Parkinson's disease (CIPD)
- Non-demented Parkinson's disease
- Dementia with Lewy Bodies (DLB) with Alzheimer's disease
- The Lewy Body Variant of Alzheimer's disease (combined pathology)

Lewy Body Dementia

Lewy Body Dementia is characterized by the presence of Lewy bodies and Lewy neurites, which have abnormal aggregations of α–synuclein in the nigral & extranigral areas, including the heart; thus, MIBG scintigraphy used to discriminate Dementia with Lewy Bodies from Alzheimer's disease and to predict the conversion to probable Dementia with Lewy Bodies

(finding associated with reduced uptake on SPECT in striatum but not with any clinical or neuropsychological factor)

Lewy Body Dementia

In 2011, the FDA approved the use of a brain scan, called a dopamine transporter scan (DaTSCAN), based on SPECT imaging, which allows for visualization of the dopamine system in the brain—evaluates whether you have a parkinsonian syndrome such as Parkinson's disease or Dementia with Lewy Bodies.

Lewy Body Dementia

Biochemically, Dementia with Lewy Bodies is associated with deficits in both acetylcholine and dopamine, which are the primary neurotransmitter deficits in Alzheimer's disease and Parkinson's disease, respectively. Thus, clinically, pathologically, and biochemically, DLB appears to fall somewhere in the middle of a disease spectrum ranging from Alzheimer's disease to Parkinson's disease.

What Causes Lewy Body Dementia

- While risk factors include age over 60, possibly males more common than females, REM sleep disorder
- No specific lifestyle risk factors identified
- Having a family member w/DLB may increase risk, DLB not considered a genetic disease, though variants in 3 genes (APOE, SNCA, GBA) been assoc w/incr risk of DLB
- Most cases unknown, no genetic test can predict
- Caused by abnl buildup & clumping of proteins named Lewy bodies; also have plaques & tangles similar to AD

Differentiating DLB & PDD

- Dementia with Lewy Bodies (DLB) and Parkinson's disease dementia (PDD) are included in DSM-5-TR as two separate entities of Major Neurocognitive Disorders with Lewy bodies, despite sharing many clinical, neurochemical, and morphological features.
- Same morphological (structural) hallmarks: cortical & subcortical α-synuclein/Lewy body inclusions, plus β–amyloid & tau pathologies

Differentiating DLB & PDD

- Despite clinical overlap, their diagnosis has been based on an arbitrary distinction concerning the time of onset of motor & cognitive symptoms, based on international consensus
  - Early cognitive impairment in DLB precedes parkinsonian motor signs or begins within 1 year from its onset; most develop parkinsonism of increasing severity over years, but 25% never develop parkinsonian sxs
  - Later onset of cognitive impairment following onset of motor symptoms in PDD, est 50-80% eventually develop dementia w/disease progression (avg about 10 yrs)
  - 78% PDD after 8 yrs of PD, longitudinal Norwegian study

Differentiating DLB & PDD

- The clinical constellations of DLB & PDD include cognitive impairment, parkinsonism, visual hallucinations, and fluctuating attention
- PET scans & postmortem studies have revealed a more pronounced cortical atrophy, elevated cortical & limbic Lewy body pathologies, higher Aβ & tau loads in cortex & striatum in DLB compared to PDD
- Multitracer PET scans have shown no differences in cortical & striatal cholinergic & dopaminergic deficits
- Clinical management of both DLB & PDD includes cholinesterase inhibitors (i.e., rivastigmine [Exelon] & donepezil [Aricept])
- Currently, no disease-modifying therapies are available

Lewy Body Disease

- DLB & PDD are important dementia syndromes that overlap in many clinical features, genetics, neuropathology, and management
- Lewy bodies more cortical in DLB, more in subcortex, basal ganglia in PD/PDD
- Considered subtypes of an α-synuclein-associated disease spectrum (Lewy body diseases)
- Both show heterogeneous pathology & neurochemistry
- Share important common underlying molecular pathogenesis with Alzheimer's disease & other proteinopathies

Lewy Body Disease

- ✔ In PD with dementia, motor symptoms usually predate the dementia by many years.
- ✔ In contrast, in DLB, the onset of dementia and parkinsonism must occur within one year of each other, and either feature can be the initial symptom.
- ✔ Although bradykinesia, rigidity, and falls are common to both diseases, tremor is often absent in DLB.
- ✔ DLB patients show an axial bias with greater postural instability, gait difficulty, and facial impassivity, but less tremor than patients with PD with dementia.
- ✔ Dementia typ progresses more quickly in DLB than PDD

What is Lewy Body Dementia

- Typically begins at age 50 or older, but sometimes younger
- Affects slightly more men than women (1.5:1)
- Gradually progressive, neurodegenerative, but often preceded by prodromal acute confusional episodes, precipitated by illness or surgery
- Lasts an avg 5-8 years from diagnosis to death, but span can range from 2 -20 years
- Prevalence est 0.1%-5% of gl elderly population and 1.7%-30.5% of all dementia cases
- Autopsy 20-35% show Lewy bodies are present
- Up to 40% of patients with AD have concomitant LBs

What is Lewy Body Dementia

- Lewy Body Dementia is a disease associated with abnormal deposits of a protein called alpha-synuclein in the brain
- In healthy brains, α-synuclein plays important roles in neurons in the brain, esp at synapses where cells communicate w/each other
- These deposits are called Lewy bodies (named for neurologist Friederich H Lewy, MD, working with Alois Alzheimer in early 1900s)
- Lewy bodies can occur alone or in combination with other brain disorders

Lewy Body Dementia

Lewy Body Dementia is characterized by the presence of Lewy bodies in the subcortical and cortical (frontotemporal) regions of the brain, as well as amyloid plaques.

Neurofibrillary tangles are less common in dementia with Lewy bodies.

Increased soluble β–amyloid 1-40 & β–amyloid 1-42 distinguish rapidly progressive form of Dementia with Lewy Bodies

Lewy Body Dementia

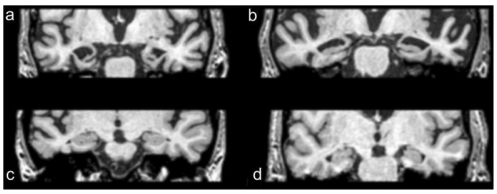
- Activity of certain brain chemicals is also affected
- Lewy bodies block the transmission of the neurotransmitters, Dopamine (which helps transmit signals that control muscle movement) & Acetylcholine (responsible for memory, thinking, & processing)
- Deposits affect chemicals in the brain that result in problems with thinking, movement, behavior, & mood
- In Dementia with Lewy Bodies, α-synuclein forms into clumps inside nerve cells, for reasons that are not fully understood, starting in areas of the brain that control aspects of memory & movement

Lewy Body Dementia

- Brain regions affected in LBD/DLB include:
  - Cerebral cortex (frontotemporal): information processing, perception, thought, & language
  - Limbic cortex: emotions & behavior
  - Hippocampus: forming new memories
  - Midbrain & Basal Ganglia: movement
  - Olfactory pathways

Lewy Body Dementia

- Less atrophy in medial-temporal lobe regions compared to AD, but much overlap



Lewy Body Dementia

LBD/DLB is a form of dementia characterized by:

- motor features, parkinsonism, incl some combo of tremor, stiffness, balance problems, postural instability & slowness;
- cognitive impairment;
- neuropsychiatric features (e.g., hallucinations, depression, sleep disorder, associated behavioral disturbances);
- and/or autonomic dysfunction.

Lewy Body Dementia

The overall clinical picture is important when making the diagnosis, because neither neuropsychological testing nor neuroimaging reliably differentiates dementia with Lewy bodies from Alzheimer's disease, and both conditions may exist in a single patient.

A useful way to remember the cardinal features of DLB:

Dementia, Delirium (fluctuating cognition), Visual hallucinations with Parkinsonism, & rapid eye movement (REM) sleep behavior disorder [RBD].

Lewy Body Dementia: Clinical

Cognition: Patients who have LBD/DLB tend to have more problems with executive functioning (e.g., planning, prioritizing, sequencing) and more visuospatial impairment, but do better with verbal & episodic memory than patients with Alzheimer's disease. Executive dysfxn very similar to Frontotemporal dementia.

Lewy Body Dementia: Clinical

Cognition: significant difficulty with visual perception & visual spatial abilities, incl diff judging distance & depth, misidentifying objects; problems with planning, multitasking, problem solving, & reasoning; confusion about time & place, difficulty with language & numbers

Lewy Body Dementia: Clinical

Cognition: In FTD, see prominent early changes in personality, social & personal behavior; stereotyped behaviors; poor judgement; inability to manage one's own affairs; disinhibition, over-activity to apathy & inertia, fatuous unconcerned affect; early loss of insight so patients are not concerned or aware of deficits; pica & compulsive behaviors; but typ no motor sxs

Lewy Body Dementia: Clinical

Cognition: In FTD, see significant executive dysfunction, problems with mental set shifting, perseveration, problems with attention & concentration, poor organization; pattern & severity very similar to that seen in LBD/DLB. LBD/DLB does not show loss of social comportment. DLB has more significant memory impairments

Lewy Body Dementia: Clinical

Fluctuating cognition occurs in 50 to 75 percent of patients who have LBD/DLB. Fluctuations may occur over minutes, hours, or days, and their presence may be particularly helpful in differentiating LBD/DLB from AD. The fluctuating cognitive state closely mimics delirium and has been referred to as "pseudodelirium"; may stare into space, seem drowsy & lethargic, sleep for extended periods day & night, even after good sleep, ideas may be disorganized, unclear, or illogical; better one day, worse the next.

Lewy Body Dementia: Clinical

In a recent study, researchers found four characteristics of fluctuations that significantly differentiated DLB from AD & FTD. These included:

(1) daytime drowsiness and lethargy,
(2) daytime sleep of two or more hours,
(3) staring into space for long periods, and
(4) episodes of disorganized speech.

The presence of three or four of these features was seen in 63% of patients who had LBD/DLB & 12% of those with AD.

Lewy Body Dementia: Clinical

In a recent study, researchers found clinical EEG testing revealed significantly greater proportion of LBD/DLB patients demonstrated much higher frequency of temporal lobe slow wave transients on EEG and these EEG findings were highly correlated with episodes of loss of consciousness in the LBD/DLB group, but not with hallucinations or global severity. These findings were not present in AD patients.

Lewy Body Dementia: Clinical

Input about the patient's cognitive state should be sought from family members and caregivers.

Physicians should not rely on clinical impressions at a single visit, because the patient's cognitive impairment may range from near normal to severe confusion.

Lewy Body Dementia: Clinical

- About 80 percent of patients who have LBD/DLB have hallucinations
- Usually these are purely visual, vivid, colorful, 3-dimensional hallucinations
- Often of humans or animals, sometimes objects
- Face on the wall, off edge of vision initially
- Often seeing things through the window, children playing, animals running, or magical creatures
- Can also experience illusions, misperception of st there, as a living thing (laundry as a cat)

Lewy Body Dementia: Clinical

- Examples of visual hallucinations:





Lewy Body Dementia: Clinical

Although these hallucinations may upset the family and caretakers, they may not be particularly distressing to the patient.

Nevertheless, because patients who have LBD/DLB can experience severe reactions to antipsychotic medications, it is important to recognize these hallucinations as part of the disease spectrum and not as evidence of a superimposed psychotic illness.

Lewy Body Dementia: Clinical

Autonomic symptoms, are typically prominent in LBD/DLB, including changes in body temperature, problems with blood pressure, especially orthostatic hypotension, dizziness, syncope/presyncope, fainting, frequent falls, sensitivity to heat & cold, sexual dysfunction, urinary incontinence, constipation, and a poor sense of smell. Also, swallowing difficulty.

Finally, patients who have LBD/DLB tend not to respond as well to levodopa with carbidopa (Sinemet) as patients who have Parkinson's disease with dementia.

Lewy Body Dementia: Clinical

REM sleep behavior disorder occurs in about 50% of patients and is often a precursor of dementia with Lewy bodies.

REM sleep behavior disorder is manifested by vivid dreams associated with simple or complex motor behavior during REM sleep.

Patients can act out their dreams, often defending themselves against attack.

Lewy Body Dementia: Cognition

Yaakov Stern and colleagues (2004) conducted a study investigating the differences in dementia characteristics among DLB (16) to AD (16) and PD with dementia (15) with comparable level of dementia.

- ✔Isolated cognitive impairment was the most common form of presentation in AD (93.8%) and DLB (31.3%) groups, while parkinsonism was in 100% of PDD subjects.
- ✔Psychoses associated with cognitive impairment at the beginning of the disease were more frequent in DLB patients (31.3%) than in AD (6.3%) and PDD (0%) groups.

Lewy Body Dementia: Cognition

Yaakov Stern and colleagues (2004) study:

- ✔There were no significant differences in Unified Parkinson Disease Rating Scale motor-subscale scores between DLB and PDD patients.
- ✔No significant differences were found between PDD group and DLB subjects on any neuropsychological test.

Lewy Body Dementia: Cognition

Yaakov Stern and colleagues (2004) study:

- DLB and PDD patients performed significantly worse on attentional functions and better on memory tests than AD.
- DLB patients also showed lower scores than AD subjects on visual memory, visuoperceptive, and visuoconstructive tests.
- Clinical features and neuropsychological deficiencies of DLB (attentional, visuoperceptive, and visuoconstructive deficits) and PD (attentional deficits) compared to AD (amnesic syndrome) can contribute to accurate identification.

Lewy Body Dementia: Cognition

- Previous studies have suggested that visuoperceptual problems are salient in DLB, including basic figure-ground discrimination worse in DLB, & problems identifying silhouettes of real versus non-real objects.
- More complex visual tasks produced similar deficits in both DLB and AD groups.
- Among clinical variables, presence/recent history of visual hallucinations was the most specific to DLB (99%), and visuospatial impairment was the most sensitive (74%).

Lewy Body Dementia: Cognition

Attention may be a second area of weakness in DLB which, together with the related areas of working memory and executive function, influences adaptive functioning and performance on formal tests.

Whereas patients with AD show set shifting, letter fluency, and selective attention deficits, the DLB group has problems in sustained and divided attention tasks.

Lewy Body Dementia: Cognition

Differences in long term episodic memory and semantic memory, two major hallmarks of AD.

One important finding is that delayed recall represents one of the apparently few areas in which patients with AD have a disproportionately greater weakness than their DLB counterparts, even though the patients with DLB do show substantial deficits on recall and recognition tasks.

Lewy Body Dementia: Cognition

Category fluency and picture naming were also substantially but equally impaired in both AD & LBD, so semantic memory itself does not distinguish these two disorders.

The more marked visuoperceptual problems in patients with LBD seem, however, to exacerbate their semantic memory performance in some tests when presentation uses the visual modality.

Lewy Body Dementia: Cognition

LBD patients showed significantly more qualitative executive impairment as compared with AD patients, including:

- greater distractibility,
- poor mental set establishment and shifting,
- circumstantial thought,
- intrusions, and
- perseverative responses (repeating).

Lewy Body Dementia: Psychosis

- Psychotic symptoms of any type are more common in LBD than AD, most frequent are visual hallucinations (54%-67%).
- In contrast, delusions were most common psychotic symptom in AD (31%), with much lower rates of all types of hallucinations.
- Whereas AD-associated delusions tend to be secondary to the amnesia (e.g., paranoia around theft and misidentification), delusions in LBD related to visual hallucinations and perceptual problems, such as phantom boarder and Capgras syndromes.
- Overall rate of psychotic symptoms in AD catches up with LBD as function of greater dementia severity.

Lewy Body Dementia: Psychosis

- ✔Delusions of misidentification make up 25%–47% of delusions in AD (Burns et al 1990; Mendez et al 1992; Binetti et al 1993; Forstl et al 1994a).
- ✔Delusions of misidentification and hallucinations appear earlier and with greater frequency in dementia with Lewy bodies than in other forms of dementia (Ballard et al 1999).
- ✔Patients suffering from delusions of misidentification show lower MMSE scores at onset and higher Blessed Dementia Scale ratings than matched nondelusional dementing controls (Forstl et al 1994a).
- ✔Capgras & Phantom Boarder make up the majority of delusional misidentifications, ranging from 6-36%.

Lewy Body Dementia: Psychosis

Capgras syndromes

a disorder in which a person holds a delusion that a friend, spouse, parent, or other close family member has been replaced by an identical-looking impostor. The Capgras delusion is classified as a delusional misidentification syndrome, a class of delusional beliefs that involves the misidentification of people, places, or objects. It can occur in acute, transient, or chronic forms. Cases in which patients hold the belief that time has been "warped" or "substituted" have also been reported. The syndrome, named for French psychiatrist Jean Marie Joseph Capgras, can be related to epilepsy, damage to the temporal lobes in the brain, and various forms of dementia. The Capgras' patient identifies his or her spouse as being an imposter - identical in every possible way, but an identical replica. The patient will accept living with these imposters but will secretly "know" that they are not the people they claim to be.

Lewy Body Dementia: Psychosis

Phantom Boarder: A delusion in which patients believe their house is inhabited by unwelcome guests. They may complain their "guests" eat their food or make excessive noise, and can usually detail the daily routines of these phantoms.

Lewy Body Dementia: Psychosis

Misidentification of objects makes up 9%–18%.

- ✔Most commonly, patients insist their residence is not their home, and must be watched closely lest they attempt to relocate to their "real" home.
- ✔Mirror sign (3%) and tv sign (5%–7%) are phenomena in which the patient misidentifies his or her own mirror image or treats television characters and events as reality.
- ✔Finally, nurturing syndrome is an increasingly recognized (Schlimme et al 2002) delusion, clustering with phenomena of misidentification, in which the patient believes a dead family member to be alive. These patients often request the police to search for their missing relatives and feed and sleep with pictures of the dead family members.

Lewy Body Dementia: Treatment

Pharmacological treatment for LBD/DLB:

- Studies found donepezil (Aricept) & rivastigmine (Exelon) superior to placebo in improving cognition in DLB & PDD (but not galantamine, i.e., Razadyne)
- Rivastigmine showed signif benefit for improving behavioral disturbance (psychiatric sxs) compared to control treatments, only long duration (>12 weeks) group
- No signif improvements were noted in motor functions on any of the cholinesterase inhibitors

[Matsunaga et al., Cholinesterase inhibitors for Lewy Body Disorders: A meta-analysis, Int J Neuropsychopharm. 2016 Feb;19(2)]

Lewy Body Dementia: Treatment

Pharmacological treatment for LBD/DLB:

- donepezil (Aricept) & rivastigmine (Exelon) superior to placebo in improving activities of daily living (ADLs), assessed by Alzheimer's Disease Cooperative Study-ADL Inventory, Unified Parkinson's Disease Rating Scale-ADLs, & Zarit Caregiver Burden
- donepezil (Aricept) & rivastigmine (Exelon) superior to placebo in improving global function assessment (clinician's interview-based impression of change & caregiver input)

Lewy Body Dementia: Treatment

Pharmacological treatment for LBD/DLB:

- Cholinesterase inhibitor treatment was associated with higher incidence of nausea and tremor compared to placebo
- Rivastigmine was associated with higher incidence of vomiting & dizziness compared with placebo
- Rivastigmine was associated with higher all-cause discontinuation rate than placebo (but not statistically significant)
- NOTE: only Rivastigmine FDA approved for LBD

Lewy Body Dementia: Treatment

Pharmacological treatment for LBD/DLB:

- Medications for PD, such as carbidopa-levodopa (Sinemet), may help reduce parkinsonian sxs like rigid muscles & slow movement, but may also increase confusion, hallucinations, & delusions
- Anticholinergic & antihistamines medications (incl Benadryl) can worsen cognition & cause behavioral problems
- Dopamine agonists can cause hallucinations
- Avoid benzodiazepines: risk sedation, falls, paradoxical agitation

Lewy Body Dementia: Treatment

Pharmacological treatment for LBD/DLB:

- First generation antipsychotic medications (Haldol, & Zyprexa & Risperdal) should *not* used; cause severe confusion, severe parkinsonism, sedation & sometimes even death
- Rarely can use certain second generation antipsychotics short time
- If needed, prefer atyipical antipsychotics, Quetiapine (Seroquel) or Clozapine (Clozaril, FazaClo)
- Newer drug, Pimavanserin (Nuplazid) FDA approved to treat hallucinations & delusions assoc w/PD psychosis, but serious side effects have been reported

Lewy Body Dementia: Treatment

Pharmacological treatment for LBD/DLB:

- Clonazepam (Klonopin) effective at very low doses for REM sleep behavior disorders in DLB [can have side effects of dizziness, unsteadiness, & problems with thinking]
- Melatonin, naturally occurring hormone, used to treat insomnia, may be beneficial alone or in combination with Clonazepam
- Stimulants (Armodafinil (Nuvigil), Modafinil [Provigil]) can be used to treat excessive daytime sleepiness (boost dopamine)
- Less support for Memantine use

Lewy Body Dementia: Experimental Potential Treatments

New Research on Potential Pharmacological treatment for LBD:

- Researcher Na Zhao, MD PHD, Mayo in Florida, studying "mini-brain models" or "brain organoids" lab-grown clusters of cells mimic human brain structure
- Developed from skin cells taken from pts w/LBD who are alive & converted them to stem cells for research
- A protein, alpha-synuclein, encoded by the SNCA gene, can build up into masses called Lewy Bodies, believed to contribute to sxs of dementia
- Mini-brains mirrored changes seen in human brains of LBD pts
- Found 4 drug candidates that may help to prevent alpha-synuclein build-up in neurons & restore energy production in neurons derived from LBD pts

Lewy Body Dementia: Experimental Potential Treatments

- RewinD-LB trial phase 2b (looks at effective dosing in defined pt populations) from CervoMed Pharmaceuticals study, drug neflamapimod, may slow cognitive decline in DLB; phase 2a trial showed benefit on cognitive decline esp for those w/o evidence of co-existing AD; Initial results dose was too low; on extension with higher dose drug, showed benefit on cognitive decline; study ongoing (March 2025)
- SHIMMER trial—positive results phase 2 clinical trial CT1812—slowed cognitive decline in attention fluctuations (91%), slowed progression neuropsychiatric features, anxiety, hallucinations & delusions (82%), caregiver distress assoc w/those sxs improved, parkinsonian motor decline slowed (62%), slowing of decline in ADLs (52%)
- Nilotinib—(FDA approved leukemia) well tolerated, improved cognition in DLB at 3 mos less at 6 mos, also had fewer falls; rec for phase3 study

Lewy Body Dementia: Experimental Potential Treatments

- COBALT trial UK—studying combination of memantine & a cholinesterase inhibitor (either donepezil, rivastigmine or galantamine) in LBD, both DLB & PDD
- France studying feasibility & potential benefit in reducing cognitive fluctuations in DLB using repetitive transcranial magnetic stimulation rTMS
- Ambroxol (used to treat coughs) being studied in DLB for cognition, functioning, & neuropsychiatric sxs; enhancing fxn of lysosomes, cellular components that clean out protein waste; believed may improve motor & behavioral deficits by reducing alpha-synuclein pathology & improving dopaminergic fxn

Lewy Body Dementia: Behavioral Management

Once a diagnosis is made, need to know:

- Neurocognitive deficits
- Preserved strengths of the person's traits and basic abilities
- Potential environmental triggers
- How an individual's affect/emotion affects their behavior
- Premorbid personality

Lewy Body Dementia: Behavioral Management

To change unwanted behaviors, need to know:

- How to decrease effect of cognitive deficits
- Utilize preserved strengths of the person's traits and basic abilities
- Avoid or alter potential environmental triggers
- Maintain positive affect/emotion and decrease negative emotions to influence behavior
- Use old preferences to shape future behavior

Best Strategies for Lewy Body Dementia

- Do more on good days, less on bad days
- Need lots of rest breaks, even on good days, don't overdo it
- Recognize visual spatial difficulties, modify spatial environment i.e., maybe can wash or wipe dishes but can't put them away, use type of calendars they can process (diff spatial styles)
- Use specific, concise verbal instructions for visual directions
- Reassure them, visual hallucinations are not real and not harmful
- Keep their visual environment simple and uncluttered, well lit

Lewy Body Disease

End of life in Lewy Body Disease:

- Dysphagia (swallowing difficulty, secondary to pharyngeal dysfxn in DLB) resulting in aspiration pneumonia (mortality rate of 62%); Fall et al. showed it was most common cause of death in PD (29%) [assess using EAT-10 scale]
- Failure to thrive, complications from motor dysfunction, complications from falling, other medical conditions (Armstrong et al. 2019, J Am Geriatr Soc)
- Use Hospice and discuss end of life decisions early on with patient & family members
- There is no evidence (of longer survival, less pneumonia, improved weight gain, or quality of life) that supports the use of feeding tubes in advanced dementia [https://www.lbda.org/go/lbd-story-facing-tough-choices-end-life]

Dementia with Lewy Bodies Websites

The Dementia with Lewy Bodies Association : http://www.lbda.org/

Family Caregiver Alliance: http://www.caregiver.org/caregiver/jsp/content_node.jsp?nodeid=570

https://www.nia.nih.gov/health/lewy-body-dementia-research

Dementia with Lewy Bodies Websites

https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Lewy-Body-Dementia-Hope-Through-Research

https://www.ninds.nih.gov/health-information/disorders/lewy-body-dementia

Reads

Living with Lewy Body Dementia by Judy Towne Jennings PT, MA

Caregiver's Guide to Lewy Body Dementia by Whitworth

Dementia with Lewy Bodies & PD Dementia by Dr. J. Eric Ahlskog

Love, Dignity & Parkinson's by Terri Pease PhD

Dancing with Elephants: Mindfulness Training for those Living with Dementia (he has Huntington's) by J Sawatsky

Where the Light Gets In by Kimberly Williams-Paisley on PPA