Banner Health

Different from Alzheimer's: Lewy body dementia

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Objectives

1. Understand how Lewy body dementia is diagnosed.

2. Learn what the symptoms of Lewy body dementia are, and how they can be treated.

3. Understand what medical research is relevant to individuals with Lewy body dementia.

What is Lewy body dementia?

- Parkinson disease with dementia (PDD)
  - Parkinsonism
  - Later dementia
- Dementia with Lewy bodies (DLB)
  - Early Dementia (in the first year)
  - Parkinsonism, cognitive fluctuations, hallucinations, dream enactment
- Collectively, “Lewy body dementia” (LBD)

Lewy body dementia- not just memory loss

- Impaired Attention
  - Cognitive fluctuations
- Visual-spatial perception problems
- Executive function difficulties

What is “parkinsonism?”

- Motor Symptoms
  - Tremor
  - Bradykinesia (Slowness of movement)
  - Rigidity (Stiffness, or resistance of the limbs to passive movement)
  - Postural Instability (Impaired balance)

Parkinson disease

- Motor symptoms (parkinsonism)
- Absence of “red flags”
  - Offending medications
  - Early, severe falls; orthostatic hypotension
- Dementia is usually a later problem
- Impacts 80% of people over the course of the illness.

Dementia with Lewy Bodies: Diagnosis

- Central Features
  - Dementia in first year
    - Attention, executive, visuospatial impairment
    - Memory loss may occur later
- Core Features (2/3=prob, 1/3=possible)
  - Parkinsonism
  - Cognitive Fluctuations (esp of attention/alertness)
  - Visual Hallucinations
  - Dream enactment
- Biomarker Tests
  - DatScan (Dopamine transporter SPECT)
  - Sleep study (for REM atonia)
  - MIBG (not available in US)

Lewy body dementia: Not just dementia

- Neuroleptic sensitivity
  - Anti-psychotics (haloperidol, risperidone, olanzapine, aripiprazole)
  - Anti-emetics (metoclopramide, prochlorperazine, promethazine)
- Motor symptoms
- Non-levodopa responsive symptoms
  - Softer voice, trouble swallowing, drooling
  - Nonmotor

REM sleep behavior Disorder

- Dream enactment behavior during Rapid Eye Movement (REM) stage sleep
- Recall of active dream content
- Muscles are not paralyzed during REM stage (loss of REM atonia)
- Affects 40-60% of PD (20% of DLB)
- Treatable with melatonin or clonazepam

RBD is a risk factor for PD, DLB

- 70% or more of those with RBD will eventually develop PD, DLB or multiple system atrophy (MSA)
- Individuals with idiopathic RBD are encouraged to participate in research
  - Annual neurological exam and testing
  - Brain and body donation
  - www.brainandbodydonationprogram.org

Schenck CH, Boeve BF, Mahowald MW. Delayed emergence of a parkinsonian disorder or dementia in 81% of older men initially diagnosed with idiopathic rapid eye movement sleep behavior disorder: a 16-year update on a previously reported series. Sleep Med. 2013 Aug;14(8):744-8.

Iranzo A, Fernández-Arcos A, Tolosa E, Serradell M, Molinuevo JL, Valldeoriola F, Gelpi E, Vilaseca I, Sánchez-Valle R, Lladó A, Gaig C, Santamaría J. Neurodegenerative disorder risk in idiopathic REM sleep behavior disorder: study in 174 patients. PLoS One. 2014 Feb 26;9(2):e89741

Medications for parkinsonism

- Carbidopa/Levodopa (Sinemet, Rytary)
- MAO-B inhibitors
  - Azilect, selegiline
- Used with caution: Amantadine, dopamine agonists (pramipexole, ropinirole, Neupro)
- Avoided: Anticholinergics
  - Artane (trihexiphenidyl)
  - Cogentin (benztropine)

Neurotransmitters depleted by LBD

- Dopamine (leading to motor symptoms)
- Acetylcholine (even more than in AD)
- Serotonin (impacting mood)
- Norepinephrine (aka noradrenaline)
  - Mood/anxiety
  - Autonomic problems (orthostatic hypotension)

Non-motor symptoms

- Diminished sense of smell
- Fatigue, Anxiety/Depression, Apathy
- Sleep fragmentation, RBD
- Dementia, cognitive fluctuations
- Psychosis (Hallucinations and delusions)
- Constipation
- Urinary frequency/urgency
- Sensory (pain, restless legs/body)
- Orthostatic Hypotension
  - Low blood pressure/dizziness/fainting with standing

Mood symptoms

- Depression
  - No “one size fits all” approach
  - Need to screen for suicidal thoughts
- Apathy
  - Nonmedical measures vs stimulants
- Anxiety
  - Buspirone, mirtazapine, antidepressants
  - Minimize or avoid tranquilizers

Sleep symptoms

- REM sleep behavior disorder
  - Treatable with melatonin or clonazepam
- Sleep-wake transition problems
- Sleep fragmentation
  - May Require sleep hygeine (fewer naps)
  - Trazodone and mirtazapine are gentler
- Excessive daytime sleepiness
  - Minimize offending medications
  - Address sleep apnea, fragmentation

Cognitive Treatments for LBD

- Aricept (donepezil)
  - Recently approved in Japan for LBD
- Exelon (rivastigmine) Patch
  - FDA approved for PDD
- Namenda (memantine)
- Exercise

Emerging Treatments for LBD

- LY3154207 (Eli Lilly)
- E2027 (Eisai)

Hallucinations and Delusions

- Frequently, early symptoms include minor hallucinations such as a sense of presence or passage.
- These an be confused with vision problems, delirium, or confusion related to memory loss.
- Over time, the hallucinations become more persistent and troubling. Additionally, delusions may occur.
- The most common symptom are visual hallucinations – seeing things that arent really there
  - Hearing things and feeling things on or under the skin may also occur
- People with PD/LBD related hallucinations are often aware that their symptoms are abnormal

Hallucinations and Delusions (Psychosis): Treatment

- Nuplazid (pimavanserin)
  - *First FDA approved treatment for PD psychosis*
- Commonly used:
  - Seroquel (quetiapene), clozapine
- Often used but may ***worsen*** *other symptoms*:
  - Abilify (aripiprazole), Risperdal (risperidone); Zyprexa (olanzapine); Geodon (ziprasidone); Saphris, Fanapt; Latuda

Treatments: Constipation

- Amitizia (lubriprostone)
  - 64% Marked or very good improvement(vs. 18.5% placebo)
- Commonly used for maintenance
  - Senna, docusate
- Commonly used “as needed”
  - Miralax (polyethylene glycol)
  - Dulcolax (biscodyl)

Treatments: Bladder urgency/incontinence

- Avoid oral oxybutynin
  - Metabolites block acetycholine in the brain
  - Patch or gel is OK (bypasses the liver)
- Commonly used
  - Sanctura (trospium)
  - Vesicare, Enablex, Detrol (tolterodine), Toviaz
- Other procedures
  - Botox, bladder stimulators, accupuncture

What is Neurogenic Orthostatic Hypotension (nOH)

- Defined as OH that is caused by a disease that causes nerve damage, such as LBD:
- The nerve damage or dysfunction seen in nOH results in decreased levels of a chemical called “norepinephrine” (NE)
- NE is involved in maintaining normal blood pressure as well as the “flight or flight” response among other things

What are the Common Symptoms of nOH?

Symptoms result from reduced blood flow to internal organs:

- Feeling dizzy or lightheaded after standing up
- Blurry vision
- Weakness
- Fainting (syncope)
- Confusion
- Nausea
- Head or neck pain

Freeman R. *N Engl J Med*. 2008;358(6):615-624.

Factors that Can Affect OH Symptoms

- How fast you rise from a lying or sitting position to standing
- Lying down for long periods before standing
- Time of day (morning usually worse)
- Warm environment (hot bath, warm weather, central heating)
- Food (worse after meals) and alcohol
- Physical exertion
- When going to the bathroom

Current Treatments: Orthostatic Hypotension

- Commonly used:
  - Limit antihypertensive use
  - Increase salt/fluid intake
  - Florinef (fludrocortisone)
  - Pyridostigmine (safer in heart failure)
  - Midodrine
  - Northera (droxidopa)
- Under study:
  - TD-9855
  - Atomoxetine

Future research directions

- Better symptomatic therapies
- Disease modifying therapies
- Understanding RBD as an LBD risk factor

Dementia With Lewy Bodies

Resources

Lewy Body Dementia Association

http://www.lbda.org/

Banner Sun Health Research Institute www.bannershri.com

- Clinicians
  - David Shprecher, Sara Dhanani (Movement)
  - Alireza Atri, Danielle Goldfarb (Dementia)
  - NP: Stephanie De Santiago, Marina Reade, Deb Witthar
- NeuroWellness classes
- Neuropsychological testing services
- Social Work/Counseling
- Clinical Research