Current interventions in Parkinson’s Disease (PD) & Lewy Body Dementia (LBD)

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Parkinson's Disease is diagnosed when a person is found on exam to have key MOTOR symptoms of 
Bradykinesia PLUS either muscle rigidity OR resting tremor
Common Non-Motor Symptoms in Parkinson’s Disease – Timing is key!

REM Sleep Behavior disorder/Insomnia
Depression/Anxiety
Loss of smell
Constipation
Orthostatic Hypotension
Sexual Problems
Urinary Dysfunction
*Mild cognitive impairment

Dementia and Psychosis
Severe Orthostatic Hypotension and Autonomic Dysregulation
Urinary Incontinence
Severe Dysphagia and Choking

Can Precede Diagnosis
Later in Disease
Earlier in Disease

Lewy Body Dementia vs. Parkinson’s disease Dementia?

Which came first?
Psychosis in PD and LBD

• **Illusions** – Misinterpretations of real stimuli. Can be unformed, such as a sense of presence or a fleeting false impression

• **Hallucinations** – Spontaneous, fully formed. Most often visual, but can be auditory, tactile, olfactory (smell), or gustatory (taste)
  - With insight the hallucinations are not real
  - Without insight they are not real

• **Delusions** – False thinking. Can be paranoia.
Finding the balance between treating the Motor symptoms and Hallucinations

- Motor Symptoms
  - Improved by dopamine medications

- Hallucinations
  - Worsened by dopamine medications

Currently Available Therapies

- Classic Motor Symptoms
  - Bradykinesia, Tremor, Rigidity
  - Hypomimia, Micrographia

- Mixed Motor/Non-Motor Symptoms
  - Hypophonia and Dysarthria
  - Walking and Balance Problems

- Non-Motor Symptoms
  - Mild Cognitive Impairment and Dementia
  - Psychosis (hallucinations and delusions)
  - Sleep disorders (RBD)
  - Depression/Apathy, Anxiety, Fatigue
  - Constipation, Orthostatic hypotension, Urinary frequency, urgency, incontinence
Currently Available Therapies

Dopamine
- Helps Motor
- Does not help Cognitive
- Might worsen some Cognitive functions
- Causes Hallucinations in PD dementia or LBD

DBS
- Helps Motor
- Does not help Cognitive
- Can worsens word finding
- In patients with moderate to severe cognitive impairment DBS can worsen all cognitive functions.

Other for Cognitive
- Cholinesterase Inhibitors
- Mild benefit to Cognition and Memory
- Does not prevent progression to Dementia
Treating cognition and memory in PD and LBD: Cholinesterase Inhibitors

- Rivastigmine (Exelon) was FDA-approved for PD Dementia in 2006.
- Evidence-based reviews in PD recommend rivastigmine as “efficacious” for the treatment of PD Dementia, with an acceptable safety risk without need for specialized monitoring.
- Other cholinesterase inhibitors:
  - Donepezil (Aricept)
  - Galantamine
- Smaller studies on memantine (Namenda)
  - Was rated as having “insufficient evidence” in the treatment of PD Dementia, though they had acceptable safety risk profiles without need for specialized monitoring.

Currently Available Therapies for Hallucinations and Psychosis

- Most common reason for a sudden onset or change in symptoms is general medical illness or other medications
  - Infection (such as a UTI or a cold/flu)
  - Medications (for pain, urinary frequency)
  - Physical stress (constipation, poor sleep, travel, new physical environment)
  - Emotional stress (anxiety)
  - Being in the hospital (all of the above)
Currently Available Therapies for Hallucinations and Psychosis

- **Reduce or stop certain medications:**
  - Artane (any other anticholinergics)
  - Amantadine
  - Dopamine agonists
  - Comtan (entacapone)
  - Sinemet CR (carbidopa/levodopa CR)
  - Rytary (continuously released levodopa)
  - Stalevo (levodopa + entacapone)
  - Inbrija (inhaled levodopa)
  - Sinemet IR (carbidopa/levodopa immediate release)
  - Duopa (levodopa intestinal gel)

Most likely to cause hallucinations/psychosis

Least likely to cause hallucinations/psychosis

- **Quetiapine (Seroquel)** may be considered. Works within a day or a few days. However, the clinical trials have not clearly shown this is effective.

- **Cholinesterase inhibitors (rivastigmine and donepezil)** - No evidence yet on in PD or LBD associated psychosis, but I use them all the time.

- **Pimavanserin (Nuplazid)** – FDA approved for PD Psychosis.
  - 199 PD Psychosis patients (at least weekly hallucinations, which were severe enough to warrant treatment).
  - Primary outcome: SAPS-PD (Scale for Assessment of Positive Symptoms-Parkinson’s disease adapted) at 6 weeks.
Current interventions in Parkinson’s Disease & Lewy Body Dementia

- No current interventions to stop the progression of Motor or Non-Motor symptoms.
  - Very active area of research
- Symptomatic therapies need to be balanced between what symptoms they make better and the potential to worsen other symptoms.
  - Requires a very individualized approach to determine the exact right medications for the patient at this time
  - Balance between benefit and side effects can change over time.
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