

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



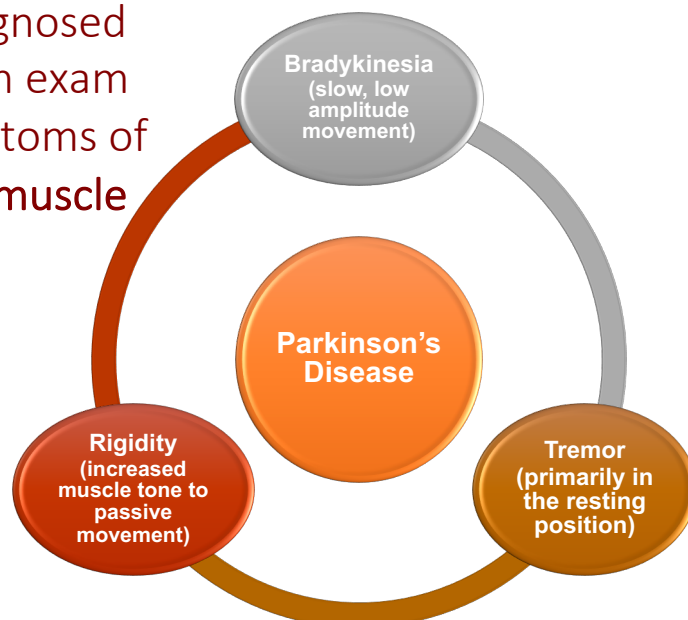
**Stanford**  
MEDICINE

Kathleen Poston, MD, MS  
Division Chief, Movement Disorders  
Associate Professor of Neurology



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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



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## Common Non-Motor Symptoms in Parkinson's Disease – Timing is key!

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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

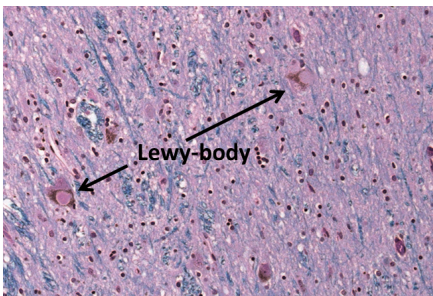


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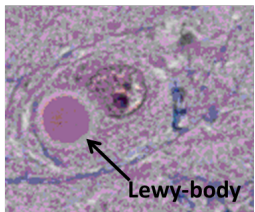
## Lewy Body Dementia vs. Parkinson's disease Dementia?

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Lewy-body Pathology



Lewy-body



Lewy-body

Cognition & Behavior

Motor

Dementia


Bradykinesia

Psychosis


Rigidity

Tremor

Time



Which came first?



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## Psychosis in PD and LBD

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- **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.



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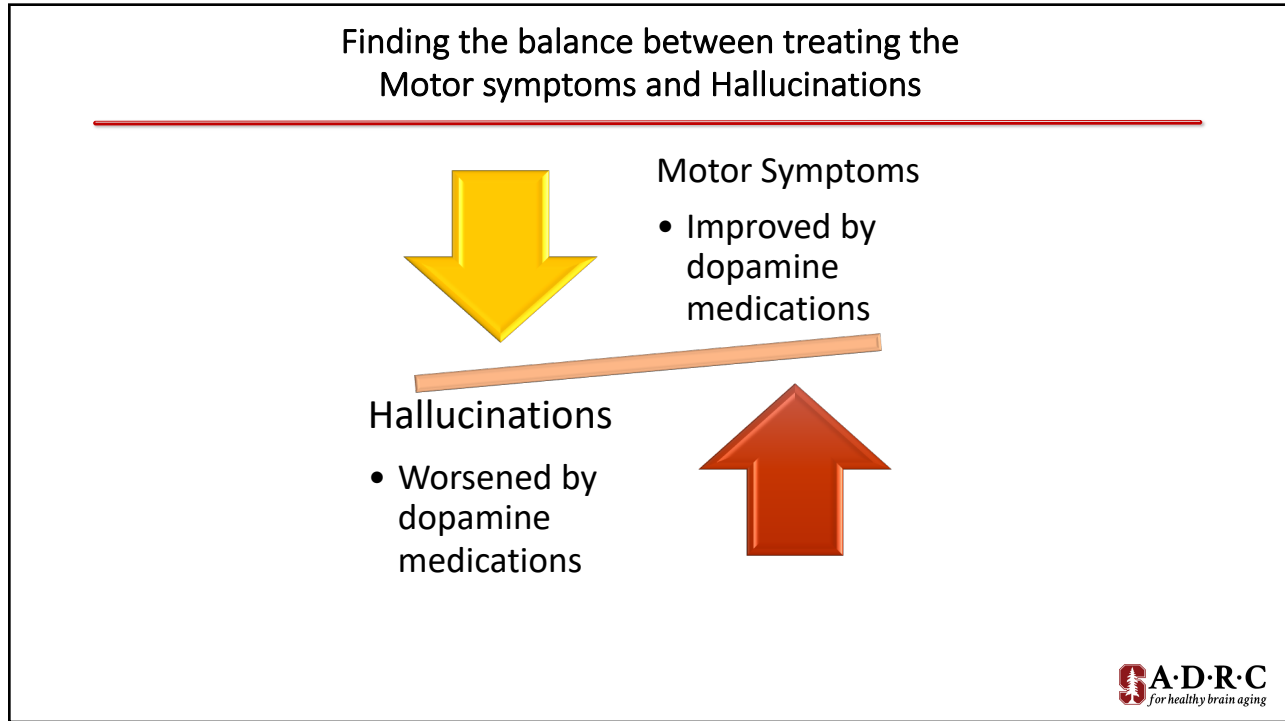
## Psychosis in PD and LBD

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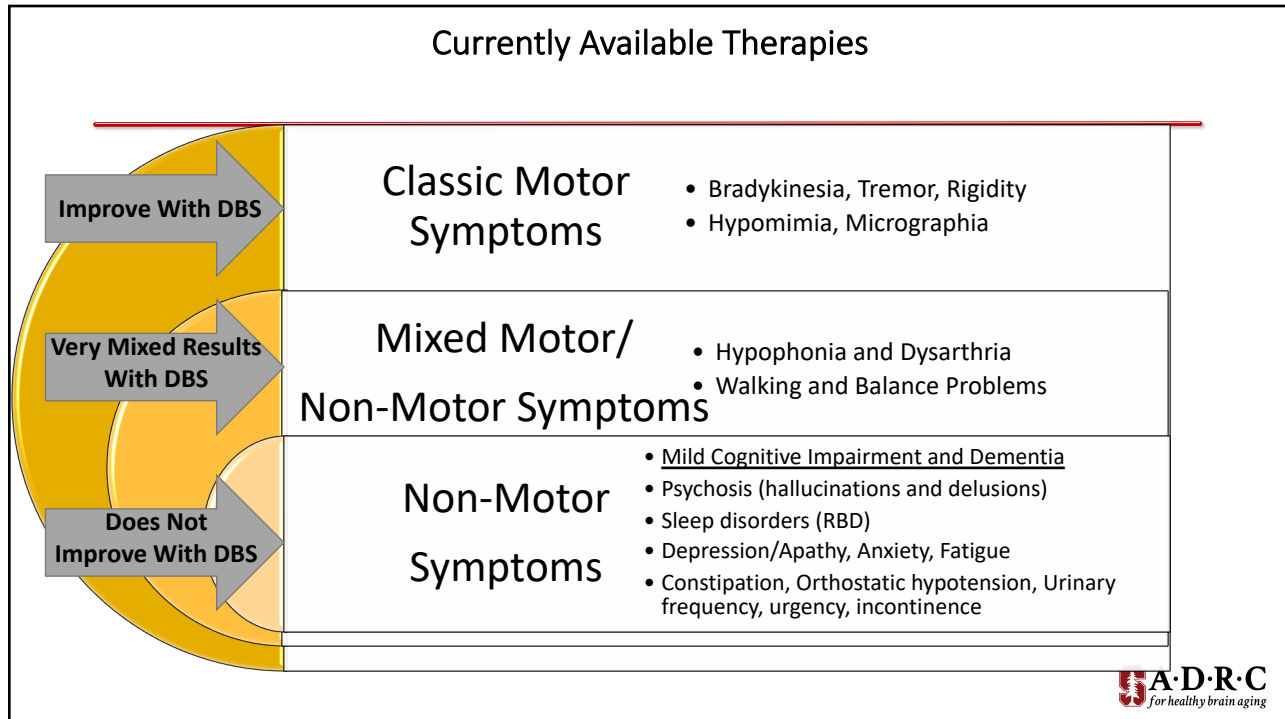
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## Currently Available Therapies

Dopamine	DBS
<ul style="list-style-type: none"> <li>• Helps Motor</li> <li>• Does not help Cognitive</li> <li>• Might worsen some Cognitive functions</li> <li>• Causes Hallucinations in PD dementia or LBD</li> </ul>	<ul style="list-style-type: none"> <li>• Helps Motor</li> <li>• Does not help Cognitive</li> <li>• Can worsens word finding</li> <li>• In patients with moderate to severe cognitive impairment DBS can worsen all cognitive functions.</li> </ul>



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## Currently Available Therapies

Dopamine	DBS	Other for Cognitive
<ul style="list-style-type: none"> <li>• Helps Motor</li> <li>• Does not help Cognitive</li> <li>• Might worsen some Cognitive functions</li> <li>• Causes Hallucinations in PD dementia or LBD</li> </ul>	<ul style="list-style-type: none"> <li>• Helps Motor</li> <li>• Does not help Cognitive</li> <li>• Can worsens word finding</li> <li>• In patients with moderate to severe cognitive impairment DBS can worsen all cognitive functions.</li> </ul>	<ul style="list-style-type: none"> <li>• Cholinesterase Inhibitors</li> <li>• Mild benefit to Cognition and Memory</li> <li>• Does not prevent progression to Dementia</li> </ul>



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## Treating cognition and memory in PD and LBD: Cholinesterase Inhibitors

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- 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.



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## Currently Available Therapies for Hallucinations and Psychosis

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- 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)



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## Currently Available Therapies for Hallucinations and Psychosis

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Most likely to cause  
hallucinations/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)

Least likely to cause  
hallucinations/psychosis



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## Currently Available Therapies for Hallucinations and Psychosis

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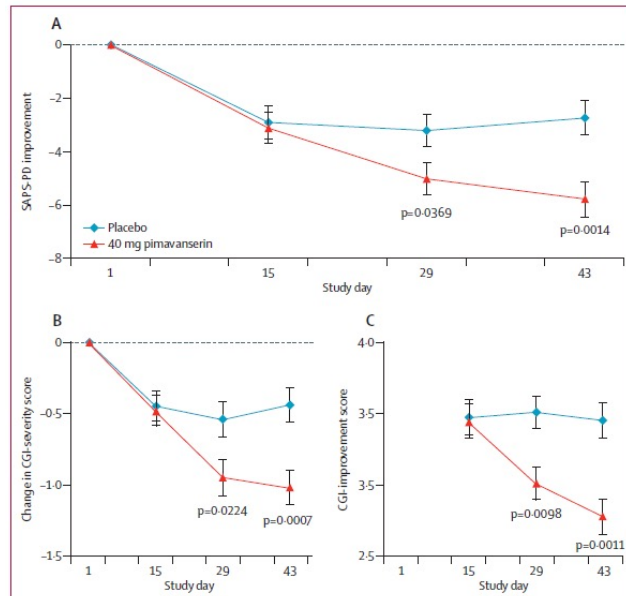
- **Quetiapine (Seroquel)** may be considered. Works within a day or a few days. However, the clinical trials have not clearly shown this is effective.
- **Cholinesterase inhibitors (rivastigmine and donepezil)** - No evidence yet on in PD or LBD associated psychosis, but I use them all the time.
- **Pimavanserin (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.



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### Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial

Jeffrey Cummings, Stuart Isaacson, Roger Mills, Hilde Williams, Kathy Chi-Barris, Anne Corbett, Rohit Dhall, Clive Ballard



**Figure 2: Treatment effects on psychosis severity reduction in the 6 week study period in the full analysis set**  
The full analysis set includes all patients who received  $\geq 1$  dose and had a SAPS assessment at baseline and at least one afterwards. Datapoints show least squares means (standard error). (A) SAPS-PD improvement. (B) Change in CGI-severity score. (C) CGI-improvement scores. SAPS=scale for assessment of positive symptoms. CGI=clinical global impression.

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## 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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# The Stanford Movement Disorders Center



Helen Bronte-Stewart, MD, MS  
Neurology, Movement disorders specialist



Kathleen Poston, MD, MS  
Neurology, Movement disorders specialist



Veronica Santini, MD  
Neurology, Movement disorders specialist



Laurice Yang, MD, MHA  
Neurology, Movement disorders specialist



J. William Langston, MD  
Neurology, Movement disorders specialist



Bill Marks, MD  
Neurology, Movement disorders specialist



Maya Katz, MD  
Neurology, Movement disorders specialist



Leila Montaser Kouhsari, MD, PhD  
Neurology, Movement disorders specialist



Jennifer O'Malley, MD, PhD,  
Child Neurology, Movement disorders specialist



Katherine Mackenzie, MD  
Child Neurology, Movement disorders specialist



Jaimie Henderson, MD  
Neurosurgery, DBS specialist

