

# Medication Considerations in Parkinson's



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## About Me



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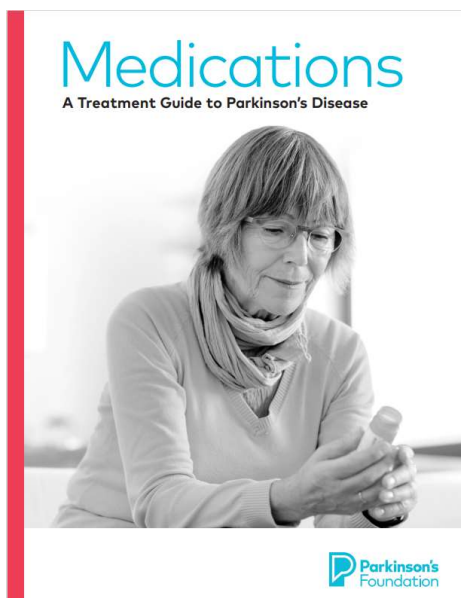
## Outline

- ▶ Pathophysiology of Parkinson's Disease
- ▶ Goals of treatment
- ▶ Medication therapy
  - ▶ What to use and when
  - ▶ How they work
  - ▶ Possible side effects and drug interactions
- ▶ Management of non-motor symptoms

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## Resources



### American Academy of Family Physicians

#### Parkinson Disease

Anne D. Halli-Tierney, MD, and Jacquelynn Luker, MD, University of Alabama, Tuscaloosa, Alabama  
Dana G. Carroll, PharmD, Auburn University Harrison School of Pharmacy, Auburn, Alabama

Parkinson disease is a progressive neurodegenerative disorder with significant morbidity and mortality. Most patients consult with their primary care physician about Parkinson disease symptoms before seeking care from a specialist. The diagnosis of Parkinson disease is clinical, and key disease features are bradykinesia, rigidity, and tremor. The main diagnostic signs of Parkinson disease are motor symptoms; however, Parkinson disease is also associated with nonmotor symptoms, including autonomic dysfunction, depression, and hallucinations, which can make the initial diagnosis of Parkinson disease difficult. Disease progression is variable and clinical signs cannot be used to predict progression accurately. Therapies, including levodopa, have not demonstrated the ability to slow disease progression. Motor symptoms are managed with carbidopa/levodopa, monoamine oxidase-B inhibitors, and nonergot dopamine agonists. Prolonged use and higher doses of levodopa result in dyskinesias and motor symptom fluctuations over time. Deep brain stimulation surgery is performed for patients who do not achieve adequate control with levodopa therapy. Deep brain stimulation is most effective for significant motor fluctuations, dyskinesias, and tremors. Nonmotor symptom therapies target patient-specific conditions during the disease course. Interdisciplinary team care can alleviate multiple symptoms of Parkinson disease. (*Am Fam Physician*. 2020;102(11):679-691. Copyright © 2020 American Academy of Family Physicians.)

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# Overview

## Pathophysiology and Goals of Treatment

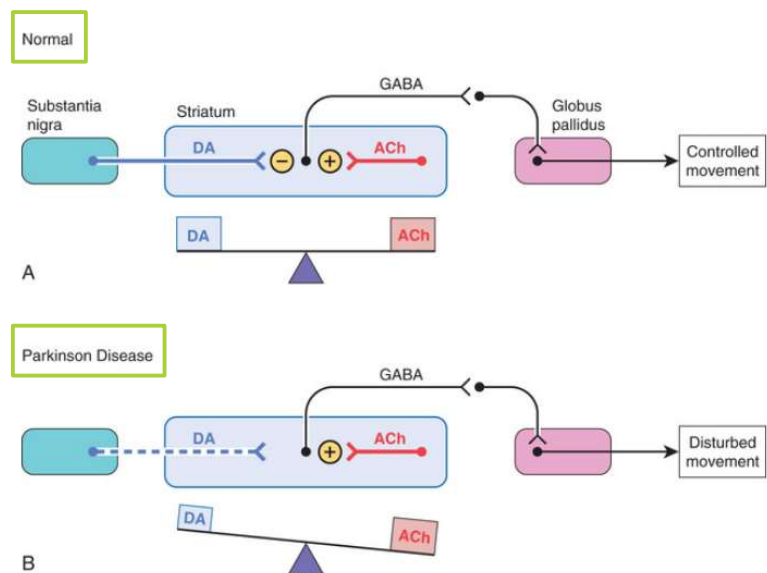
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## Pathophysiology

- ▶ Loss of dopamine-producing neurons in the substantia nigra
- ▶ Excitatory influence of acetylcholine goes unopposed
- ▶ Excessive stimulation of neurons that release GABA



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## Causes of Degradation of Dopamine Neurons

- ▶ No one knows for sure
- ▶ Some evidence implicates the abnormal clumping of a protein called alpha-synuclein within Lewy bodies in the brain.
- ▶ Combination of genetic and environmental factors

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## Goals of Treatment

- ▶ ***Ideally*** reverse the neuron degradation or prevent further degradation.
- ▶ Unfortunately, no medications can do this.
- ▶ Medications can only provide symptomatic relief.
- ▶ Goal: Improve quality of life
- ▶ Overview of medication mechanism of action
  - ▶ Restore balance between dopamine and acetylcholine

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# High-intensity Exercise Can Reverse Neurodegeneration in Parkinson's Disease

February 23, 2024 by Isabella Backman



High-intensity exercise induces brain-protective effects that have the potential to not just slow down, but possibly reverse, the neurodegeneration associated with Parkinson's disease, a new pilot study suggests.

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MENU

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# Medications

## For the Treatment of Parkinson's Disease

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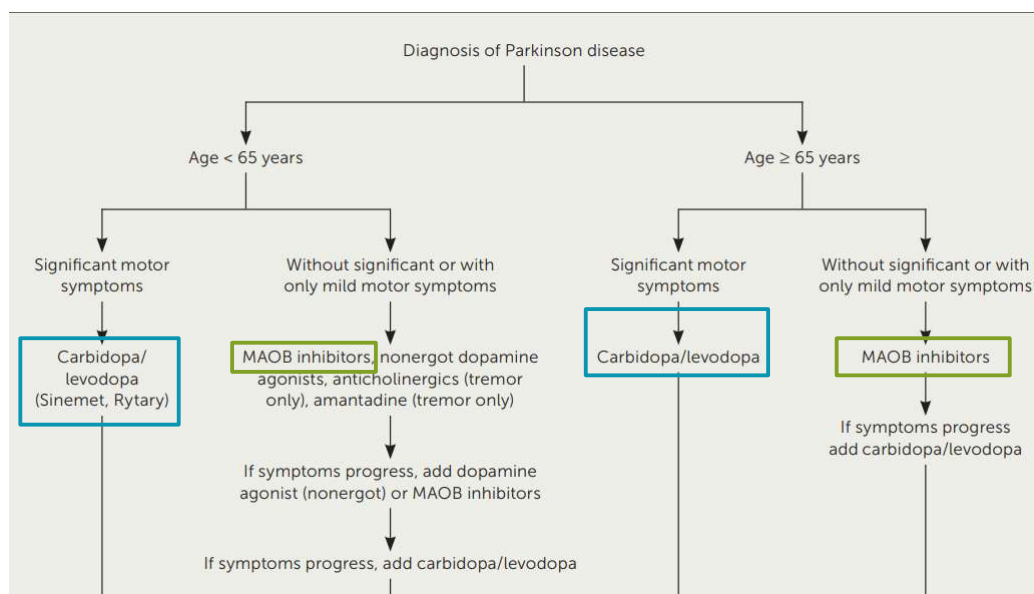
## When to start treatment?

- ▶ Treat motor symptoms when they impact the functions of daily life or decrease quality of life.
  - ▶ Movement symptoms: slowness (bradykinesia), stiffness (rigidity), tremor, cramping (dystonia), balance and coordination problems

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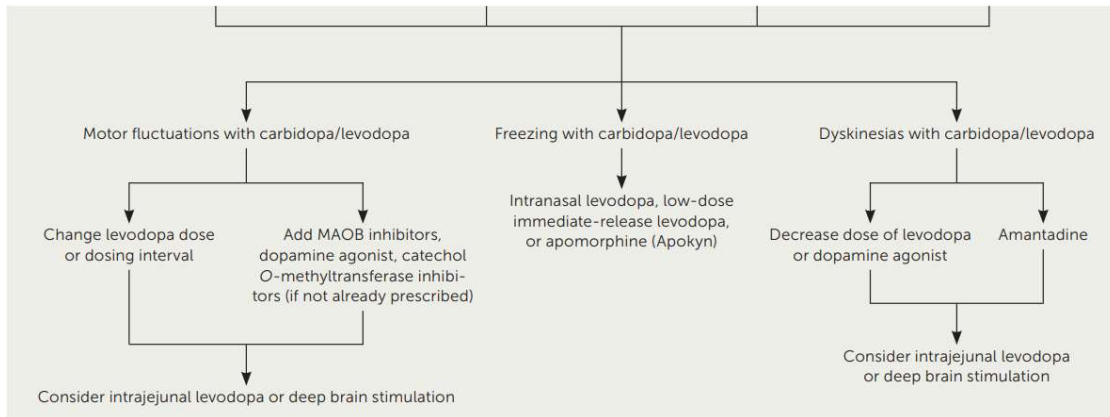
## Overview of Initial Treatment



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## Overview of Initial Treatment

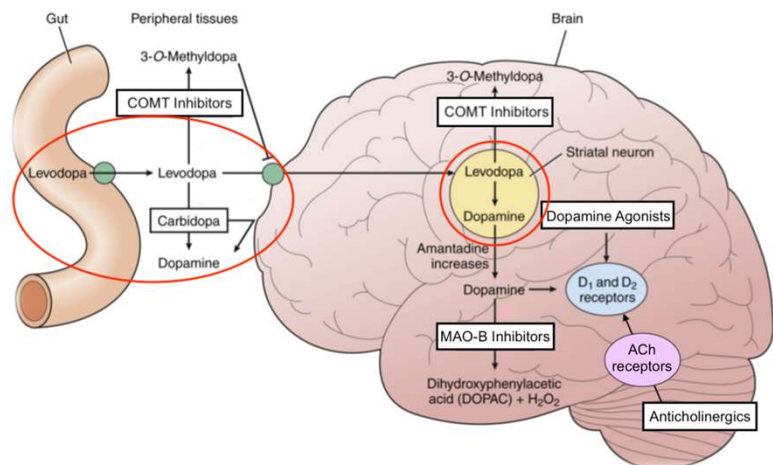


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## Levodopa

- ▶ Generic name: Carbidopa/levodopa
- ▶ Brand names: Sinemet, Dhivy, Rytary, Duopa
- ▶ Dopamine precursor
- ▶ Formulated with carbidopa which reduces or prevents the nausea of levodopa



### Role

- ▶ Most effective for treating motor symptoms

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## Levodopa: Impact on Symptoms

- ▶ Greatly improves slowness and rigidity for most people
- ▶ Some experience significant tremor improvement, others may not
- ▶ May also improve some non-movement symptoms such as pain, depression and anxiety
- ▶ May *not* help balance, swallowing, and memory issues

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## Levodopa: Tips for Taking

- ▶ Initially taken 3 times daily, evenly spaced throughout the day
  - ▶ May need to take more frequently to reduce “off” time
- ▶ Symptoms typically improve within 45 minutes of taking
- ▶ Ideally taken on an empty stomach 30-60 minutes before a meal
  - ▶ High protein meals may interfere with levodopa absorption from the gut so try to take medication at least 30 min before.
  - ▶ If nausea, take levodopa with crackers or bread

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## Levodopa: Side Effects

- ▶ More common when beginning treatment or increasing the dose
  - ▶ Start with a low dose and increase slowly

### Nausea

Eat with a cracker or piece of toast.

Dose may need to be lowered.

Add additional carbidopa.

### Dyskinesia

Uncontrolled, involuntary movements

Usually develops around 5 years after starting levodopa.

Reduce dose of levodopa or dopamine agonist.

Add amantadine.

### Other

Low blood pressure

Dizziness

Confusion

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## Levodopa: Wearing Off

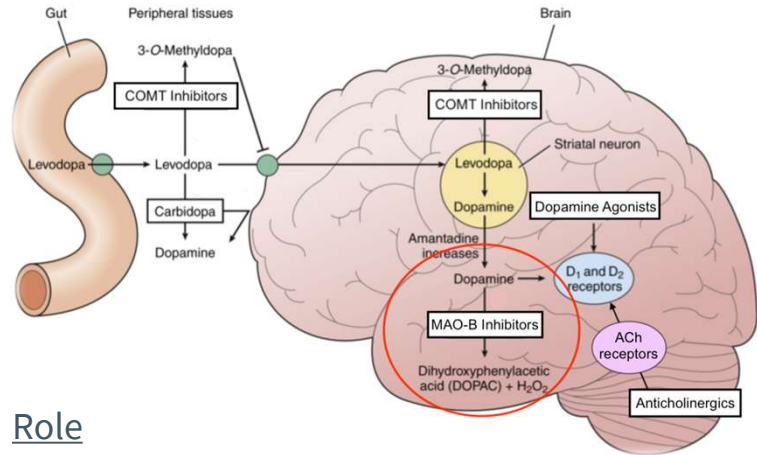
- ▶ After taking levodopa for some time – typically years – may notice more “off time” before next dose.
- ▶ Strategies for helping this
  - ▶ More frequent dosing
  - ▶ Use extended-release formulations
  - ▶ Add other medications to keep dopamine levels more consistent
    - ◆ COMT inhibitors
    - ◆ MAO-B inhibitors
    - ◆ Dopamine agonists

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## MAO-B Inhibitors

- ▶ Rasagiline (Azilect)
- ▶ Selegiline (Zelapar)
- ▶ Saffinamide (Xadago)
  
- ▶ Block the enzyme (MAO-B) that breaks down dopamine



### Role

- ▶ Used alone for mild symptoms
- ▶ Added to levodopa to reduce “off”

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## MAO-B Inhibitors: Side Effects

- ▶ Mild nausea
- ▶ Headache
- ▶ Insomnia (selegiline – take morning and midday to avoid this)
- ▶ Confusion (selegiline – avoid in older adults)
  
- ▶ Rasagiline is generally preferred due to fewer side effects

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## MAO-B Inhibitors: Drug Interactions

- ▶ Review any new medications with your doctor or pharmacist
- ▶ Possible serotonin syndrome with other medications that increase serotonin
  - ▶ Rare with doses used to treat PD

### OTC Medications to Avoid

St. John's Wort  
Dextromethorphan (cough suppressant)

### Prescription Medications to Use with Caution

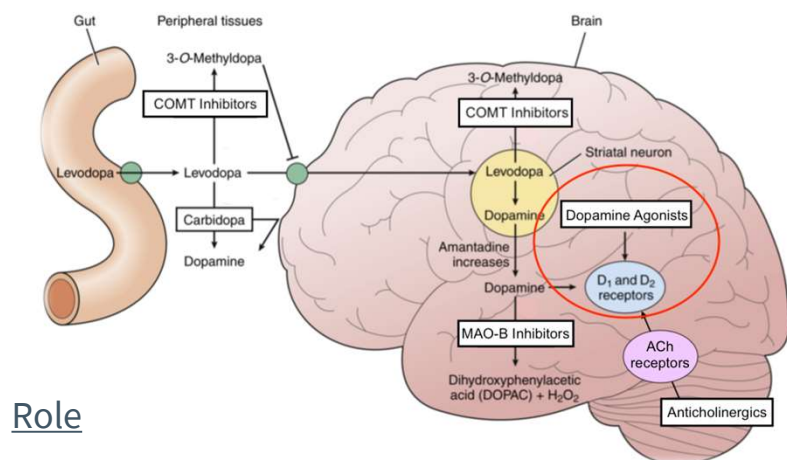
Antidepressants (SSRIs, tricyclics)  
Cyclobenzaprine (Flexeril)  
Tramadol, methadone, meperidine

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## Dopamine Agonists

- ▶ Ropinirole (Requip)
- ▶ Pramipexole (Mirapex)
- ▶ Rotigotine (Neupro) patch
- ▶ Mimic the effect of dopamine in the brain



### Role

- ▶ Used alone for mild symptoms
- ▶ Added to levodopa to reduce “off” time

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## Dopamine Agonists: Side Effects

- ▶ Similar to carbidopa/levodopa
  - ▶ Less common: dyskinesia
  - ▶ More common: daytime sleepiness, hallucinations, confusion (caution with older adults)
  - ▶ More common: Impulse control disorders (uncontrolled gambling, increased sexual urges, excessive eating and shopping, repetitive activities)

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## Dopamine Agonists: Other Tips

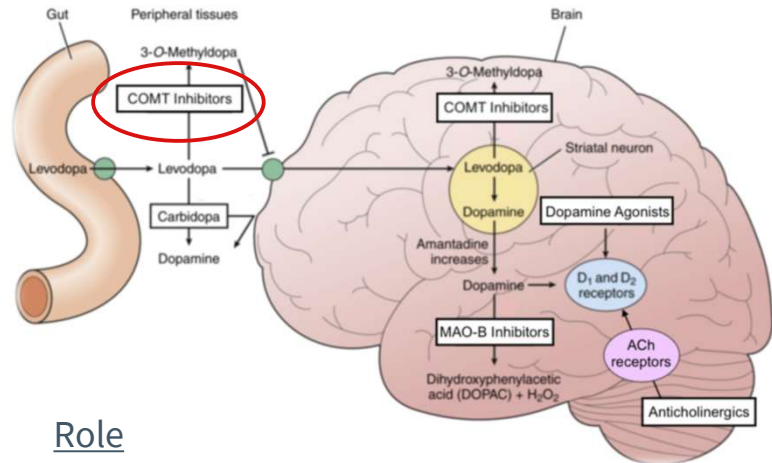
- ▶ Take consistently.
- ▶ Missing just once dose may lead to withdrawal symptoms such as anxiety, drug cravings, sweating, fatigue, low blood pressure, or pain.

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## COMT Inhibitors

- ▶ Entacapone (Comtan)
- ▶ Levodopa/carbidopa/entacapone (Stalevo)
- ▶ Opicapone (Ongentys)
  
- ▶ Blocks an enzyme (COMT) that deactivates levodopa in the blood stream before it gets to the brain



### Role

- ▶ Add to levodopa to reduce “off” time
- ▶ Never taken alone

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## COMT Inhibitors: Side Effects

- ▶ Minimal, but may intensify some levodopa-related side effects, particularly dyskinesia.

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## Amantadine

- ▶ Brand names: Osmolex ER, Gocovri
- ▶ Exact mechanism is unknown
- ▶ Likely impacts multiple neurotransmitters – including dopamine and glutamate – to achieve its benefits

### Role

- ▶ Added to levodopa to treat dyskinesia (most commonly)
- ▶ Can be used on its own in early disease

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## Amantadine: Side Effects

- ▶ Nausea
- ▶ Dry mouth
- ▶ Lightheadedness
- ▶ Insomnia
- ▶ Confusion
- ▶ Hallucinations
- ▶ Swollen feet
  
- ▶ Side effects can limit its long-term use and may be more bothersome in older adults

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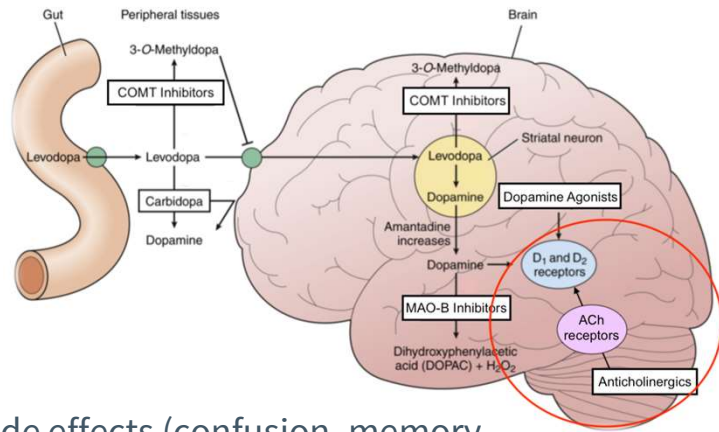
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## Anticholinergics

- ▶ Trihexyphenidyl
- ▶ Benztropine (Cogentin)
- ▶ Block acetylcholine receptors to restore the balance

### Role

- ▶ Limited due to significant side effects (confusion, memory impairment, dry mouth, urine retention, constipation)
- ▶ Mild relief for tremor



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## Drugs to AVOID in Parkinson's Disease

- ▶ Antipsychotics (e.g. haloperidol, risperidone, olanzapine)
  - ▶ Safe options: quetiapine, pimavanserin (Nuplazid), clozapine
- ▶ Antiemetics (e.g. promethazine, metoclopramide)
  - ▶ Safe option: ondansetron

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# Management of Non-Motor Symptoms

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## Managing Non-Motor Symptoms

### Constipation and feeling full or bloated

The GI tract slows down in PD.

Drink plenty of water and fluids.

Get regular exercise.

Includes lots of fiber in your diet (beans, whole grains, fruits, vegetables).

Polyethylene glycol (Miralax).

### Low blood pressure when standing (orthostatic hypotension)

Closely review medications that lower blood pressure.

May reduce dose of PD medications.

Change positions slowly.

Increase fluids and salt in diet if it is safe for you.

Wear compression socks.

Medications: fludrocortisone, midodrine

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## Managing Non-Motor Symptoms

### Mood: Depression and Anxiety

Under-recognized and have greatest impact on well-being.

Counseling (talk therapy plus medication is more effective)

Cognitive behavioral therapy

Exercise and mindfulness

Medications: Escitalopram, sertraline, duloxetine, venlafaxine, amitriptyline.

### Sleep Disorders

A sleep study can provide more info.

Restless leg syndrome (RLS):  
Dopamine agonist at night, carb/levo ER formulation, gabapentin

Insomnia: non-medication options, adjust PD meds if wearing off, antidepressants, melatonin

Excessive daytime sleepiness:  
selegiline, low-dose stimulants

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## Managing Non-Motor Symptoms

### Cognitive Impairment and Dementia

Thorough medical work up to assess other causes. Careful evaluation of medications for cause of symptoms.

Medications: rivastigmine, donepezil, galantamine

### Psychosis

20-40% will experience hallucinations or delusions.

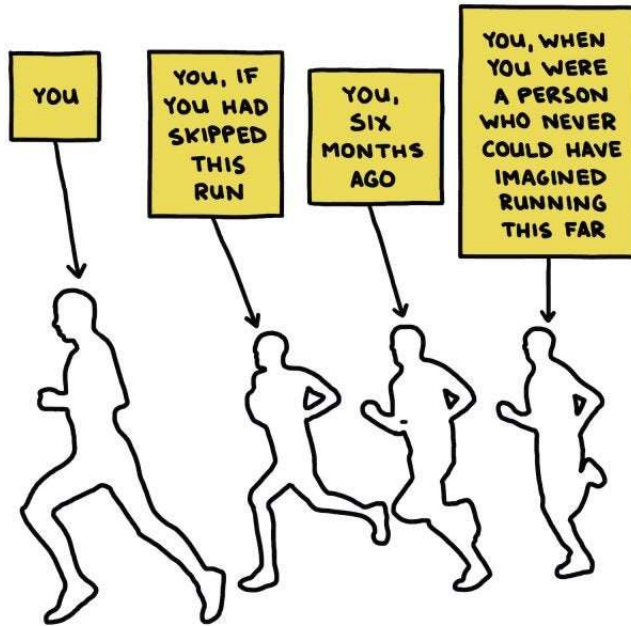
Evaluate PD medications especially if at higher doses.

Evaluate other medication causes.

If severe: quetiapine, pimavanserin, clozapine.

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# THANKS!

## Any questions?

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