



PARKINSON'S
ASSOCIATION OF SAN DIEGO

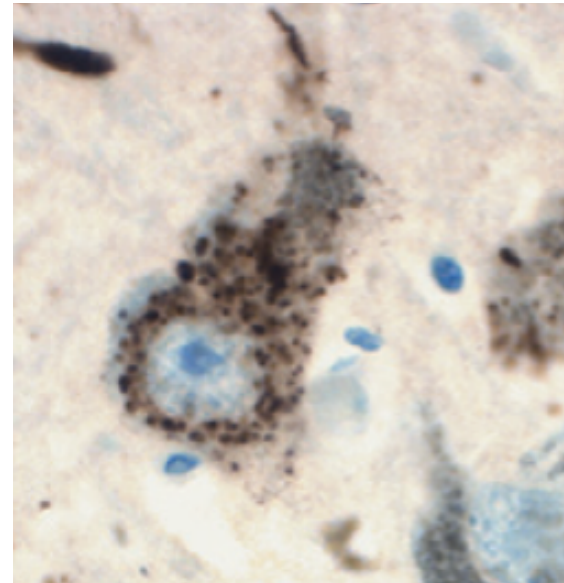
2018 Symposium: Empowerment Day for Parkinson's

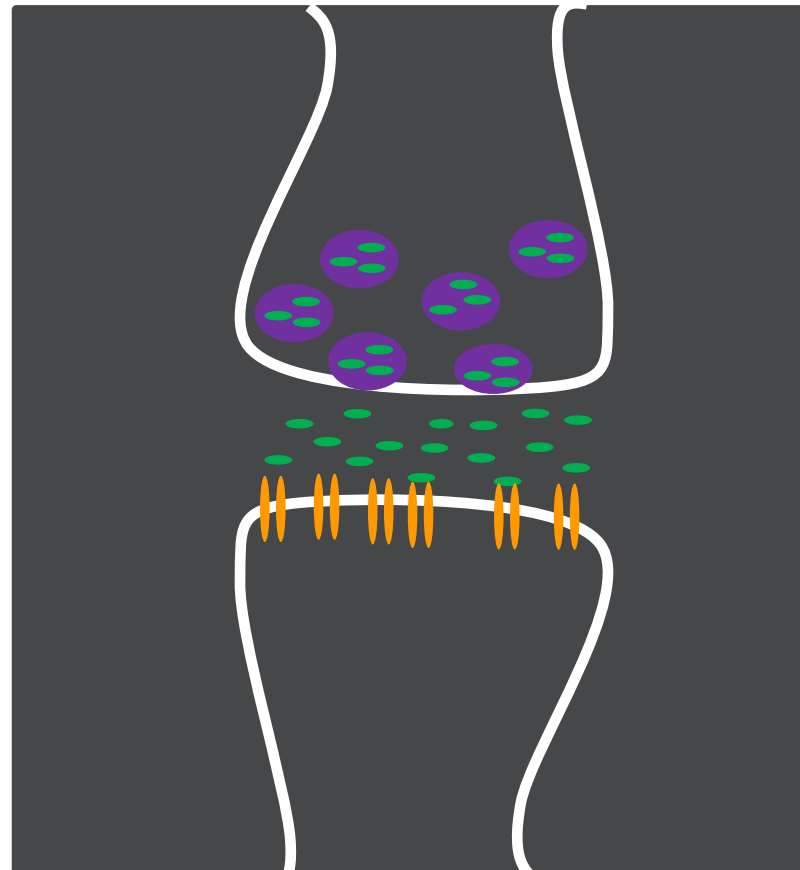
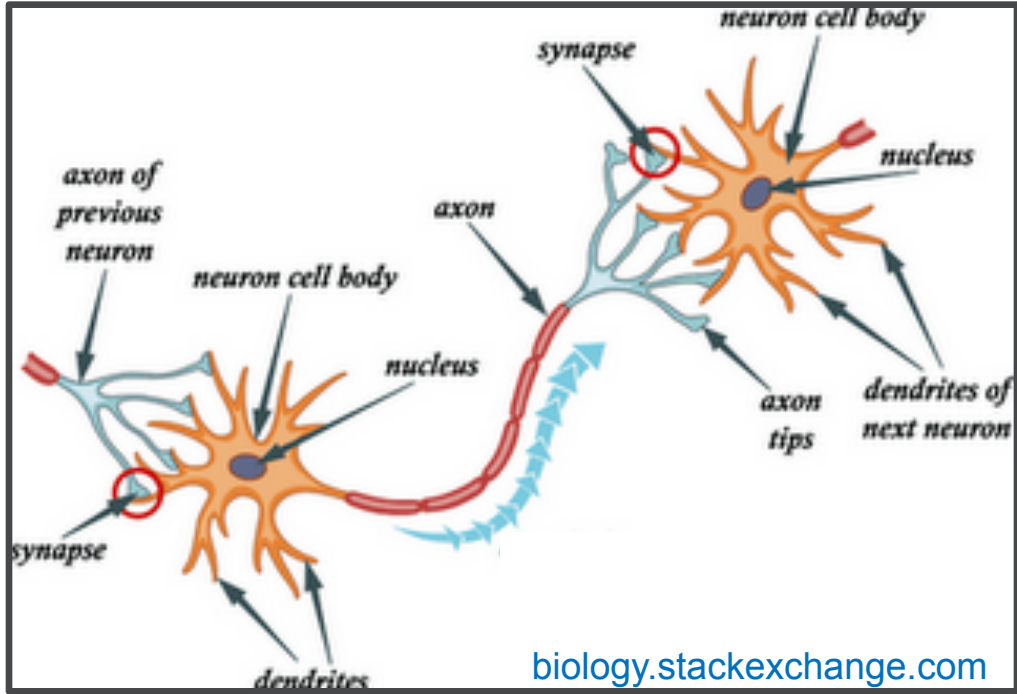
Medical Management of Motor Symptoms

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Disclosures - None



The primary pathologic event in Parkinson disease is loss of the dopamine neurons in the substantia nigra (SN_c), which send projections to the medium spiny neurons in the striatum





Dopamine Replacement Therapy:

carbidopa levodopa

- 25/100 mg  25/250 mg
- 10/100 mg 
 - Standard oral formulation (aka Sinemet®)
 - Oral dissolving tablets (aka Parcopa®)
- Usually taken a minimum of three times daily
- Possible side effects:
 - Nausea, abdominal discomfort, dyskinesias, dystonia, worsening of orthostatic hypotension, drowsiness, confusion, hallucinations, paranoia, rash

Carbidopa levodopa: What about the protein effect?

- Some patients with PD find that their levodopa works less effectively when they take it with food (especially protein) or on a full stomach
- However, only ~1/3 of PD patients have this!
- Don't arrange your life/meal schedule around dose times until you do some trial and error and find out if you are one of these patients
- Some patients become nauseated when taking their carbidopa levodopa on an empty stomach, but most do not have this problem

Remember, every person is different!

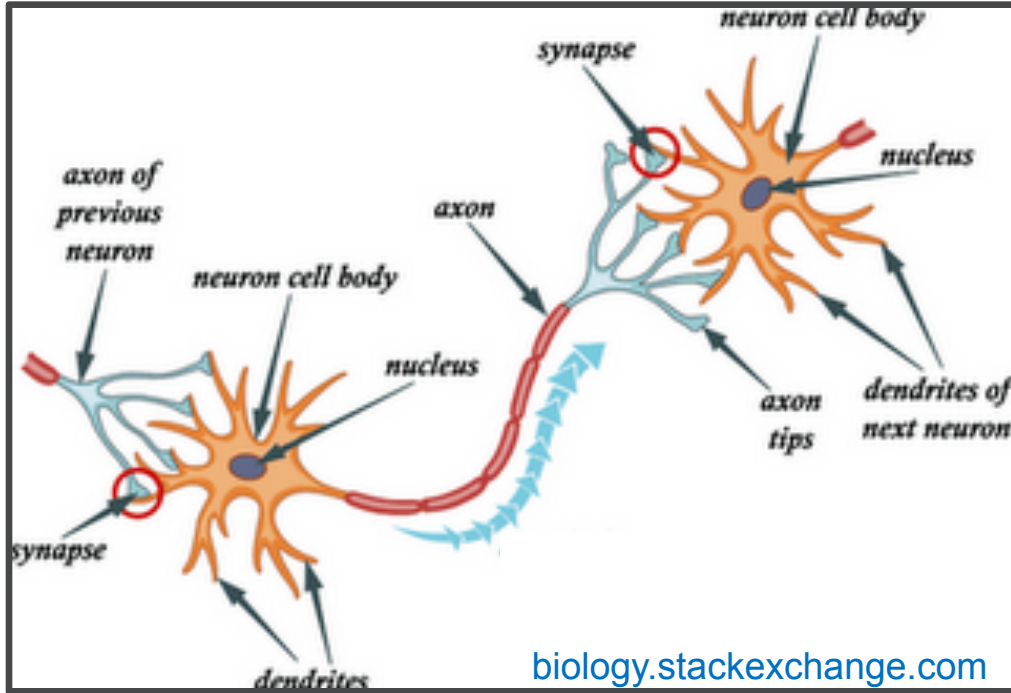
Dopamine Replacement Therapy: dopamine agonists

- **Pramipexole** (aka Mirapex®)
 - 0.125 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg ER:
0.375 mg, 0.75 mg, 1.5 mg, 2.25 mg, 3 mg, 3.75 mg, 4.5 mg
- **Ropinirole** (aka Requip®)
 - 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 5 mg ER: 2
mg, 4 mg, 6 mg, 8 mg, 12 mg
- **Rotigotine** (aka Neupro®) patch
 - 1 mg, 2 mg, 3 mg, 4 mg, 6 mg, 8 mg patches

Possible side effects:

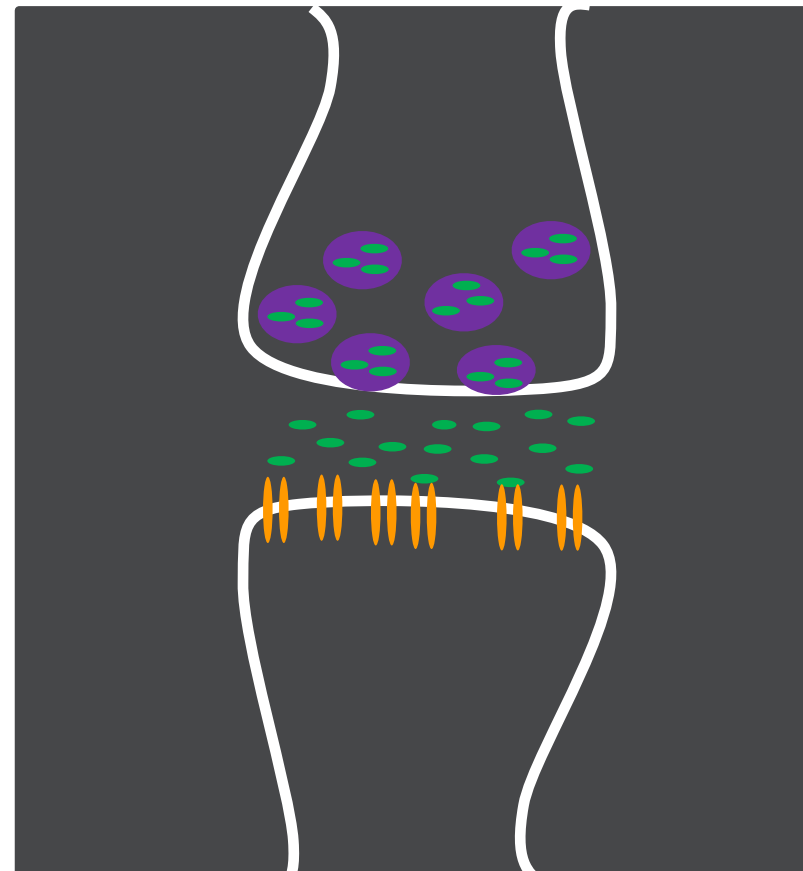
- **Worsening of orthostatic hypotension, drowsiness, confusion, hallucinations, impulse control disorders**, ankle swelling, paranoia, nausea, abdominal discomfort, dyskinesias, dystonia, rash, **withdrawal syndrome**

Why do PD patients develop “wearing off?”



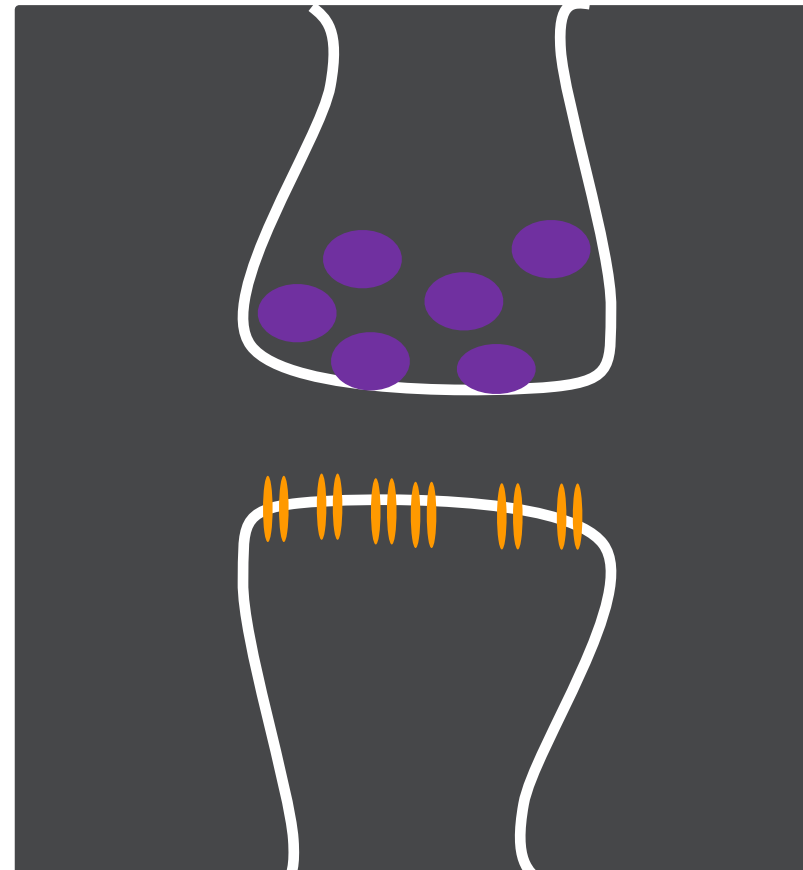
Dopamine neurons:

3-6 Hz tonic firing as well as phasic firing
in response to stimuli



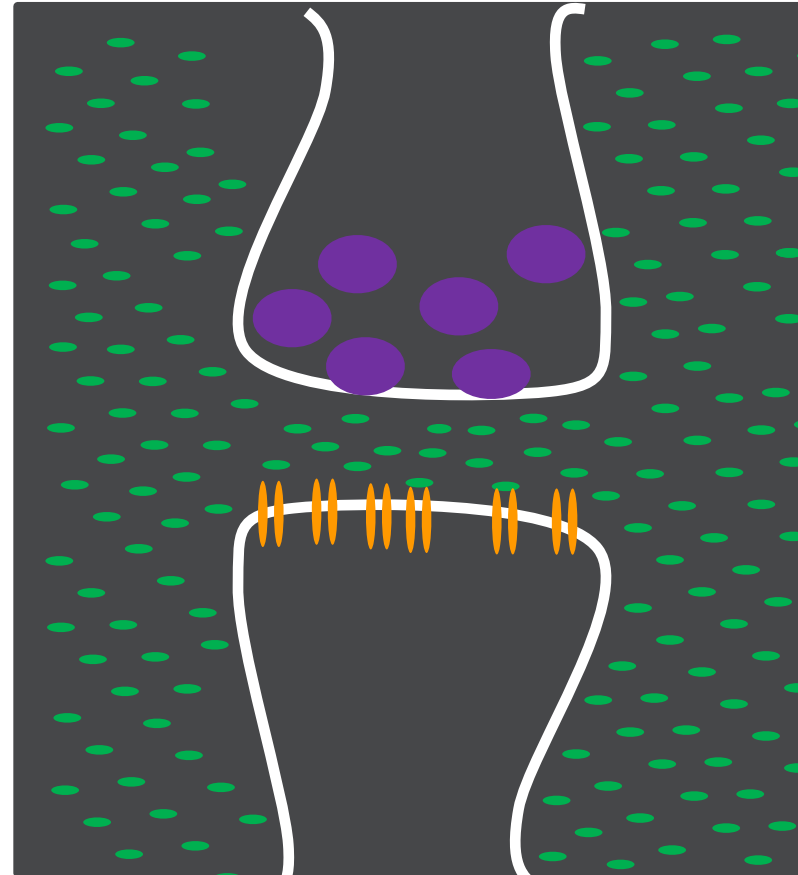
Early PD

- Remaining dopamine neurons are able to take up excess levodopa from the blood and store it as dopamine in the presynaptic terminals



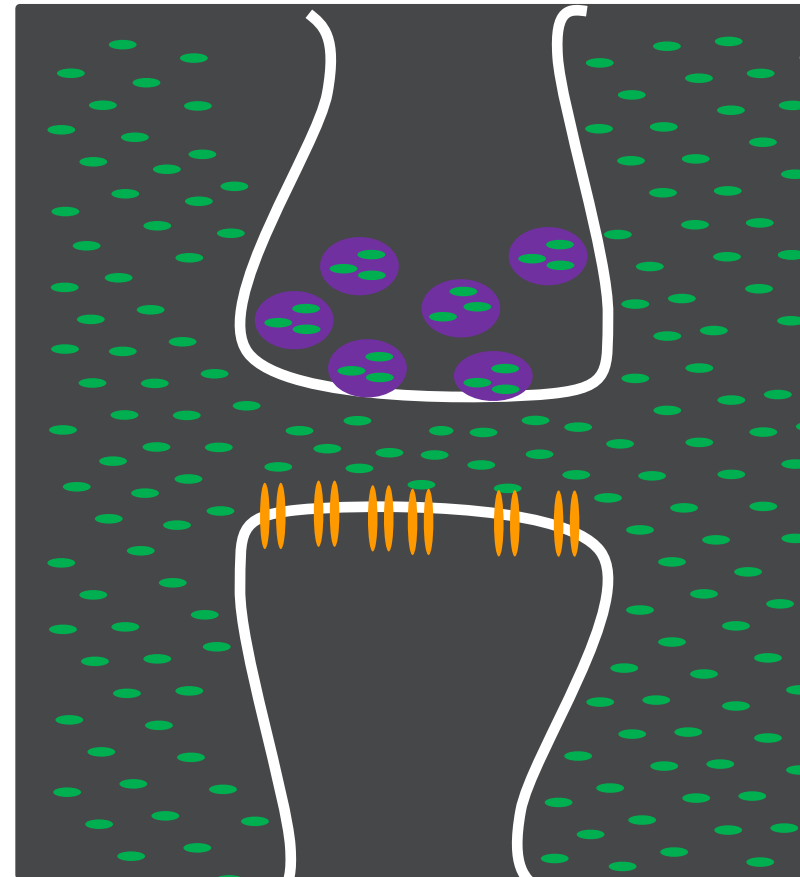
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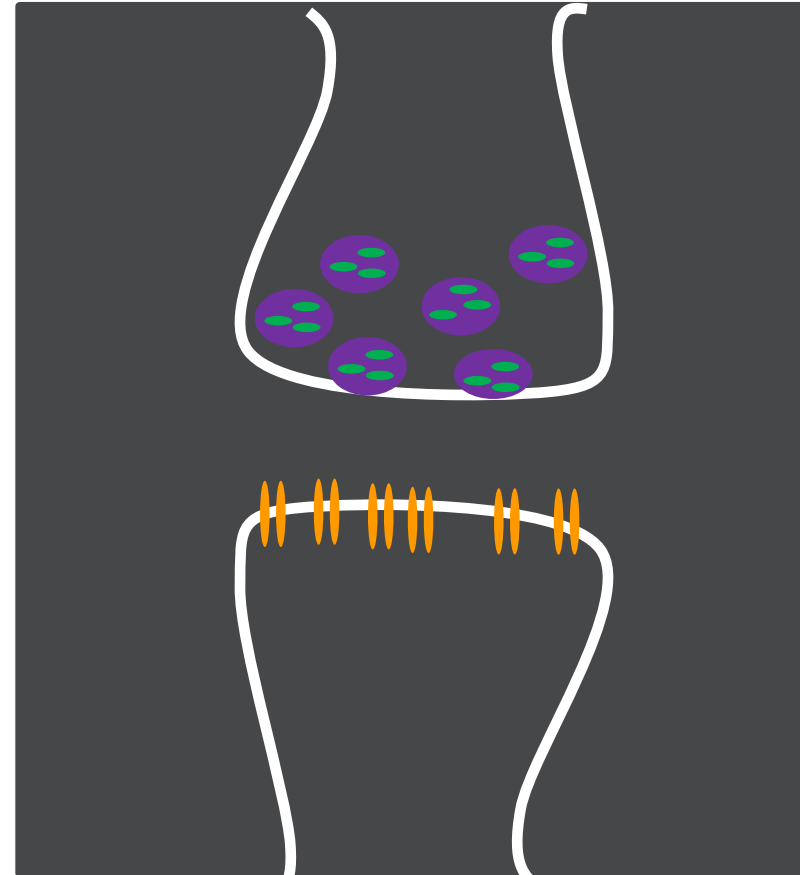
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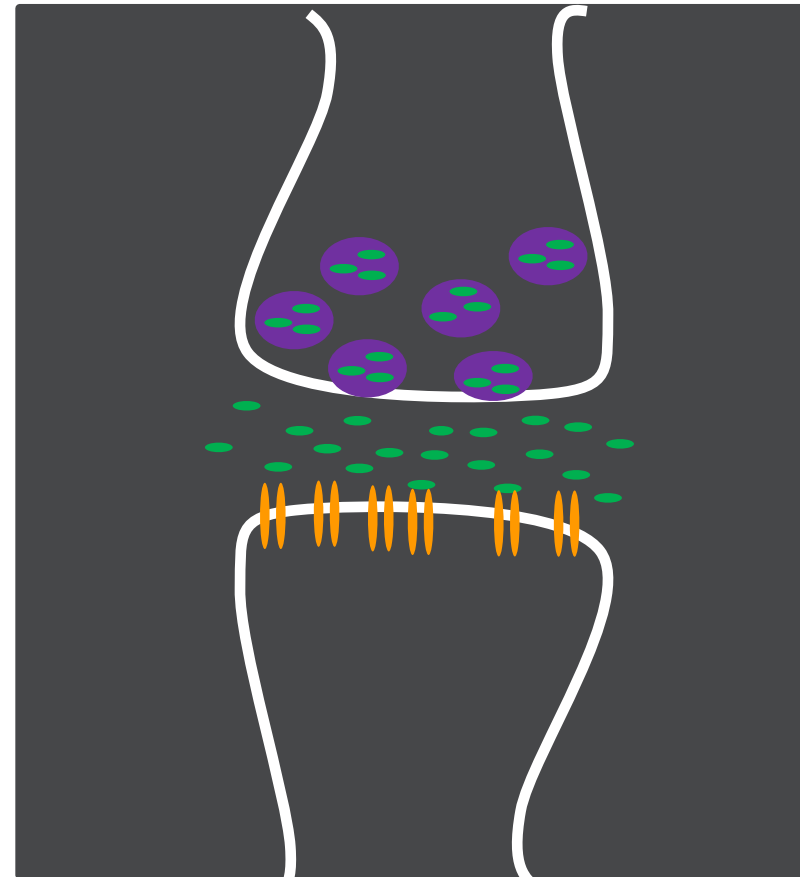
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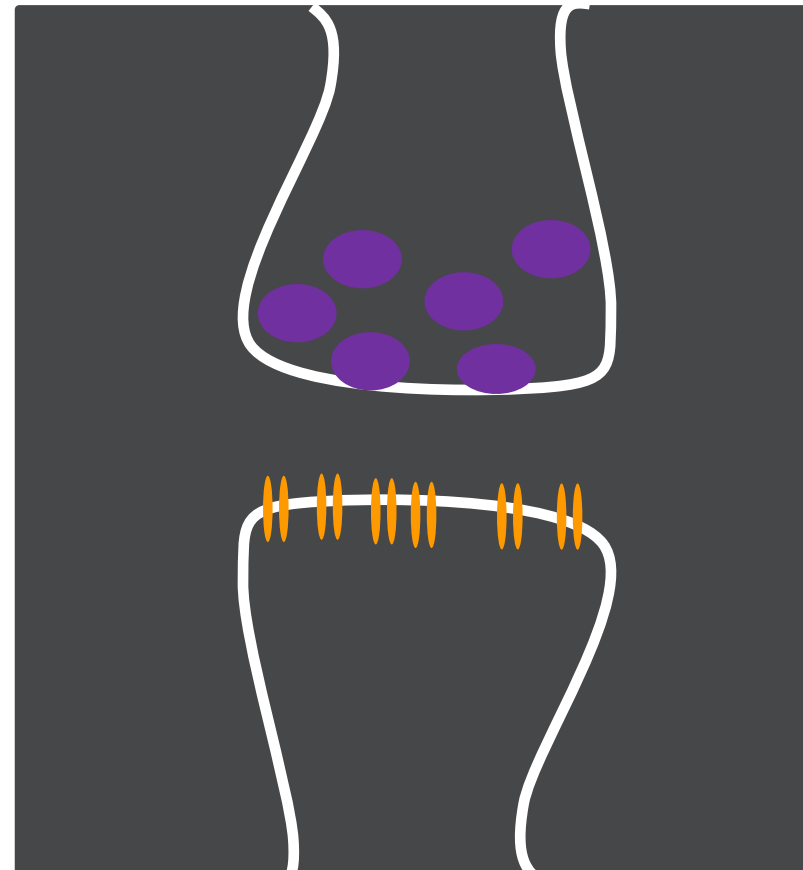
Early PD

- Dopamine concentration maintained at constant levels in part due to presynaptic storage of dopamine



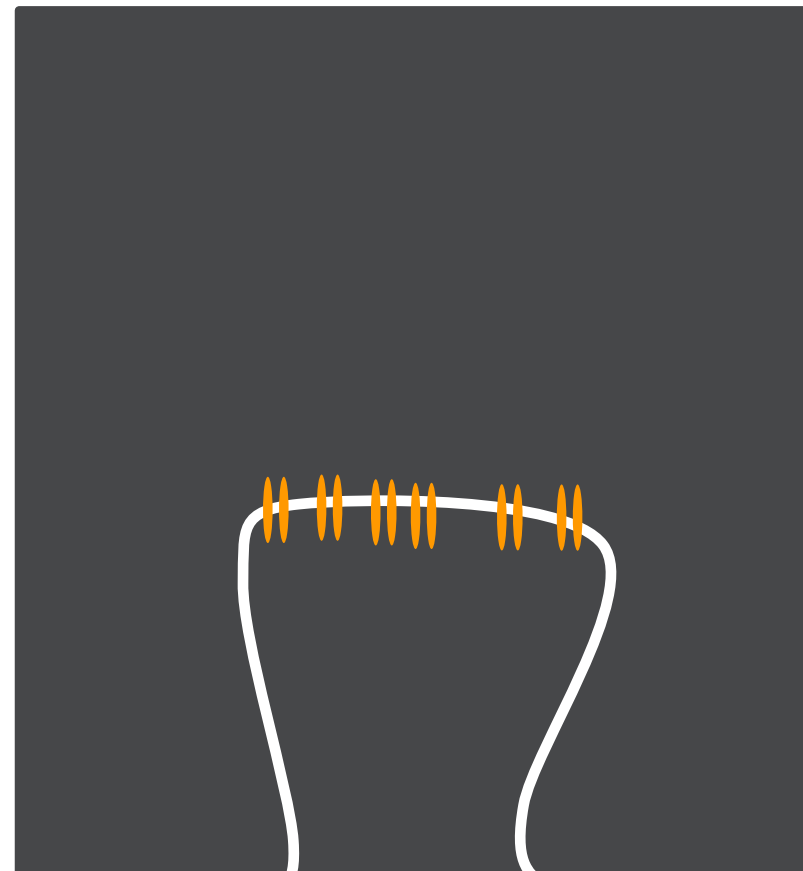
Later PD

- As more dopamine neurons are lost, the presynaptic stores of dopamine become depleted



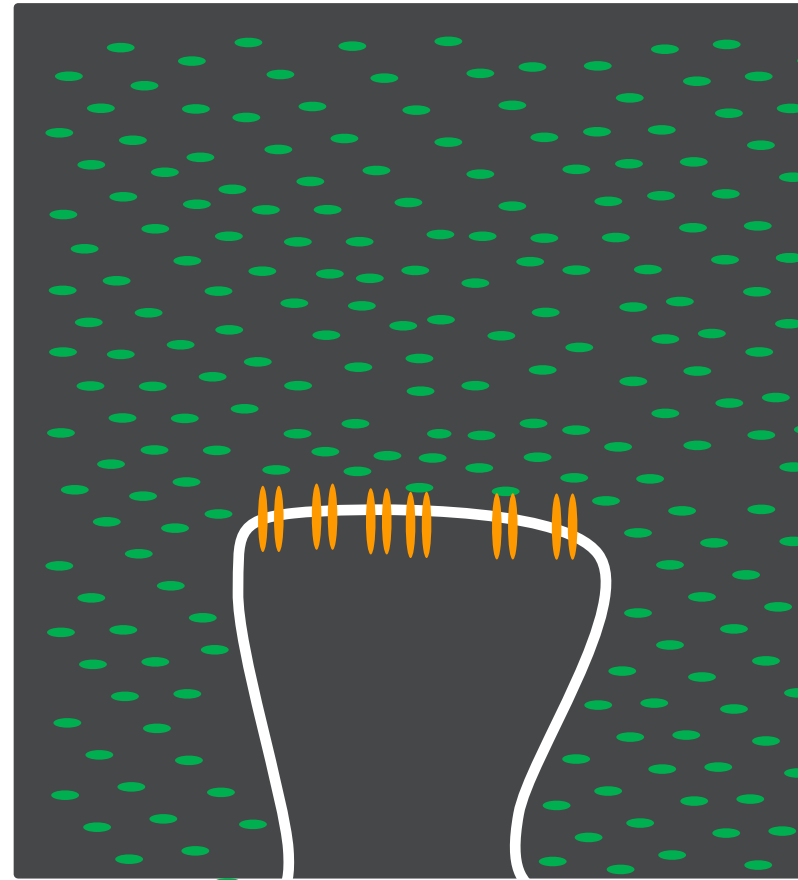
Later PD

- Postsynaptic concentration of dopamine in the striatum becomes closely linked to blood levels of levodopa



Later PD

- Postsynaptic concentration of dopamine in the striatum becomes closely linked to blood levels of levodopa
- Half life of levodopa in the blood: ~60-90 minutes



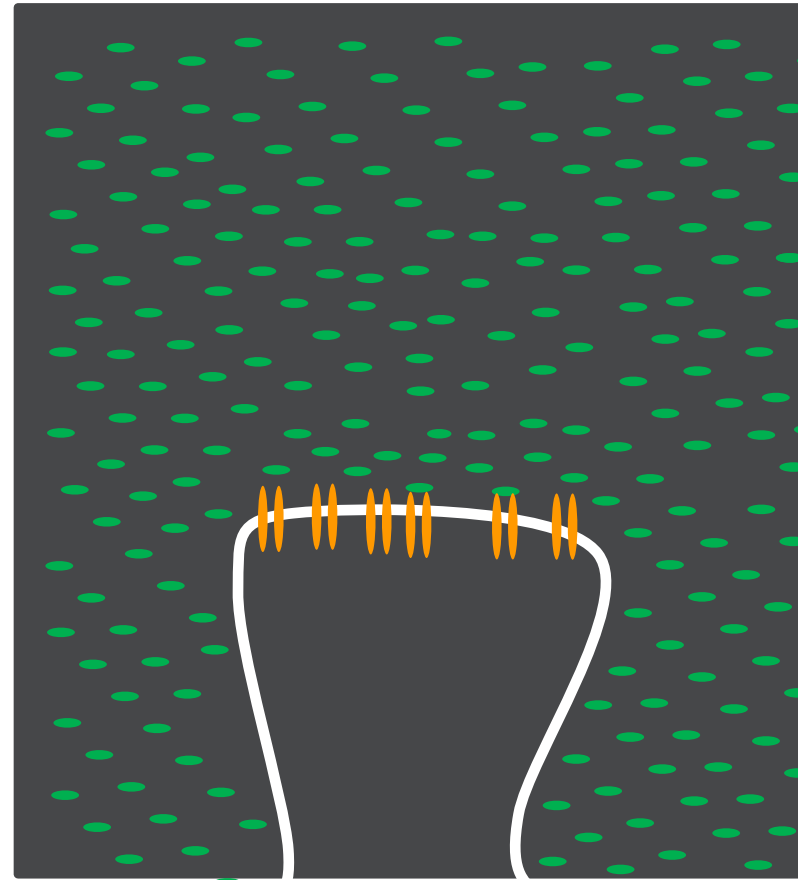
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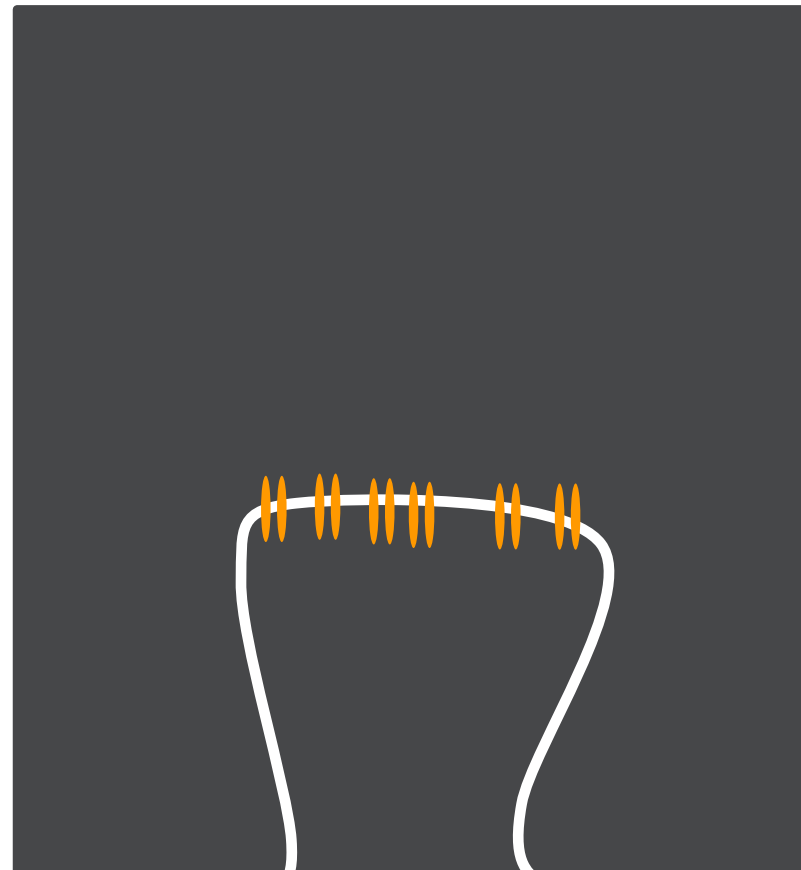
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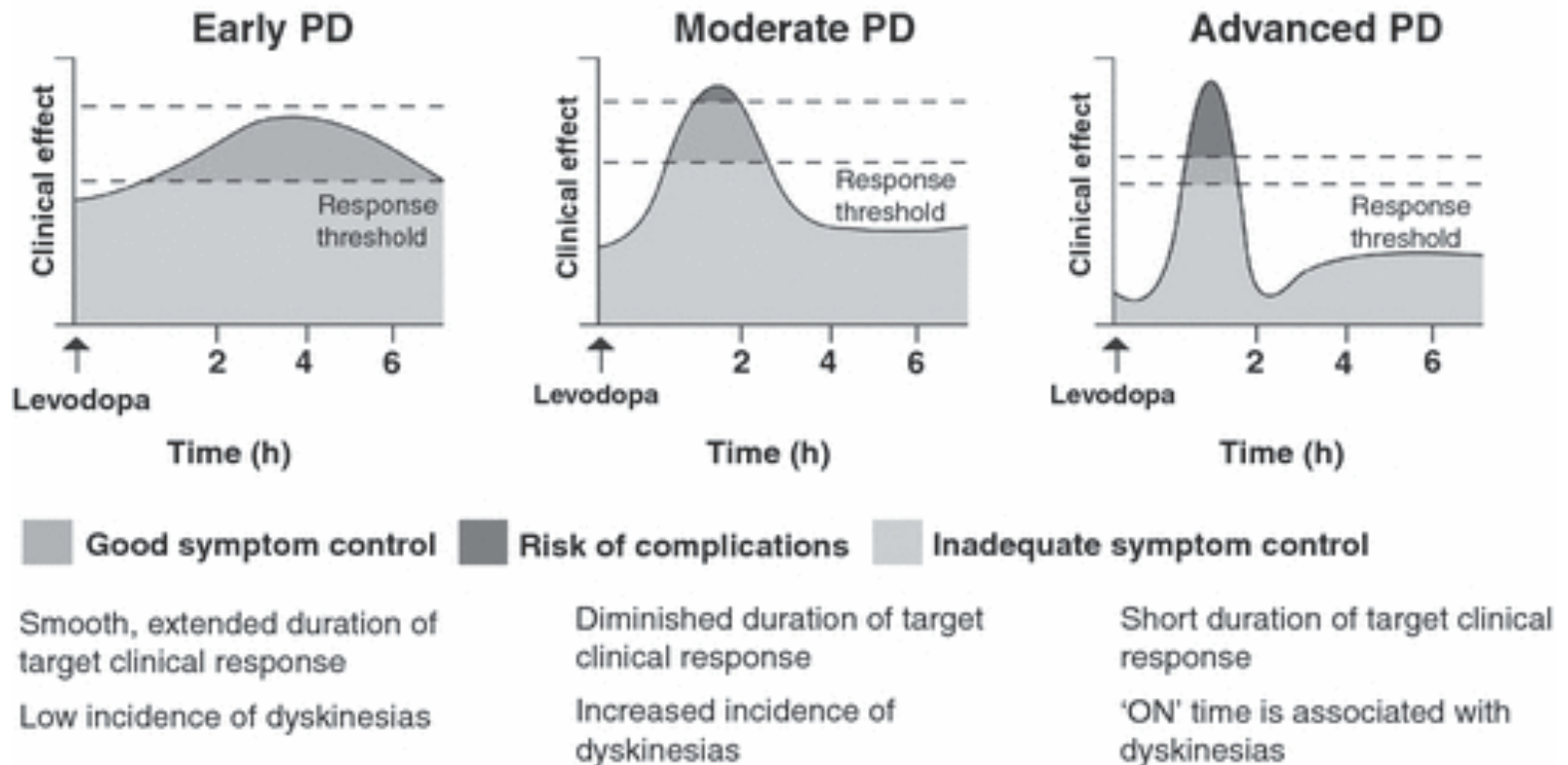


Later PD

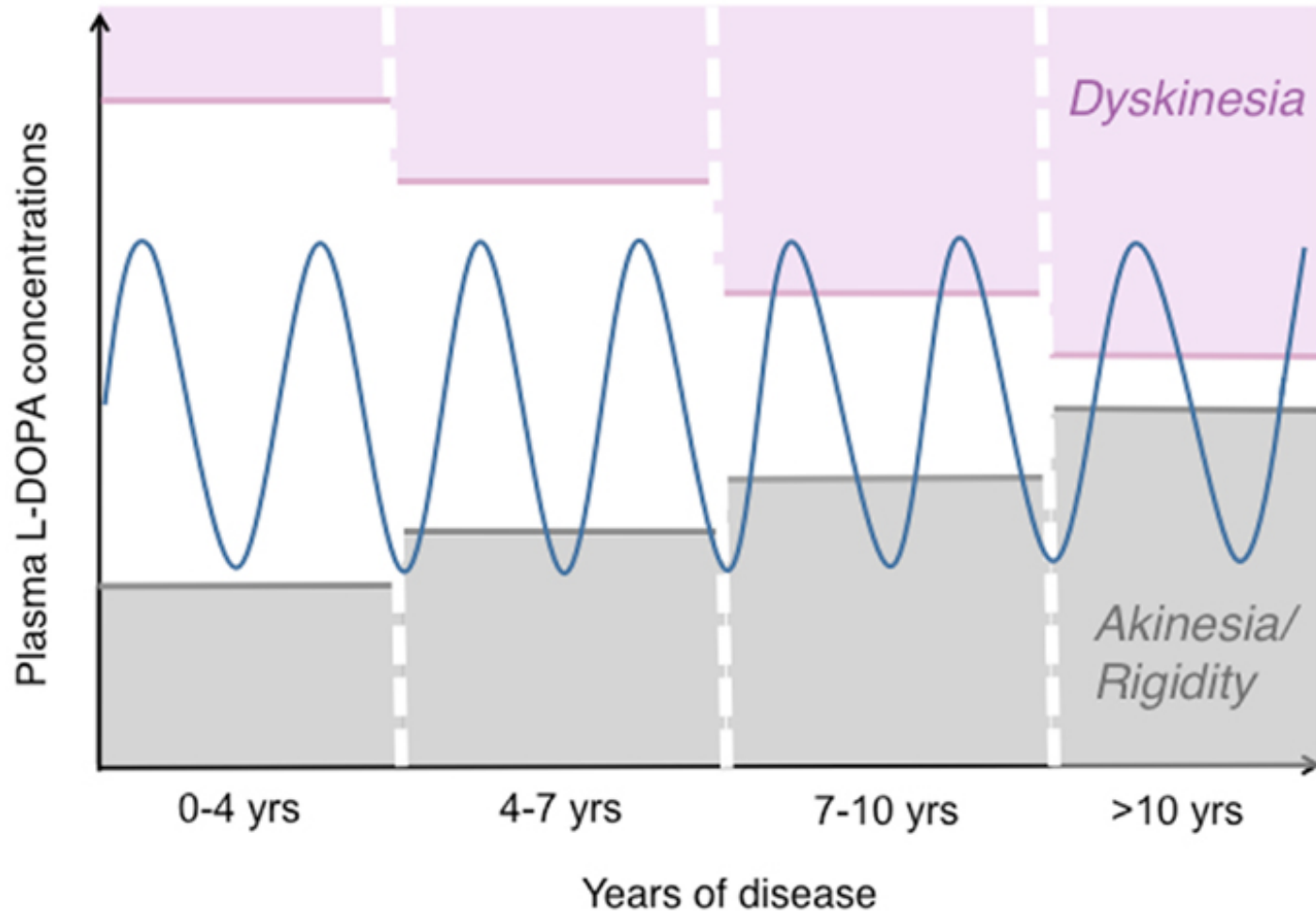
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Change in levodopa response over time



Schapira AH et al. *Eur J Neurol.* 2009;16(9):982-9.



Cenci MA. *Front Neurol.* 2014;15(5):424.

Adjunctive Medications for Motor Fluctuations

- Carbidopa levodopa ER 25/100 mg, 50/200 mg
- Pramipexole, Ropinirole, Rotigotine
- MAO-B inhibitors:
 - Rasagiline 1 mg (aka Azilect®)
 - Selegiline 5 mg twice daily
 - Safinamide (aka Xadago®) 50-100 mg daily

Adjunctive Medications for Motor Fluctuations

COMT inhibitors

- Entacapone (aka Comtan®)
 - 200 mg usually taken with each levodopa dose
 - Side effects: orange urine, diarrhea, rash, dyskinesias, other side effects of boosted levodopa dose
- Carbidopa-levodopa-entacapone (aka Stalevo®)
 - Combination tablet that comes in six different strengths
- Tolcapone (aka Tasmar®) 100 mg

Adjunctive Medications for Motor Fluctuations

Rytary®

- Capsule contains beads of both immediate release and extended-release carbidopa levodopa
- 23.75/95 mg, 36.25/145mg, 48.75/195 mg, 61.25/245 mg

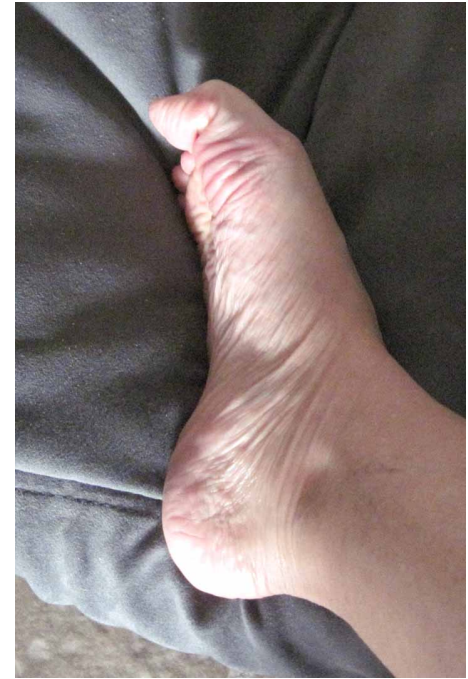
Others Medications

- **Amantadine** 100 mg one to three times daily
 - Suppresses dyskinesias, has modest effect on tremor, slowness, stiffness
- **Gocovri®** 137 mg, 274mg capsules, once daily
- **Osmolex ER®** 129mg, 193mg, 258 mg capsules – once daily
 - Extended release version of amantadine
- Anticholinergic drugs: **trihexyphenidyl, benztropine**
 - May help tremor and other motor symptoms of PD (particularly dystonia), but are almost always limited by side effects:

Side effects: dry mouth, worsened constipation, urine retention, dry eyes, confusion, forgetfulness, hallucinations, paranoia, drowsiness

Dystonia in PD

Botulinum toxin injections



Thank You!

