



PARKINSON'S DISEASE

SPOTLIGHT ON  
PARKINSON'S DISEASE:  
WHAT TO DO WHEN YOUR  
MEDICATIONS STOP WORKING

TUESDAY, APRIL 2, 2019

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WELCOME AND INTRODUCTIONS



**Stephanie Paul**

*Senior Vice President Development and Marketing*  
American Parkinson Disease Association

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## PRESENTATION



**Un Jung Kang, MD**  
*Founders Professor of Neurology*  
*Director of Translational Research*  
The Marlene and Paolo Fresco Institute for  
Parkinson's and Movement Disorders  
NYU Langone Health  
New York, NY

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## FINANCIAL DISCLOSURES

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**Consultant: None**

**Speakers Bureaus: None**

**Equity: None**

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## COMMON MISCONCEPTION ABOUT PD MEDICATIONS

Do medications stop working after a few  
years?

- Should I save the medications for later  
when I need them more?

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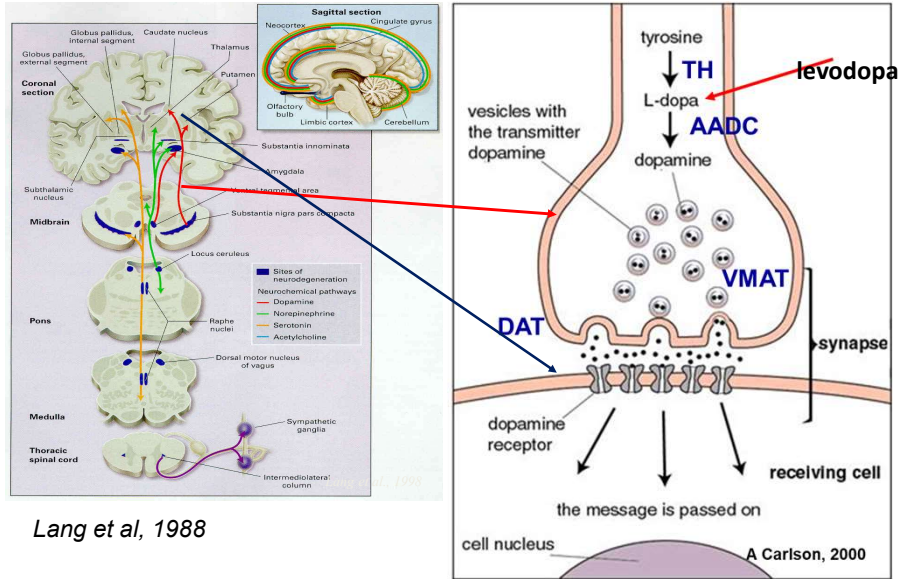
## WE WILL DISCUSS

- What the current medications are  
addressing
  - How do they work?
  - What symptoms do they treat?
- Limitations of the current medications
- How to address the symptoms not treated  
by the current medications

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## LEVODOPA REPLACES DOPAMINE IN THE BRAIN



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## WHAT PROBLEMS DO THE CURRENT DOPAMINE MEDICATIONS ADDRESS?

	Helped by DA meds	Limited benefit from DA meds
<b>Motor symptoms</b>	rest tremor, bradykinesia, rigidity, gait problems	rest tremor, speech problems, gait problems, freezing
<b>Non-motor symptoms</b>	learning, other symptoms (to be discussed)	cognitive deficit, apathy, depression, anxiety, fatigue, sleep, autonomic symptoms (constipation, sexual, urinary dysfunction, orthostatic hypotension), pain and sensory disturbances

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## WHAT DOES IT MEAN WHEN MEDICATION IS NOT WORKING?

When you first start medications:

After several years:

Reevaluation of medication response:

## WHAT DOES IT MEAN WHEN MEDICATION IS NOT WORKING?

When you first start medications:

- No response
  - Insufficient dose
  - Insufficient duration
- Inadequate response
  - Limited by side effects



## WHAT DOES IT MEAN WHEN MEDICATION IS NOT WORKING?

When you first start medications:

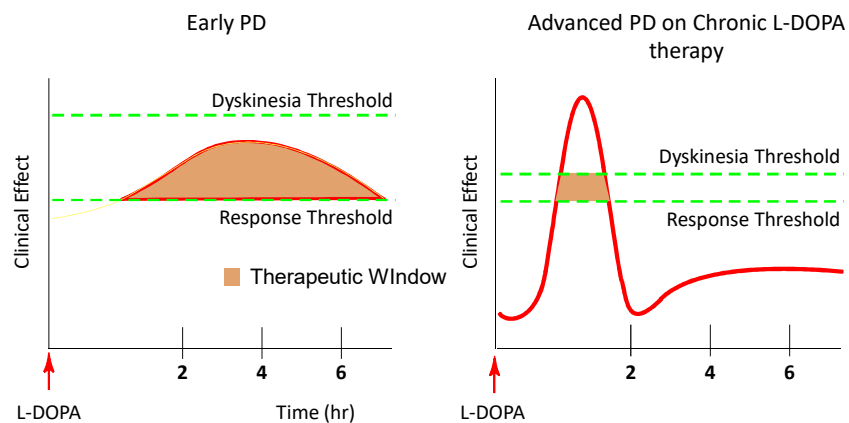
After several years:

- Dose failures
- Motor response fluctuations
  - “Wearing-off”
  - Sudden “off”
  - Levodopa-induced dyskinesias

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## MOTOR RESPONSE COMPLICATIONS IN ADVANCED PD PATIENTS AFTER CHRONIC L-DOPA THERAPY



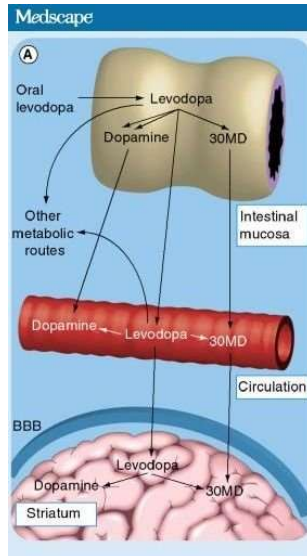
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## MAKING SURE LEVODOPA GETS TO THE BRAIN



Seeberger & Hauser, *Expert Rev Neurother.* 2009

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## NEW DELIVERY METHODS TO BYPASS GUT

### Quicker delivery

1. Sublingual orally disintegrating tablet  
Carbidopa/Levodopa (Parcopa)
2. Inhalation  
Levodopa powder (Inbrija)
3. Subcutaneous injection  
Apomorphine (Apokyn)

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## NEW DELIVERY METHODS TO BYPASS GUT

### Quicker delivery

1. Sublingual orally disintegrating tablet
2. Inhalation
3. Subcutaneous injection

### More sustained delivery

1. Transdermal preparation  
rotigotine (Neupro)
2. Subcutaneous injection pump  
apomorphine (Apokyn)



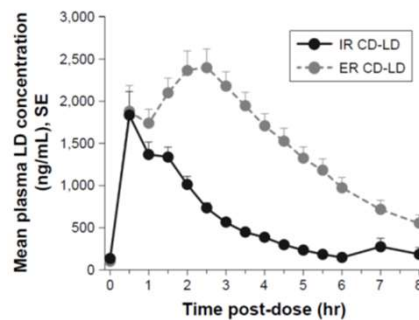
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## HOW TO MAKE LEVODOPA AND DOPAMINE LAST LONGER

### Longer acting levodopa preparations

- Sustained release oral medication (CR, ER, Rytary)
- Duodenal infusion (Duopa)



Hasuer et al., *Neuropsych Dis Treat.* 2018

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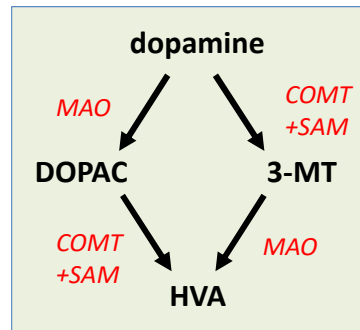
## HOW TO MAKE LEVODOPA AND DOPAMINE LAST LONGER

### Longer acting levodopa preparations

- Sustained release oral medication (CR, ER, Rytary)
- Duodenal infusion (Duopa)

### DA metabolism inhibitors:

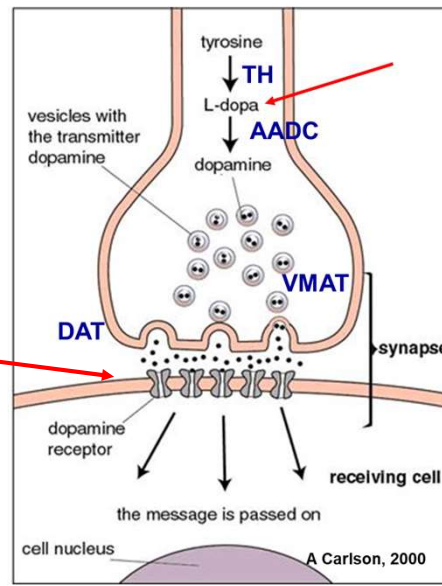
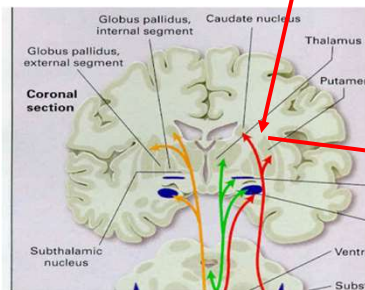
- MAO inhibitors: rasagiline (Azilect), selegiline, safinamide (Xadago)
- COMT inhibitors: entacapone (Comtan, Stalevo), tolcapone (Tasmar)



## HOW TO MAKE LEVODOPA AND DOPAMINE LAST LONGER

### Dopamine agonists:

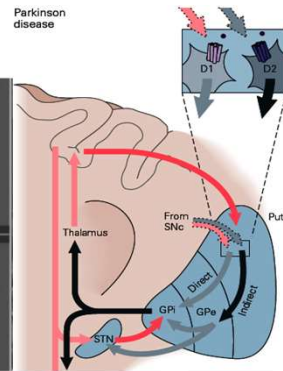
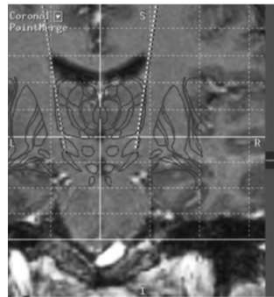
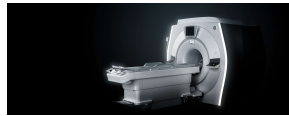
- (longer half-life)  
Pramipexole (Mirapex, ER),  
ropinirole (Requip, XL),  
rotigotine (Neupro)





## MODULATION OF NEURONS TO MAKE LEVODOPA WORK BETTER

Lesions (thalamotomy, pallidotomy)  
Deep brain stimulation (STN, Gpi)  
Focused ultrasound



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## COMMON MISCONCEPTION ABOUT PD MEDICATIONS

Do medications stop working after a few years?

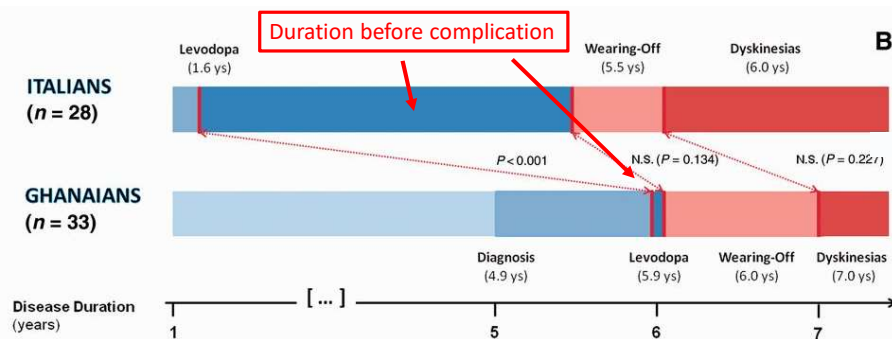
- Should I save the medications for later when I really need them?

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## MOTOR RESPONSE COMPLICATIONS: DISEASE OR MEDICATION

The modern pre-levodopa era of Parkinson's disease: insights into motor complications from sub-Saharan Africa



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## WHAT DOES IT MEAN WHEN MEDICATION IS NOT WORKING?

When you first start medications:

After several years:

Reevaluation of medication response:

- Symptoms that used to respond to medication do not respond anymore.
- Symptoms that never or partially responded to dopaminergic medications become more noticeable.

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## LIMITATIONS OF DOPAMINE MEDICATIONS

	DA medication related	Limited benefit from DA meds
<b>Motor symptoms</b>	Motor response complications: wearing-off, dyskinesia	speech problems, gait problems, freezing, tremor
<b>Non-motor symptoms</b>	Non-motor fluctuations, impulse control disorders, hallucination	cognitive deficit, apathy, depression, anxiety, fatigue, sleep, autonomic symptoms (constipation, sexual, urinary dysfunction, orthostatic hypotension), pain and sensory disturbances

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## NEW APPROACHES FOR TREATING PD

### Non-dopaminergic medications to improve symptoms

- Symptomatic treatments for non-motor symptoms
- New approaches for med-resistant motor symptoms
  - Cholinergic
  - Glutamatergic
  - Novel brain modulation

### Disease modification

- Exercise
- Isradipine
- Alpha-Synuclein antibodies
- Exenatide, nilotinib, c-abl inhibitors

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## WE DISCUSSED

- What the current medications are addressing
  - Most of the current medications are dopaminergic and treat motor deficits
- Limitations of the current medications
  - Motor response fluctuations
  - Non-motor symptoms are not fully addressed
- How to address the symptoms not treated by the current medications
  - Non-DA medications, Disease modification therapy

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## QUESTION & ANSWER



**Un Jung Kang, MD**

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## CLOSING REMARKS



**Stephanie Paul**  
*Senior Vice President Development and Marketing*  
American Parkinson Disease Association

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**FOR ADDITIONAL INFORMATION,  
ANSWERS TO YOUR QUESTIONS,  
OR FOR ADDITIONAL RESOURCES**

Please visit our website  
**[apdaparkinson.org](http://apdaparkinson.org)**

Or call us  
**1-800-223-2732**

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