

# Parkinson's Disease in 2022



Fundamentals and Updated Options



# INOVA<sup>®</sup> | Parkinson's and Movement Disorders Center

## Introducing our Team

From left to right:

Dr. Hannah Walters

Sonia Gow

Dr. Drew Falconer

Dr. Mahesh Shenai

Dr. David Whitney

Dr. Sean Rogers





# INOVA<sup>®</sup> | Parkinson's and Movement Disorders Center

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on all of our center's offerings!  
Join our newsletter!

**[Sonia.Gow@inova.org](mailto:Sonia.Gow@inova.org)**

703-375-9987

[www.inova.org/move](http://www.inova.org/move)





# INOVA<sup>®</sup> | Parkinson's and Movement Disorders Center

## 4 locations across Northern Virginia

### Alexandria

1500 N. Beauregard Street, Suite 300  
Alexandria, VA 22311

### Fairfax

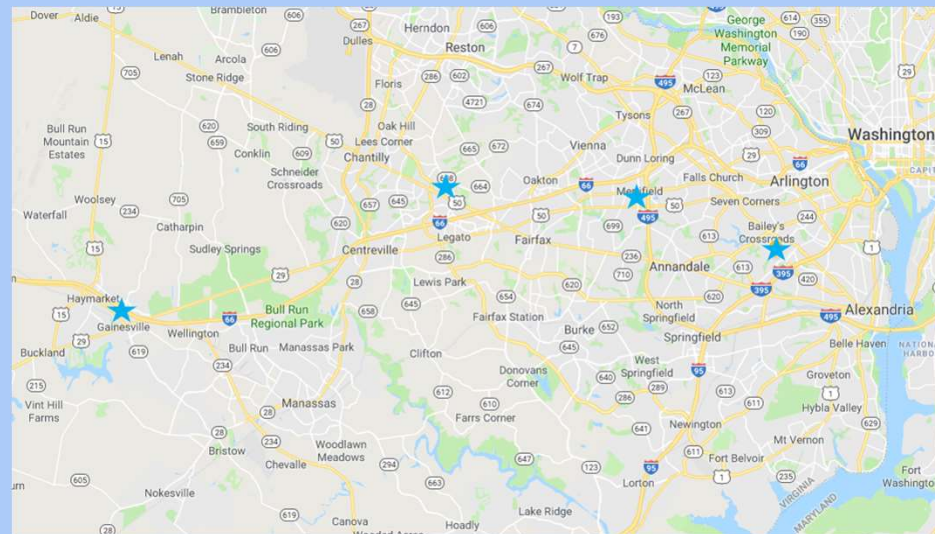
8081 Innovation Park Dr., #900  
Fairfax, VA 22031

### Fair Oaks

3580 Joseph Siewick Dr., Suite 206  
Fairfax, VA 22033

### Gainesville

7051 Heathcote Village Way, Suite 230  
Gainesville, VA 20155



[www.inova.org/move](http://www.inova.org/move)

# WHAT'S ON TAP?

- Laying the groundwork. How should we think about Parkinson's?
- Basics of treatment and medication.
- Better tools - updated medications.
- To the future!

# WHAT IS PARKINSON'S?

PARKINSON'S DISEASE AFFECTS **ONE IN 100 PEOPLE OVER AGE 60**. IN THE UNITED STATES, 60,000 NEW CASES WILL BE DIAGNOSED THIS YEAR ALONE.

**1** / 100  
OVER  
AGE 60



**1M** / US



**5M** / WORLD

TODAY, AN ESTIMATED **ONE MILLION** PEOPLE IN THE UNITED STATES AND MORE THAN **FIVE MILLION** WORLDWIDE ARE LIVING WITH PARKINSON'S DISEASE.

THERE IS  
**NO TEST**

TO DIAGNOSE  
PARKINSON'S DISEASE.  
PEOPLE WITH PARKINSON'S  
VISIT MULTIPLE DOCTORS  
AND **CAN WAIT YEARS**  
BEFORE A CORRECT  
DIAGNOSIS.



PARKINSON'S DISEASE IS CAUSED BY THE  
DEATH OF DOPAMINE CELLS.

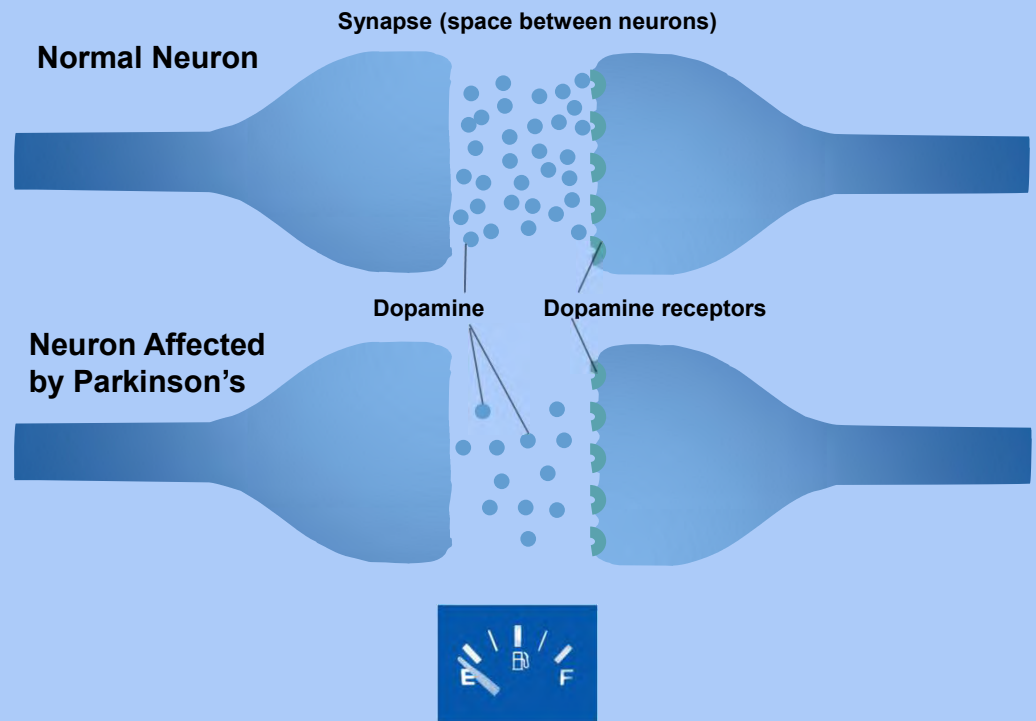
**60 TO 80%**

OF THESE CELLS ARE ALREADY LOST BY  
THE TIME MOTOR SYMPTOMS APPEAR.



# THE CAUSE?

- Just a dopamine deficiency!
- Genetics
  - Classically NOT inherited
- Environmental factors
  - Pesticides including Agent Orange
  - Well water
  - Heavy metal exposure
  - Chemical exposure
  - Head injury



# HOW DO WE DIAGNOSE PARKINSON'S?

- Symptoms/History/Exam + Response to Medications +/- DaTscan

- DaTscan

- Dopamine Active Transporter
- PET scan of brain highlighting dopamine transport system
- Tool to help with grey area
- FDA approved since 2010, covered by most insurers



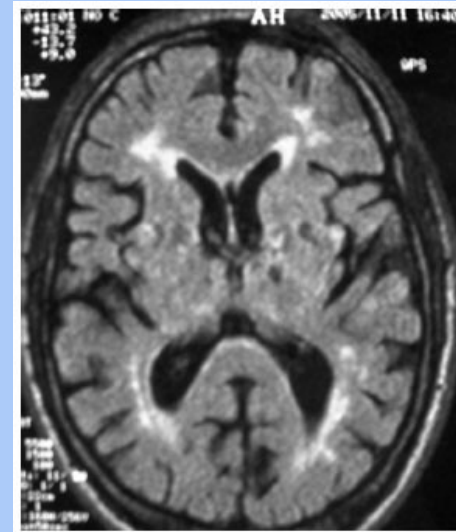
Neurology Journal 2014:

Accurate diagnosis even by a “Fellowship Trained Specialist”: 85% accuracy



# MIMICKERS OF PARKINSON'S – “PARKINSONISM”

- Syndromes that can look like Parkinson's Disease, but do not respond significantly to DOPAMINE
  - Parkinson-isms, including the following:
    - Vascular Parkinson's
    - Medication-induced Parkinson's
    - Parkinson's Plus Syndromes
      - Multisystem Atrophy
      - Progressive Supranuclear Palsy
      - Corticobasal Degeneration



**Proper diagnosis is key to proper treatment**

# WHAT HAPPENS IF YOU HAVE REDUCED DOPAMINE?

## ■ Motor and Non-motor Symptoms

- Systems which function inapp...  
in Dopamine or one of its by

## ■ Motor Symptoms

- Resting tremor
- Tremor with position
- Bradykinesia (slowness)
- Rigidity (stiffness)
- Slow walking, shuffle, reduce
- Balance issues
- Reduced facial expression (f
- Speech changes (hypophonia)



Parkinson's in 2022

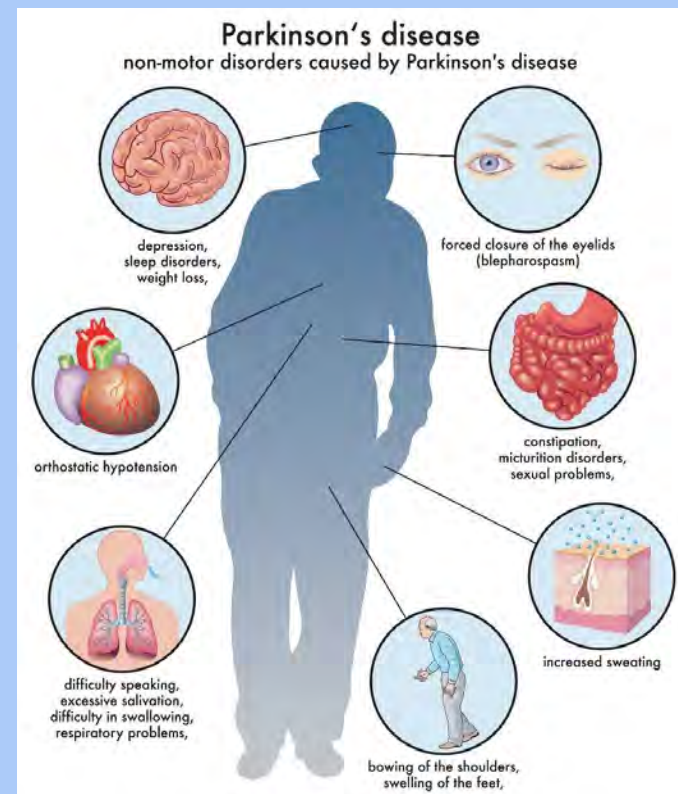


William Richard Gowers, 1886

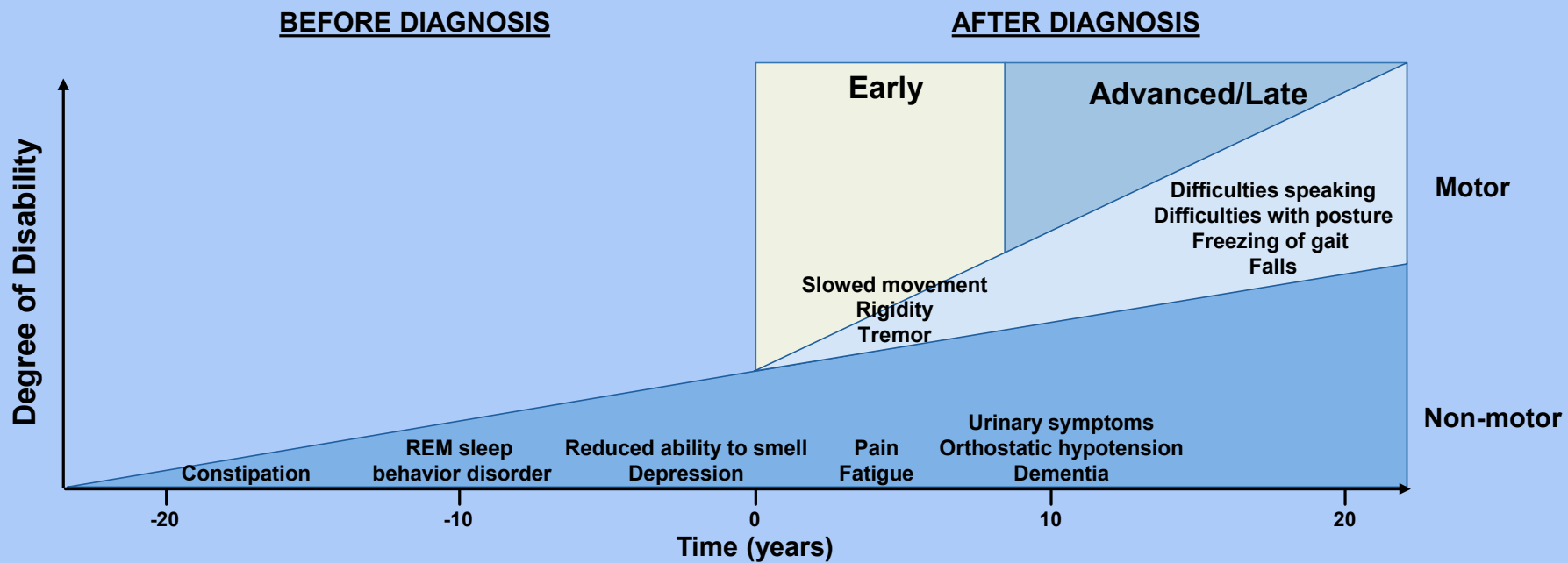
# NON-MOTOR SYMPTOMS

**\*\*Can present years before diagnosis\*\***

- Loss of sense of smell
- Constipation
- Talking in sleep or acting out dreams
- Anxiety/Depression
- Bladder issues
- Excessive saliva/drooling
- Vision changes
- Problems sweating
- Lightheadedness/Dizziness on standing
- Fatigue
- Skin problems
- Cognitive changes



# PARKINSON'S CHANGES OVER TIME

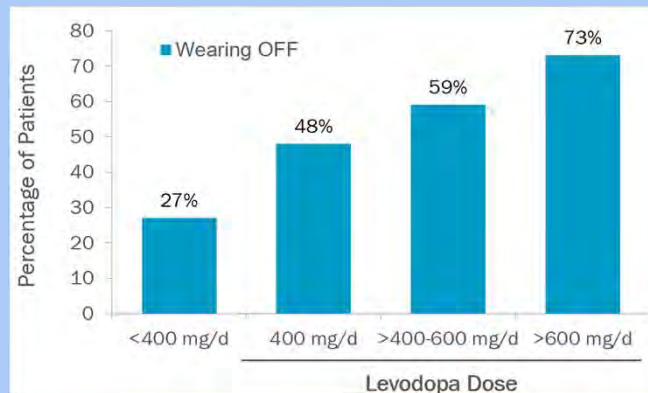


# OFF TIME – THE ENEMY

## ■ Medication problem?

- First AM off
- End of dose
- Sub-optimal on
- Sudden off
- Dose failure
- Exercise-induced
- Food-induced

## ■ Motor and non-motor OFF



Online survey of 3,000+

**70%** reported 2+ Off episodes a day.

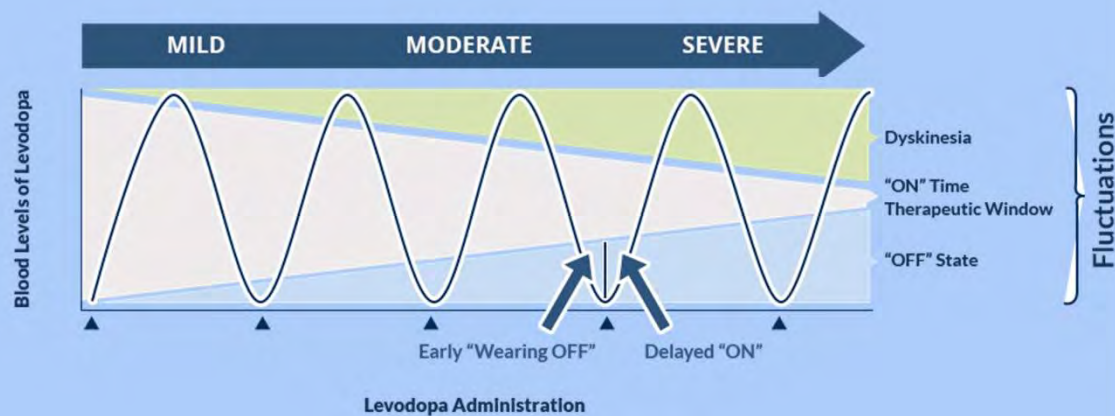
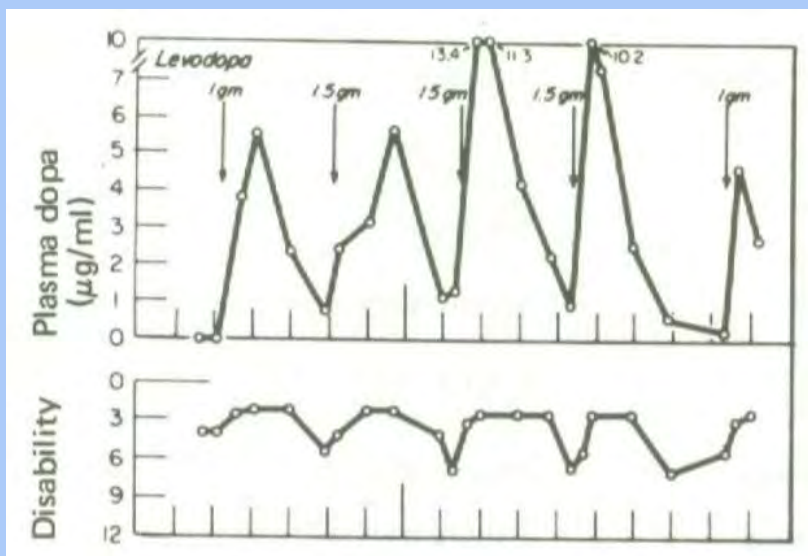
**65%** reported 2 or more hours a day

**50%** - moderate/severe, affected daily activities

**If we fix OFF, we fix Parkinson's Disease.**

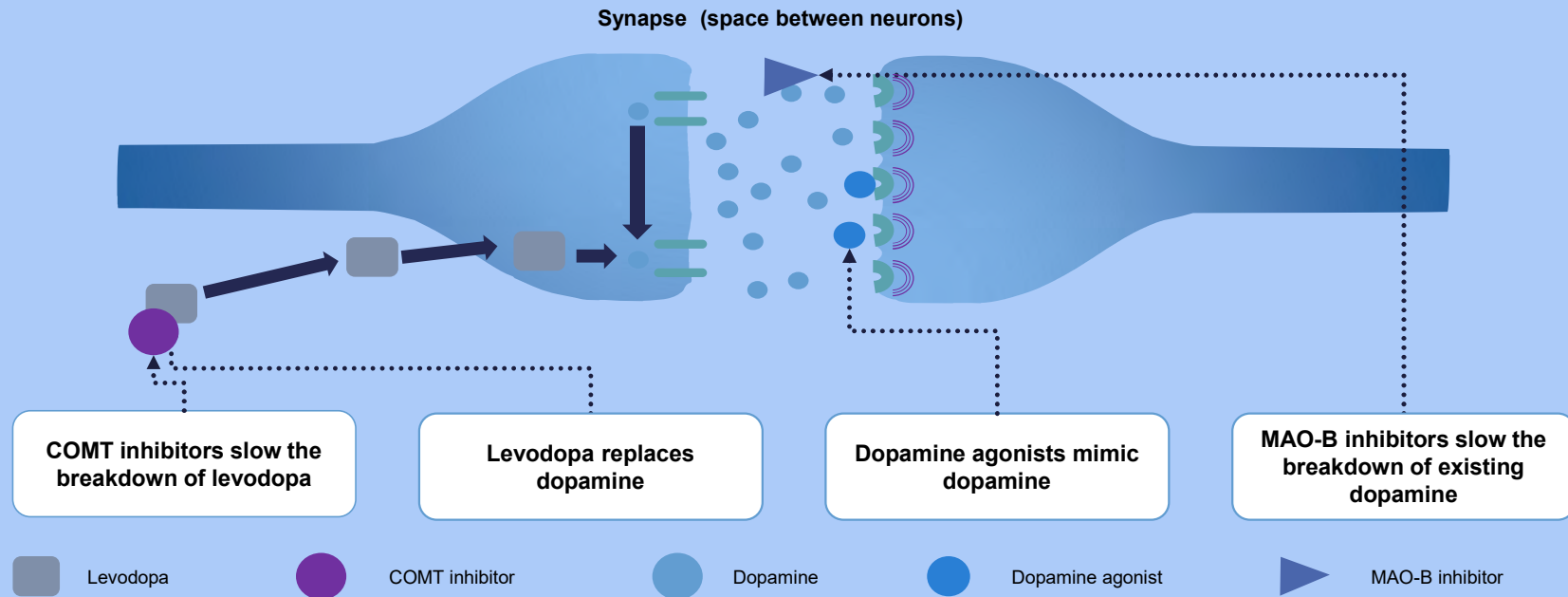
# WHY DOES PD CHANGE OVER TIME?

The disease itself and living the pharmacokinetics.



# MEDICATION CATEGORIES FOR PD

## PARKINSON'S DISEASE MEDICINES WORK TO INCREASE DOPAMINE OR ACT LIKE DOPAMINE IN THE BRAIN



COMT = catechol-O-methyltransferase.  
MAO-B = monoamine oxidase-B.  
Kalia LV et al. *Lancet*. 2015;386:896-912

# EXPANDED TOOLBOX UP UNTIL 8 YEARS AGO

- Dopamine Agonist



- Carbidopa/Levodopa formulation



- MAOB inhibitor

- COMT inhibitor

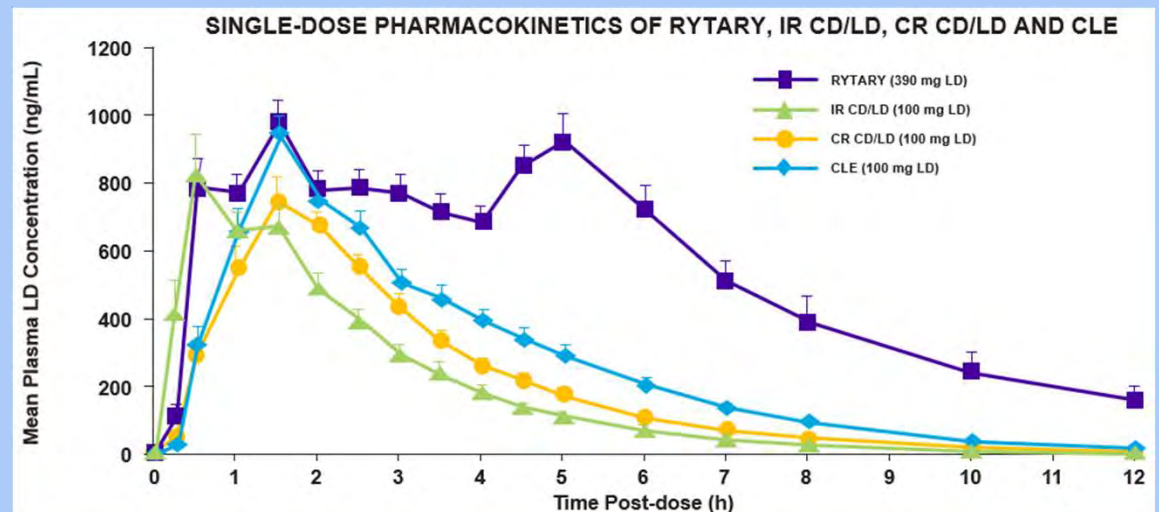
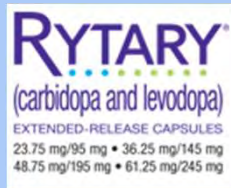




# NEW LEVODOPA FORMULATION

## Rytary™ (carbidopa/levodopa)

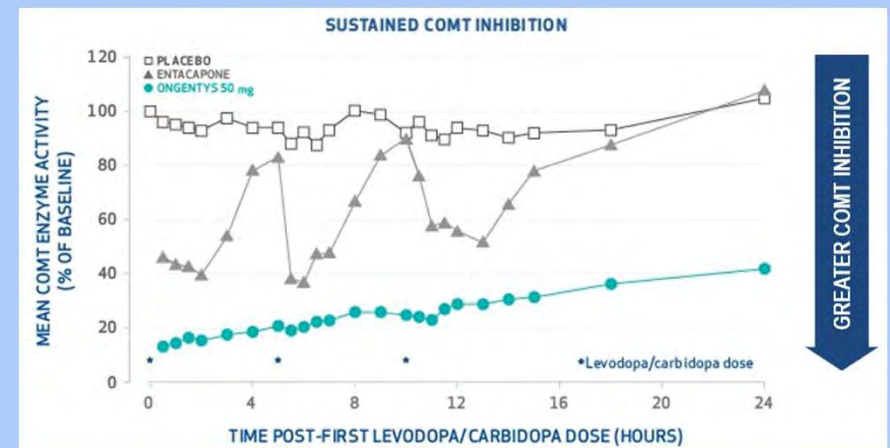
- History of evolution of levodopa delivery ----->
- Equivalent dose of Rytary on average 1.2 more hours of “on time” compared to IR.



# MAXIMIZE YOUR LEVODOPA

## Ongentys™ (opicapone)

- 1x daily inhibitor of COMT enzyme.
- Boosts levodopa for 24 hours
- Blocks breakdown of levodopa in the periphery, making more available to the brain
- In use in Europe since 2016
- Once daily at bedtime away from food

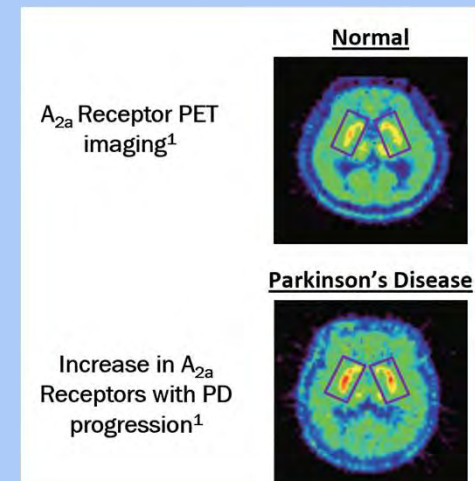


# NON-DOPAMINE APPROACH

## Nourianz™ (istradefylline)

- **INDIRECT pathway** – activation reduces motor activity
  - Direct pathway increases activity (dopamine, etc.)
  - Indirect pathway inhibits motor activity (adenosine, GABA)
- **Adenosine A<sub>2a</sub> receptor antagonist**
  - Double negative, blocks the block
- Improves off time, releasing the ‘brake’ on the system.

**NOURIANZ™**  
(istradefylline) tablets  
20mg | 40mg

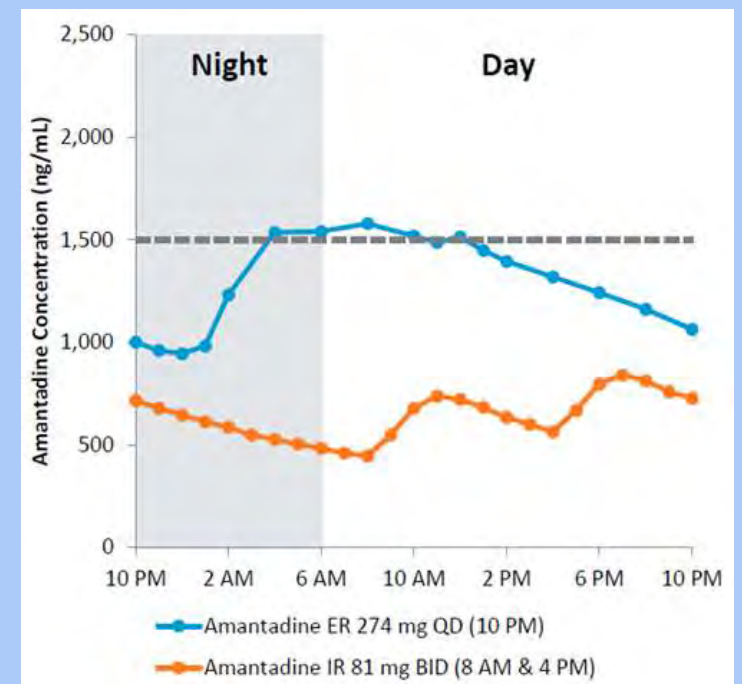


# DYSKINESIA AND OFF TIME

## Gocovri™ (amantadine ER)

- 1x daily amantadine ER at bedtime
- First “FDA approved” therapy for dyskinesia AND off periods
- Used to reduce dyskinesia (37% reduction or elimination)
- Reduced OFF time by 45% during the day

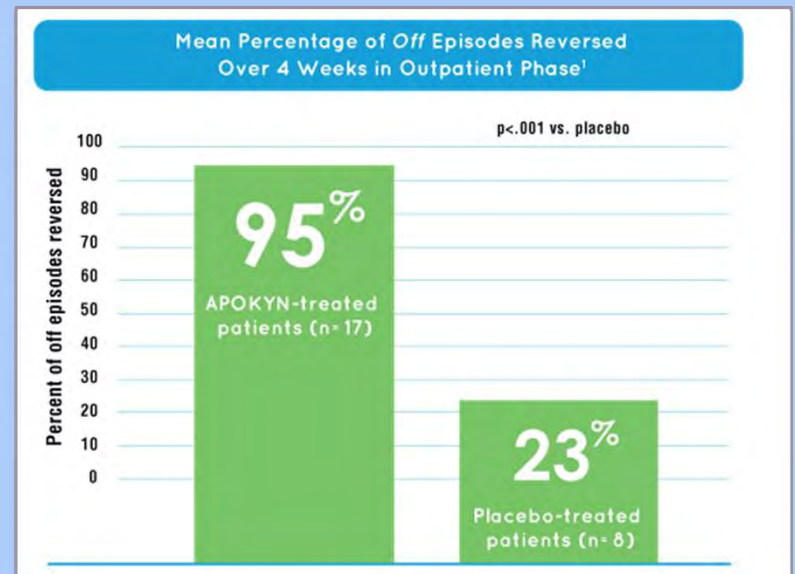
**GOCOVRI**<sup>®</sup>  
(amantadine) extended release capsules



# RESCUE OPTION #1 - APOKYN

## Apokyn™ (apomorphine injection)

- Rapid onset Dopamine Agonist via injection
- For different types of OFF episodes:
  - Rapid off, wearing off
  - Dose failure / unexpected off
  - Delayed on
  - First AM symptoms or exercise intolerance
- Achieve ON within 10-20 minutes



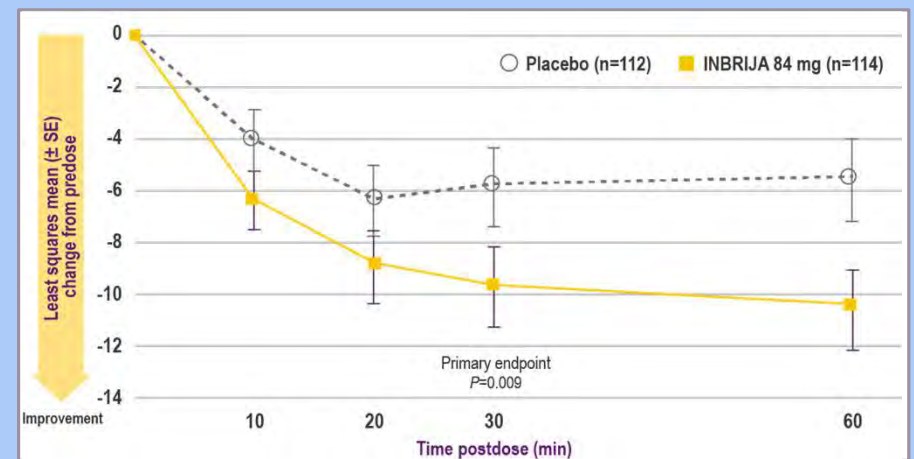
## RESCUE OPTION #2 - INBRIJA

### Inbrija™ (levodopa inhalation powder)

- Rapid onset levodopa through inhaler
- For different types of OFF episodes:
  - Rapid off, wearing off
  - Dose failure / unexpected off
  - Delayed on
  - First AM symptoms or exercise intolerance
- Achieve ON within 10 minutes, can take up to 5x daily



#### UPDRS Part III Score Change From 0-60 Minutes Postdose at Week 12



## RESCUE OPTION #3 - KYNMOBI

### Kynmobi™ (apomorphine sublingual film)

- Sublingual dissolving film for “off” episodes.
- Improvement begins after 15 min
- For different types of OFF episodes:
  - Rapid off, wearing off
  - Dose failure / unexpected off
  - Delayed on
  - First AM symptoms or exercise intolerance
- Can be taken up to 5x daily.

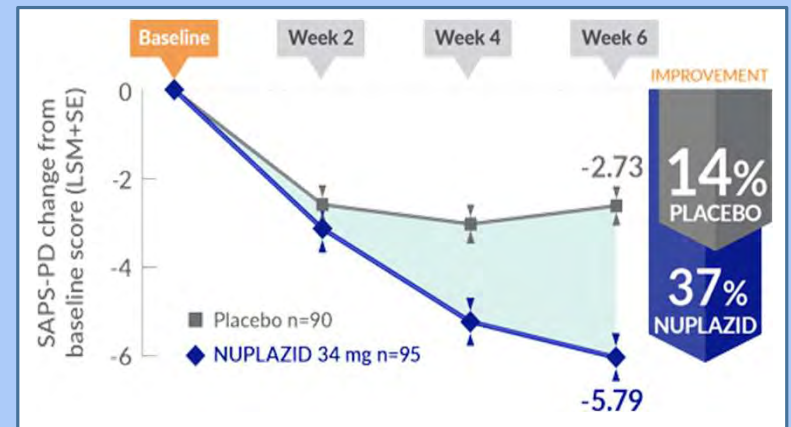


# HALLUCINATIONS AND PSYCHOSIS

## Nuplazid™ (pimavanserin)

- First antipsychotic medication specifically designed for hallucinations and 'psychosis' associated with Parkinson's Dementia and Lewy Body Dementia.
- Serotonin Agonist with no impact on dopamine receptors
- + SAPS-PD improvement with no change in UPDRS

**NUPLAZID™**  
(pimavanserin) tablets

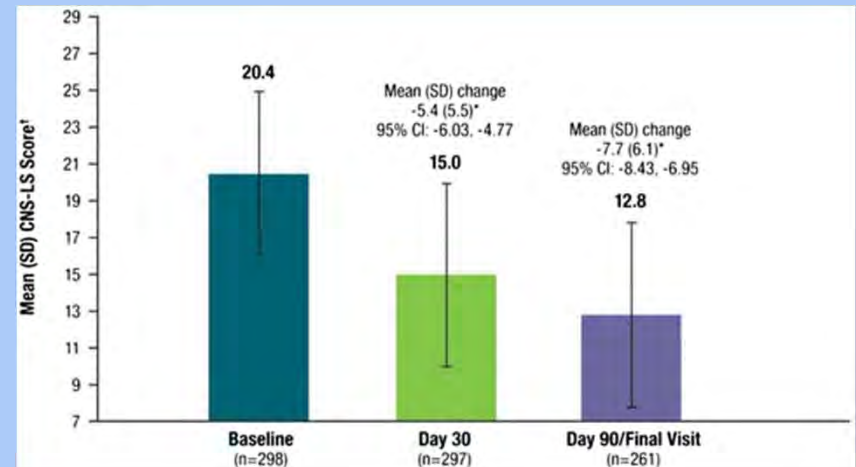




# PSEUDOBULBAR AFFECT

## Nuedexta™

- “Uncontrollable episodes of crying and/or laughing, or other emotional displays.”
- Disconnect between emotion and display, or inappropriate display
- PRISM study – 26%, though up to 40% in PD
- CNS-LS Screening reflects symptoms
- Reduction in episodes at 90 days was 72.3% if not fully resolved.



# PHYSICAL/OCCUPATIONAL/SPEECH THERAPY

*LSVTBIG<sup>®</sup> and LSVTLOUD<sup>®</sup>*

But also, non-LSVT Therapy aimed at  
balance/gait and strengthening

**The sooner the better!**

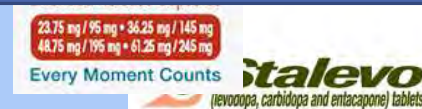


# NEW TOOLBOX...AND GROWING

- Dopamine Agonist
- Carbidopa/Levodopa formulation
- MAOB inhibitor
- COMT inhibitor
- A2a agonists
- Amantadine derivatives
- Rescue Therapies
- Symptom specific therapies



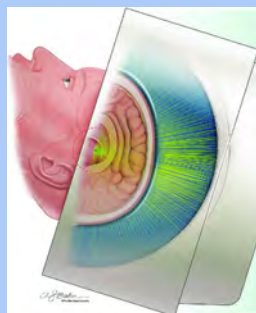
## MOVEMENT DISORDERS SPECIALTY CENTER



(pimavanserin) tablets



# TECHNOLOGY AS A TOOL



Join us March 15, 2022!

# BEING THEIR BEST

Hints for doing well:

- Teamwork is key, as is communication.
- Take advantage of telehealth.
- Take care of their part -> exercise, sleep, diet.
- Keep moving!
- Never be satisfied with “good enough.”



# TO THE FUTURE

- Longer-acting levodopa formulations (10 hours or greater)
- New inhibitors
- Pump-based and sub-cutaneous formulations
- Improved technology
- Targeted protein therapy
- Cure



All of this equals

**HOPE**

**THANK YOU!**



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**Join our newsletter!**  
<http://eepurl.com/gPkGlf>

**Stay up to date on all  
of our center's offerings!**

**Sonia.Gow@inova.org**  
**703-375-9987**

[www.inova.org/move](http://www.inova.org/move)



# Advanced Medication Management and Therapies: DBS, Duopa and More



**INOVA**<sup>®</sup>

Parkinson's and  
Movement Disorders Center





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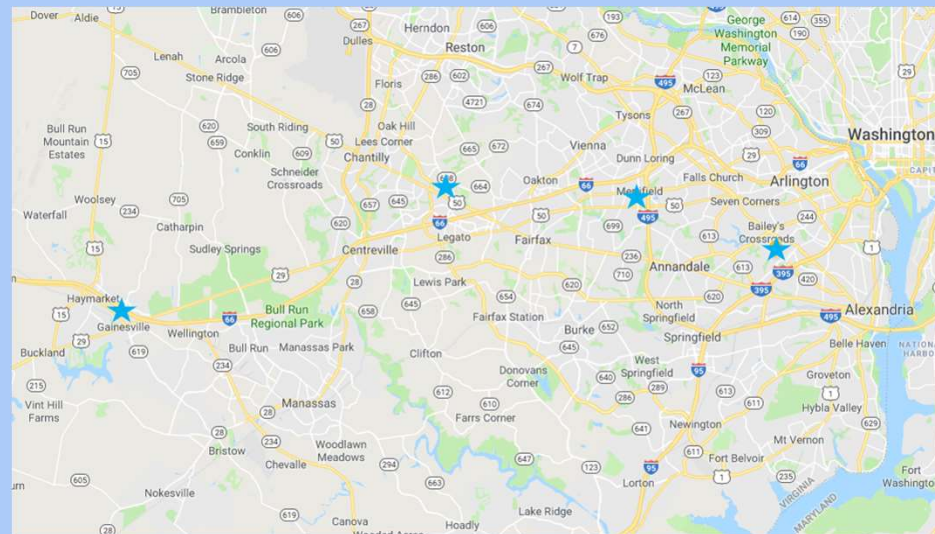
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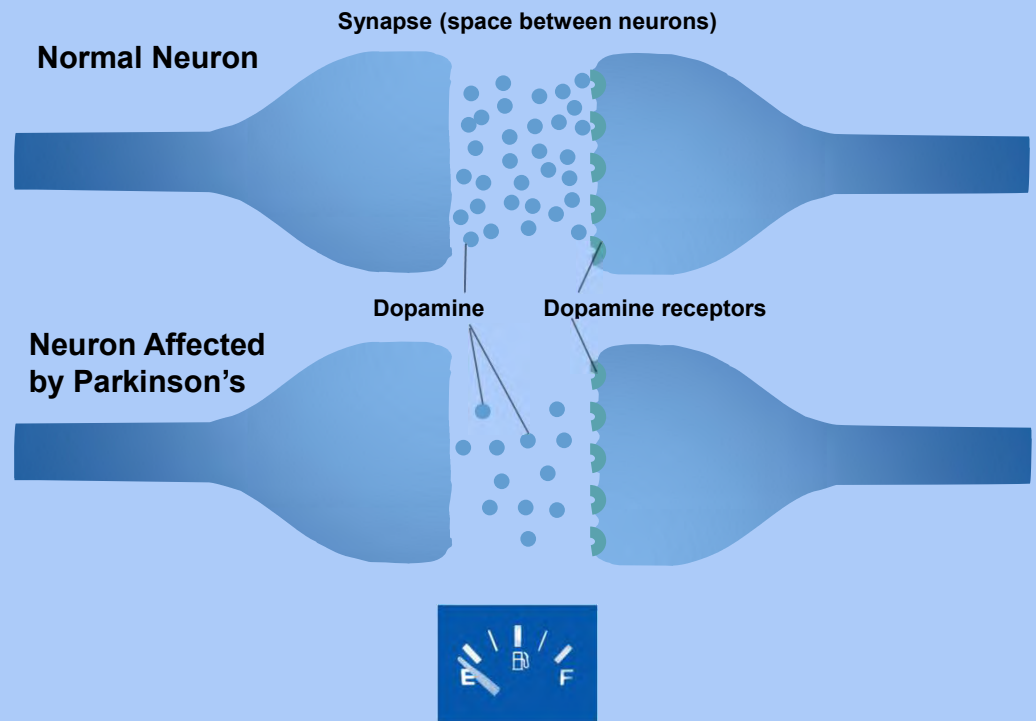
[www.inova.org/move](http://www.inova.org/move)

# WHAT'S ON TAP? PICKING UP FROM LAST TIME

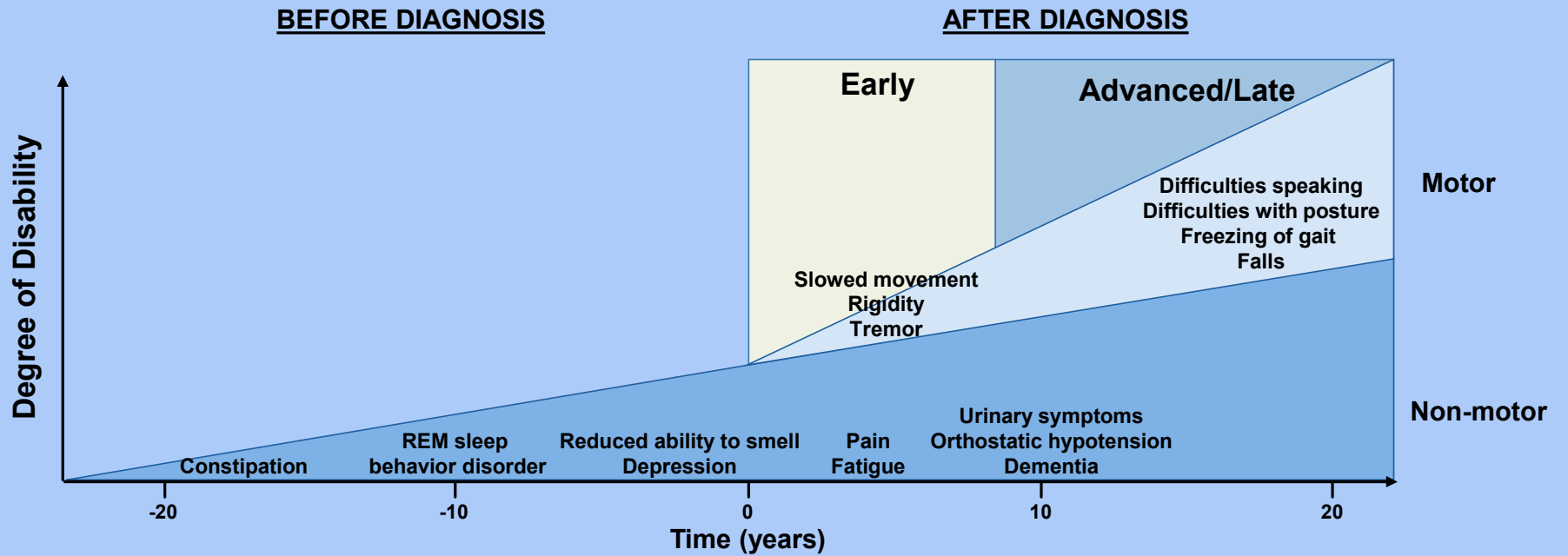
- How does Parkinson's change.
- Is “advanced” the right word?
- How to adapt medications.
- When to think about more.
- How does DBS work.
- To the future!

# THE CAUSE?

- Just a dopamine deficiency!
- Genetics
  - Classically NOT inherited
- Environmental factors
  - Pesticides including Agent Orange
  - Well water
  - Heavy metal exposure
  - Chemical exposure
  - Head injury

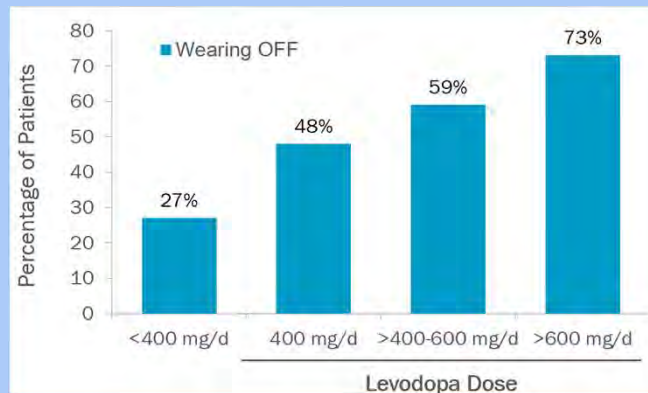


# PARKINSON'S CHANGES OVER TIME



# OFF TIME

- When medication is not doing what it is expected to or can do
- Many different types of OFF, sudden or subtle
  - First AM off
  - End of dose
  - Sub-optimal on
  - Sudden off
  - Dose failure
  - Exercise-induced
  - Food-induced
- Motor and non-motor OFF



Online survey of 3,000+

**70%** reported 2+ Off episodes a day.

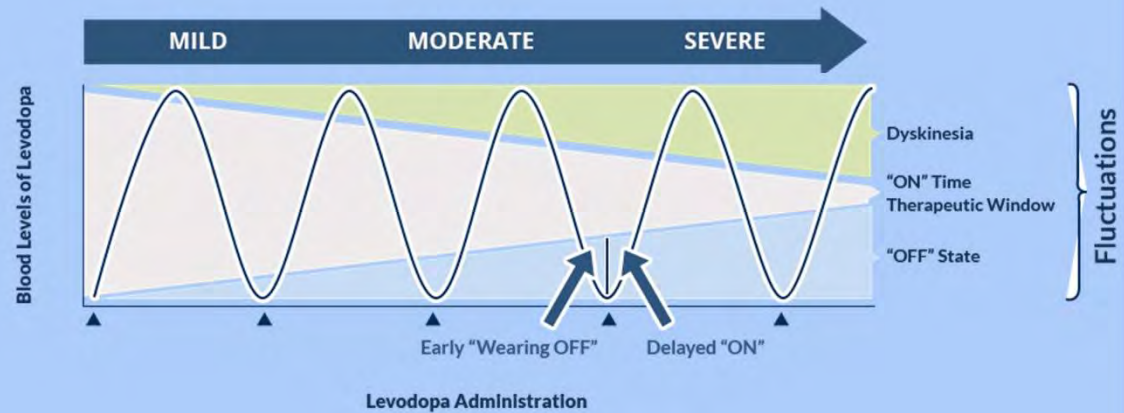
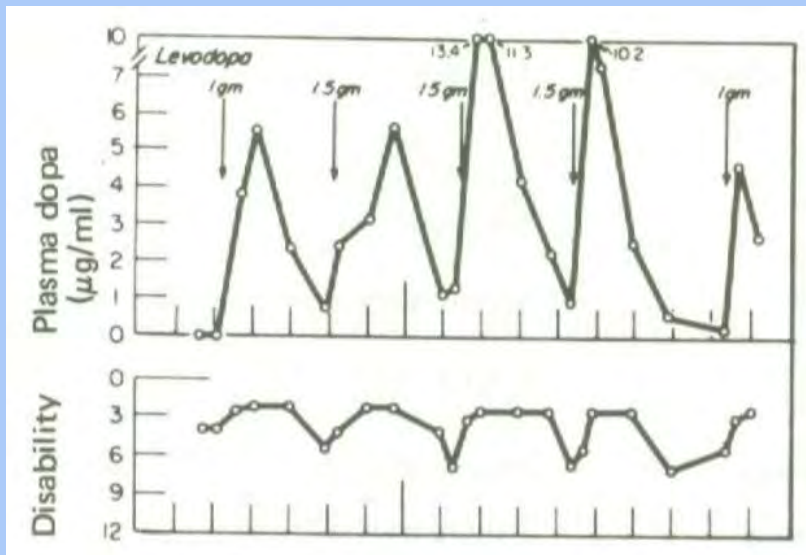
**65%** reported 2 or more hours a day

**50%** - moderate/severe, affected daily activities

**If we fix OFF, we fix Parkinson's Disease.**

# WHY DOES PD CHANGE OVER TIME?

The disease itself AND medications used.





# EXPANDED TOOLBOX UP UNTIL 8 YEARS AGO

- Dopamine Agonist



- Carbidopa/Levodopa formulation



- MAOB inhibitor

- COMT inhibitor



# NEW TOOLBOX...AND GROWING

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- A2a agonists
- Amantadine derivatives
- Rescue Therapies
- Symptom specific therapies

**Neupro**<sup>®</sup>  
(Ropinirole Transdermal System)

**REQUIP**<sup>®</sup>  
ropinirole HCl

**XADAGO**<sup>®</sup>  
(safinamide) tablets  
**Mirapex**<sup>®</sup>  
pramipexole dihydrochloride tablets

**GOCOVRI**<sup>®</sup>  
(amantadine) extended release capsules  
**AZILECT**<sup>®</sup>  
(bupropion) extended-release tablets

**NOURIANZ**<sup>™</sup>  
(istradefylline) tablets  
20 mg 40 mg

**Osmolex ER**<sup>™</sup>  
(amantadine)  
Extended-release Tablets

**PARCOPIA**<sup>®</sup>  
(carbidopa and levodopa orally disintegrating tablets)

**Rytary**<sup>™</sup>  
(Carbidopa and Levodopa)  
Extended-Release Capsules  
23.75 mg / 95 mg + 36.25 mg / 145 mg  
48.75 mg / 195 mg + 61.25 mg / 245 mg  
Every Moment Counts



**Stalevo**<sup>®</sup>  
(levodopa, carbidopa and entacapone) tablets

**COMTan**<sup>®</sup>  
(entacapone) tabl

**NUPLAZID**<sup>™</sup>  
(pimavanserin) tablets

**Inbrija**<sup>™</sup>  
(levodopa inhalation powder)  
42 mg capsules

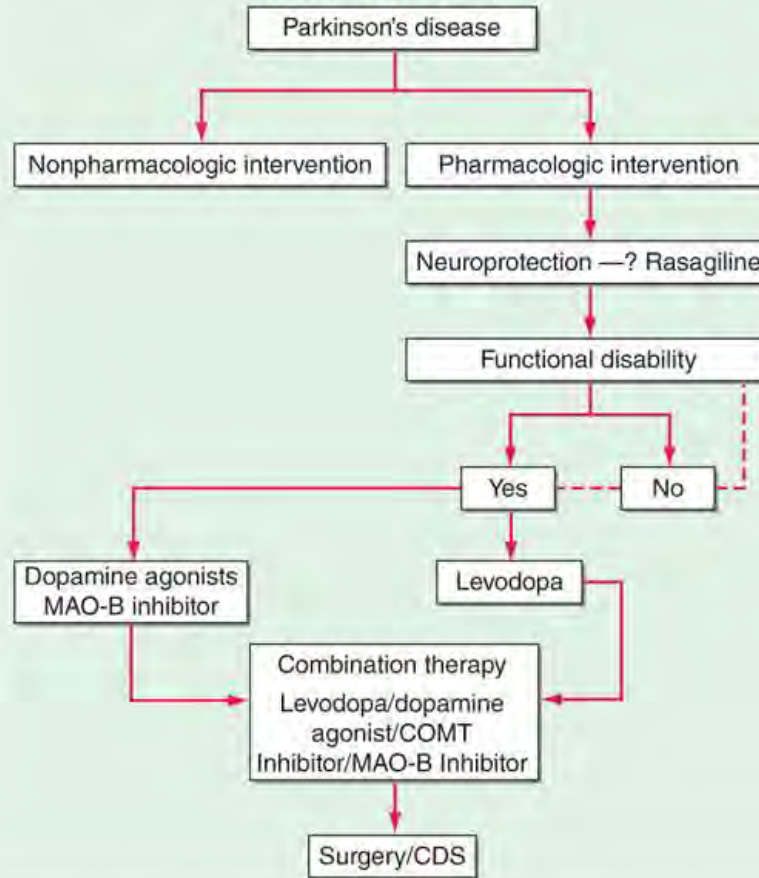
**Ongentys 50 mg**  
capsules/capsules dures  
opicapone  
via oral/via oral

**Northera**<sup>™</sup>  
(droxidopa) Capsules  
100 mg - 200 mg - 300 mg

**APOKYN**<sup>™</sup> *Be on. Live life.*  
apomorphine hydrochloride injection

**NUEDEXTA**<sup>®</sup>  
tromethorphan HBr and  
idine sulfate) capsules  $\frac{20}{10}$  mg

## TREATMENT ALGORITHM FOR THE MANAGEMENT OF PARKINSON'S DISEASE



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition Copyright © McGraw-Hill Education. All rights reserved.

## GENERAL TREATMENT ALGORITHM

Varies based on:  
Experience  
Comfort  
Place of training  
Clinic structure  
and time

# NEW TOOLBOX...AND GROWING

- Dopamine Agonist
- Carbidopa/Levodopa formulation
- MAOB inhibitor
- COMT inhibitor
- A2a agonists
- Amantadine derivatives
- Rescue Therapies
- Symptom specific therapies

**Neupro**<sup>®</sup>  
(Rotigotine Transdermal System)

**REQUIP**<sup>®</sup>  
ropinirole HCl

**XADAGO**<sup>®</sup>  
(safinamide) tablets  
**Mirapex**<sup>®</sup>  
pramipexole dihydrochloride tablets

**NOURIANZ**<sup>™</sup>  
(istradefylline) tablets

**Osmolex ER**<sup>™</sup>  
(selegiline) Tablets

**GOCC**<sup>®</sup>  
(amantadine) extended  
68.1

**Ry**<sup>®</sup>  
(Carbidopa)  
Extended  
28.75 mg  
48.75 mg

Every Moment Counts  
**Stalevo**<sup>®</sup>  
(levodopa, carbidopa and entacapone) tablets

**Inbrija**<sup>™</sup>  
(levodopa inhalation powder)  
42 mg capsules

**Northera**<sup>™</sup>  
(droxidopa) Capsules  
100 mg · 200 mg · 300 mg

**COMTAN**<sup>®</sup>  
(entacapone) tabl

**Ongentys 50 mg**  
capsules/capsules dures  
opicapone  
via oral/via oral

**APOKYN**<sup>®</sup> Be on.  
apomorphine hydrochloride injection Live life.

**NUEDEXTA**<sup>®</sup>  
tromethorphan HBr and  
idine sulfate) capsules 20 mg  
10 mg

**RAZID**<sup>™</sup>  
tablets

So when do you  
look to technology?

## NOT “ADVANCED” - DIFFERENT TOOLS

- DUOPA Intestinal Gel
- Focused Ultrasound
- Deep Brain Stimulation

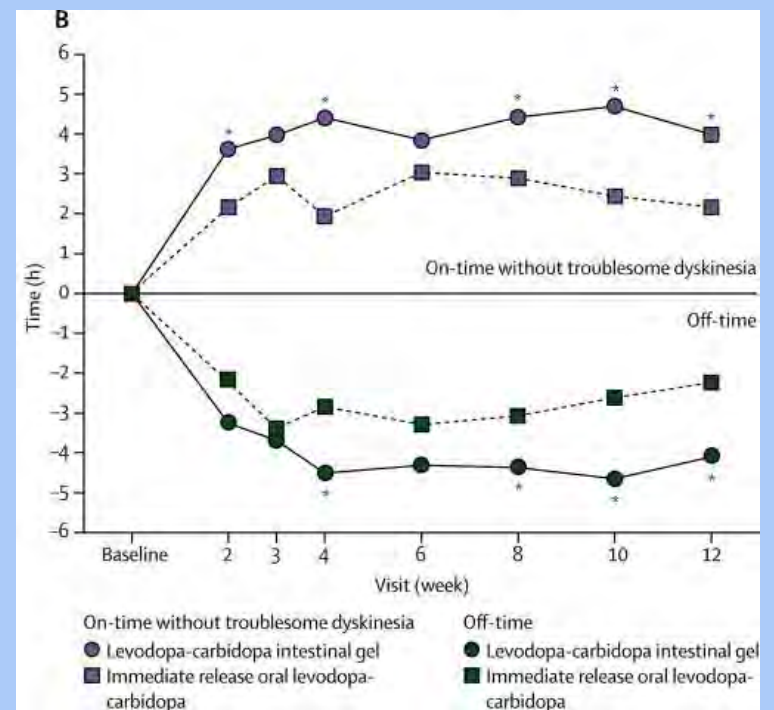


# CONSTANT DELIVERY OF LEVODOPA

## Duopa

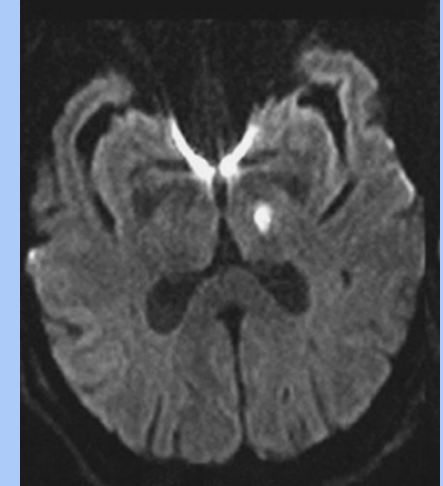
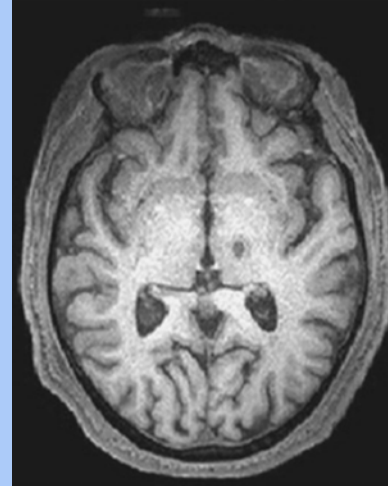
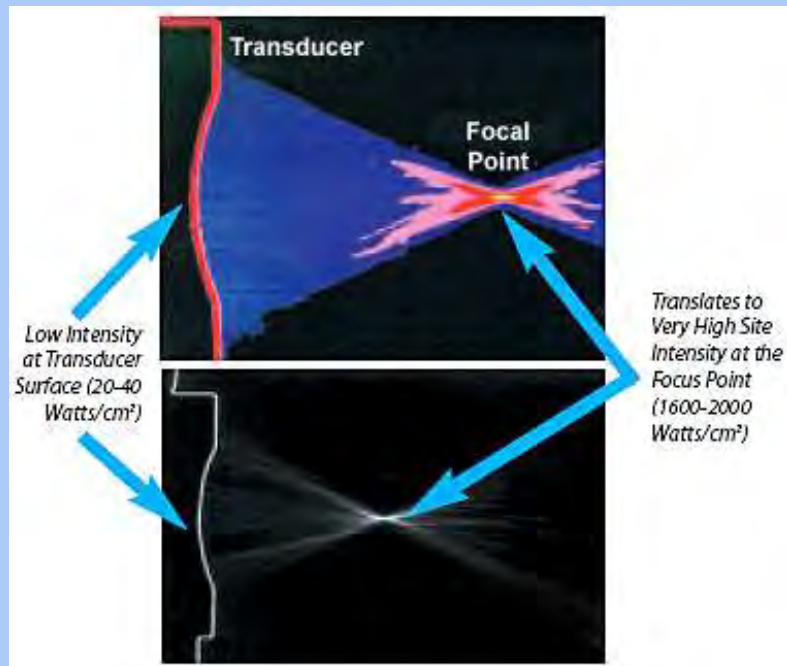
- Dopamine gel continuously administered via intra-intestinal pump
- Provides steady delivery of levodopa without the fluctuations of oral medication
- Off time decreased by 4h and on time increased by 4h<sup>1</sup>

**Duopa**  
carbidopa/levodopa  
enteral suspension  
4.63 mg/20 mg per mL



# FOCUSED ULTRASOUND (FUS)

- 1,000 ultrasound beams
- Non-invasive
- Creates focal lesion at target
- Approved unilateral ET, unilateral PD tremor

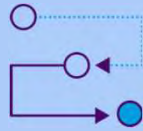


# DEEP BRAIN STIMULATION (DBS)



## Initial Discovery

**1930s–60s**  
Stimulating regions of the brain at high frequency could reduce symptoms



## Prototype Development

**1970s–80s**  
Neurostimulator developed and used for DBS for several movement disorders



## Product Standardization

**1997–2002**  
Clinical data used for DBS to receive FDA approval



## Innovation Cycle

**2015**  
Regulatory approval for directional DBS system

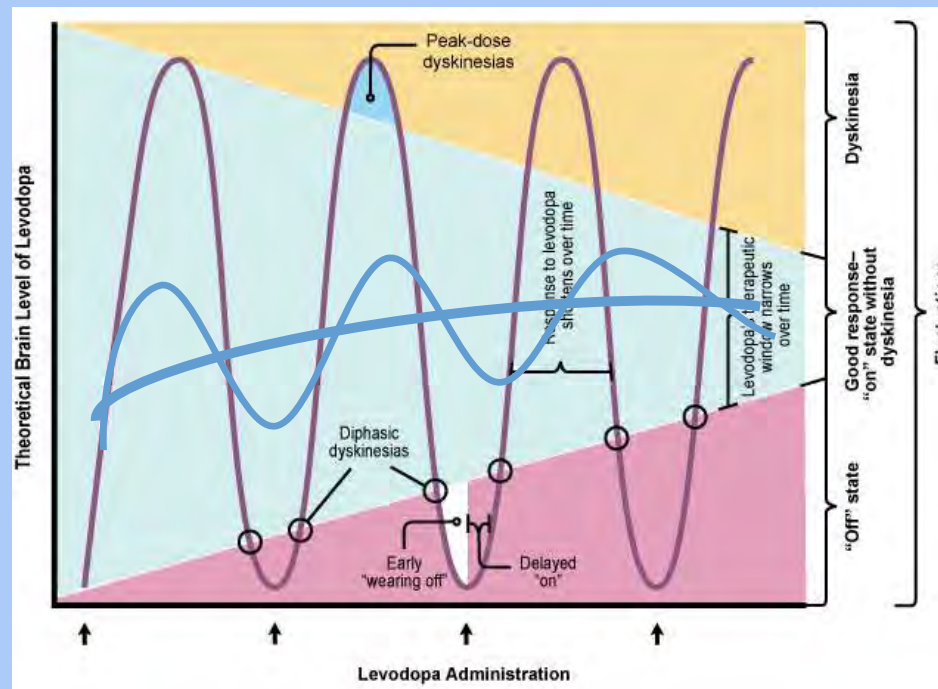


## HOW DOES IT WORK?

- Controlled stimulation of electricity to block electrical pathway.
- Surgeries for PD (pallidotomy or thalamotomy) and Focused Ultrasound destroys nerve cells, DBS does not.
- Programmable and adaptable, by MD and patient.
- Removable, if necessary, with little to no tissue damage.
- Standard of care.

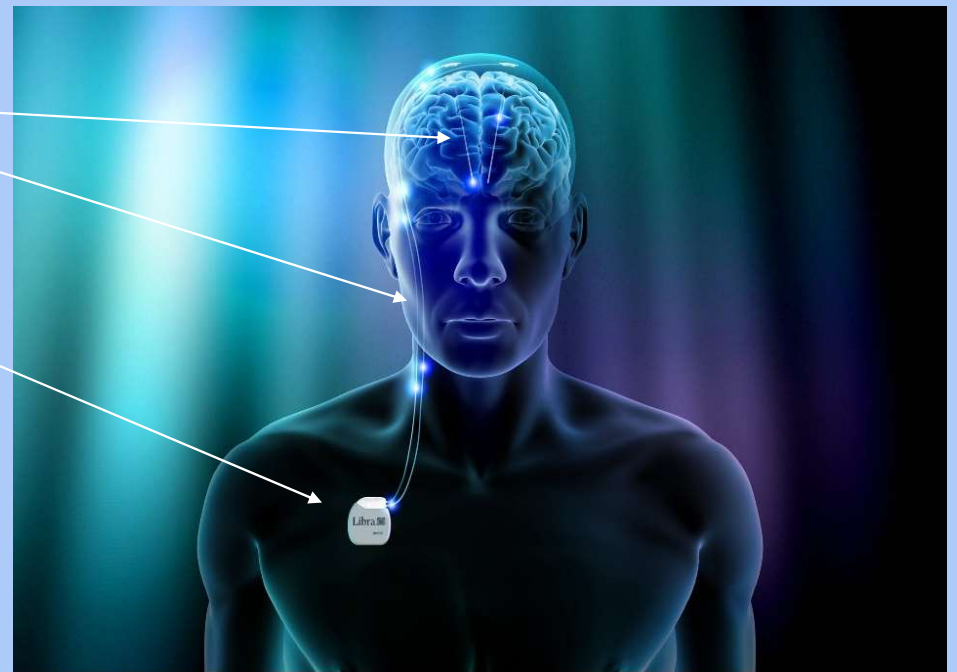


# HOW DOES IT WORK?



# COMPONENTS?

- The DBS system consists of three components:
  - Intracranial Lead
  - Extension connecting lead and generator
  - Implanted pulse generator (neurostimulator)
- Unilateral or bilateral leads
- Proper patient selection is key



# DBS INDICATIONS

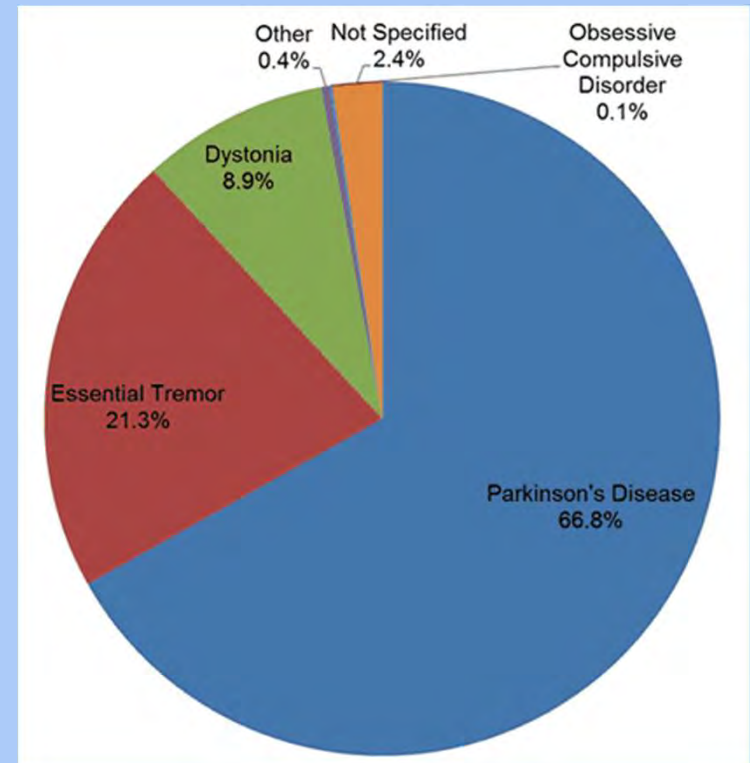
- **FDA indicated for:**

- Parkinson's Disease
- Essential Tremor
- Dystonia

- **FDA approval:**

- Essential tremor - 1997
- Parkinson's disease - 2002
- Dystonia - 2003

Covered by all insurance providers.



Implantable Systems Performance Registry (ISPR) for deep brain stimulation systems. July 2009 - July 31, 2013.

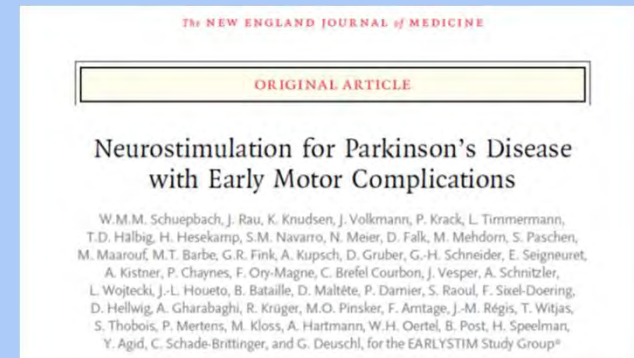
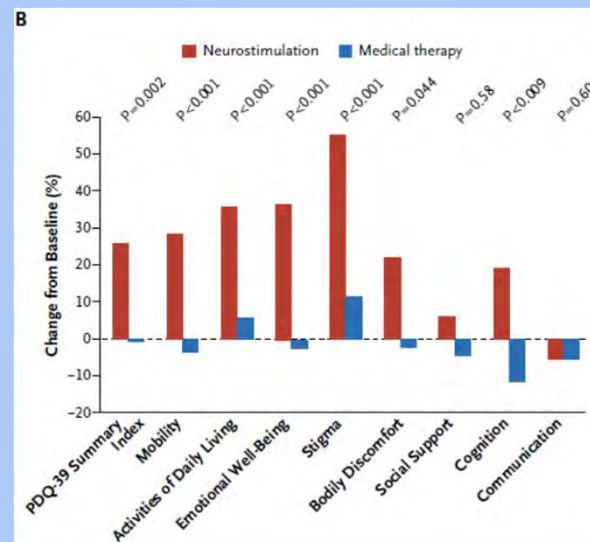
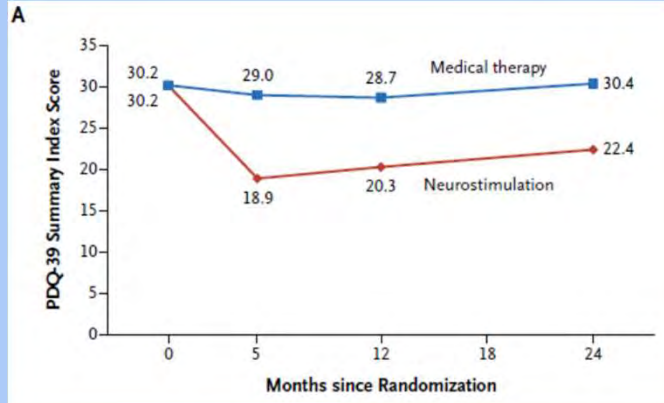
# BENEFIT FOR OUR PATIENTS

## Parkinson's Disease:

- 80-90% subjective improvement
- >60% medication reduction
- 80% improvement in “off” periods
- 10% improvement in “on” periods
  
- 4.6 hours MORE on time without dyskinesia
  
- Reduction in medications leads to decrease in the following:
  - Cost
  - Side effects (nausea, orthostasis, cognitive change, and downstream dyskinesia risk)



# EARLY-STIM STUDY



- **Conclusions:** DBS was found to be superior to medical therapy in patients with PD and early motor complications

# DBS, DISEASE MODIFYING THERAPY?

## Effects of deep brain stimulation on rest tremor progression in early stage Parkinson disease

Mallory L. Hacker, Mahlon R. DeLong, Maxim Turchan, Lauren E. Heusinkveld, Jill L. Ostrem, Anna L. Molinari, Amanda D. Currie, Peter E. Konrad, Thomas L. Davis, Fenna T. Phibbs, Peter Hedera, Kevin R. Cannard, Lea T. Drye, Alice L. Sternberg, David M. Shade, James Tonascia, David Charles

- **Classification of evidence** This study provides Class II evidence that for patients with early PD, DBS may slow the progression of rest tremor.

Neurology®

# WHO IS A CANDIDATE

- A good candidate for DBS per our center:

1. Parkinson's Disease at least 4 yrs (FDA indication)
2. Experiencing a response to medication
3. Experiencing the on-off fluctuation of medication
4. Able to participate in care
5. Good surgical candidate
6. No diagnosed dementia or severe psychiatric disorder

Also refractory tremor in Parkinson's disease





# EXPANDING FIELD: COMPETITION ONLY BENEFITS THE PATIENT

5 years ago



NOW

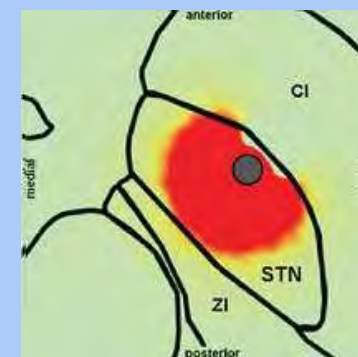
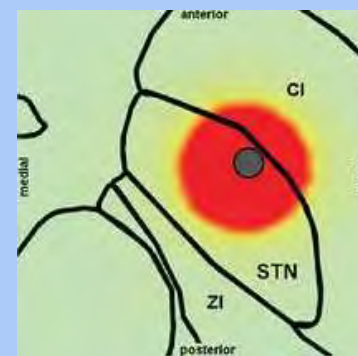
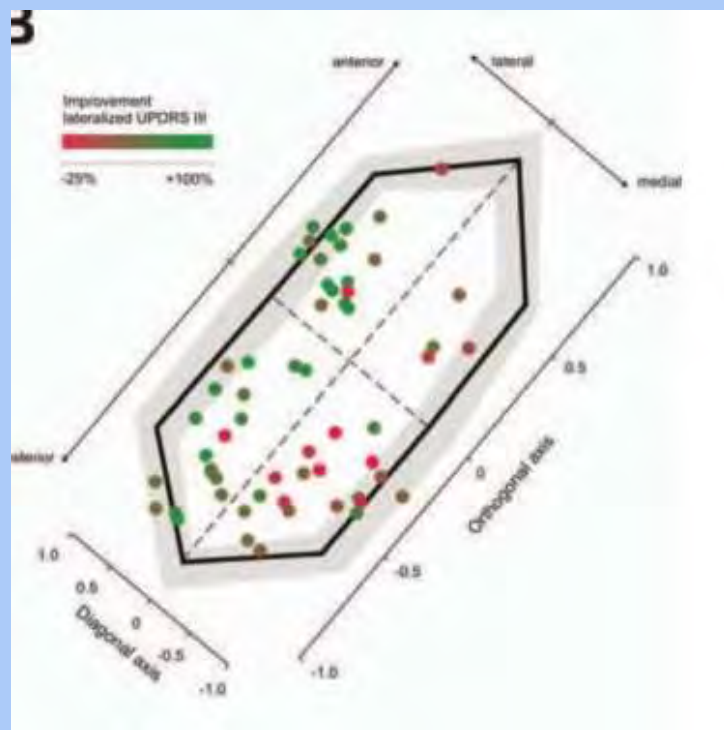


# AN EXPANDING FIELD – PICK YOUR CAR

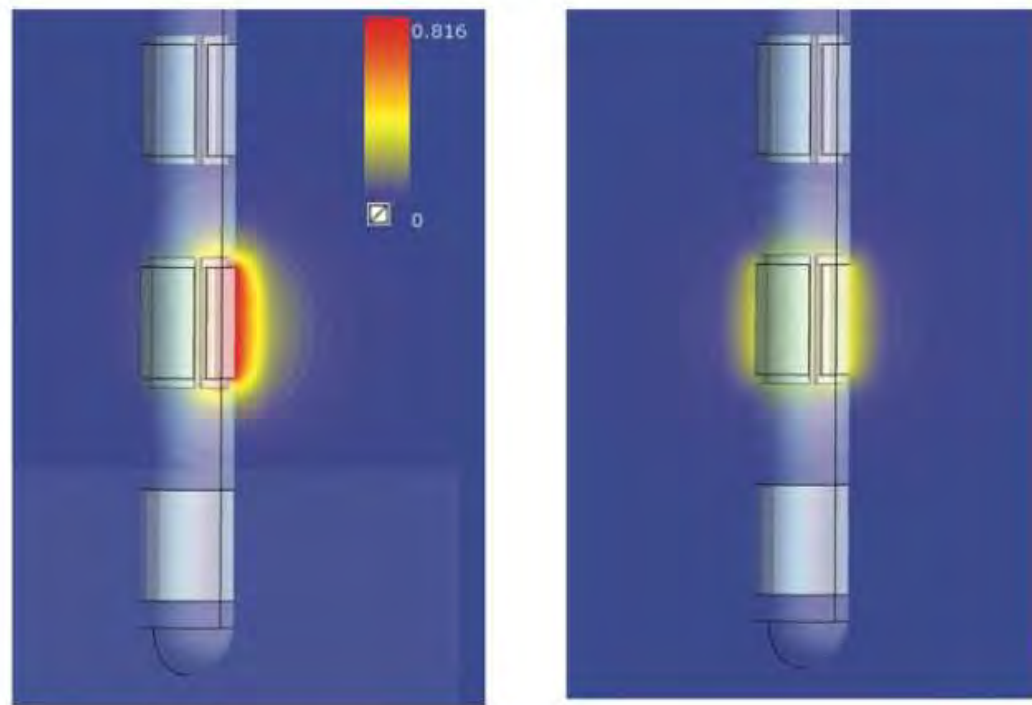
- Directional stimulation.
- Remote programming.
- Improved technology and wireless.
- Smaller technology, thinner.
- Longer battery life and rechargeable systems.
- Variety of rechargeable systems.



# DIRECTIONALITY, THE PRESENT AND FUTURE OF STIM



# DIRECTIONALITY, THE PRESENT AND FUTURE OF STIM



Reference: Poster: VTA Modelling studies- Cheeran, Venkatesan, Kent- WSSFN 2017

# THE FUTURE?

- Local field potential readings
- “Closed-loop” systems
- Longer batteries and better hardware
- Improved personalization and patient interaction



Deep Brain Stimulation Systems - Percept PC | Medtronic

# MULTIDISCIPLINARY APPROACH

*A team approach is key to a successful outcome.*

- Cognitive evaluation
  - Full Neuropsychiatric testing
- Psychiatric evaluation, if necessary
- Physical therapy, occupational therapy and speech therapy
- Neurosurgical evaluation
  - Work together for pre-surgical planning
    - GPI vs STN, Unilateral vs Bilateral
  - Intra-operative cooperation
- Movement Disorders Specialist



## IN SUMMARY – DBS IS STANDARD OF CARE

- Longstanding, well-studied tool.
- Therapy at the source.
- Adaptable, adjustable with no treatment horizon.
- Average implant – 11 years from diagnosis.
- FDA approved – 4 years from diagnosis.
- The gap? Education, training and comfort.



**THANK YOU!**



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