University of Nebraska Medical Center Parkinson's Disease 2025

A Conference for Parkinson's Disease Patients and their Family/Care Partners

Embassy Suites by Hilton Omaha La Vista Hotel & Conference Center

October 1, 2025

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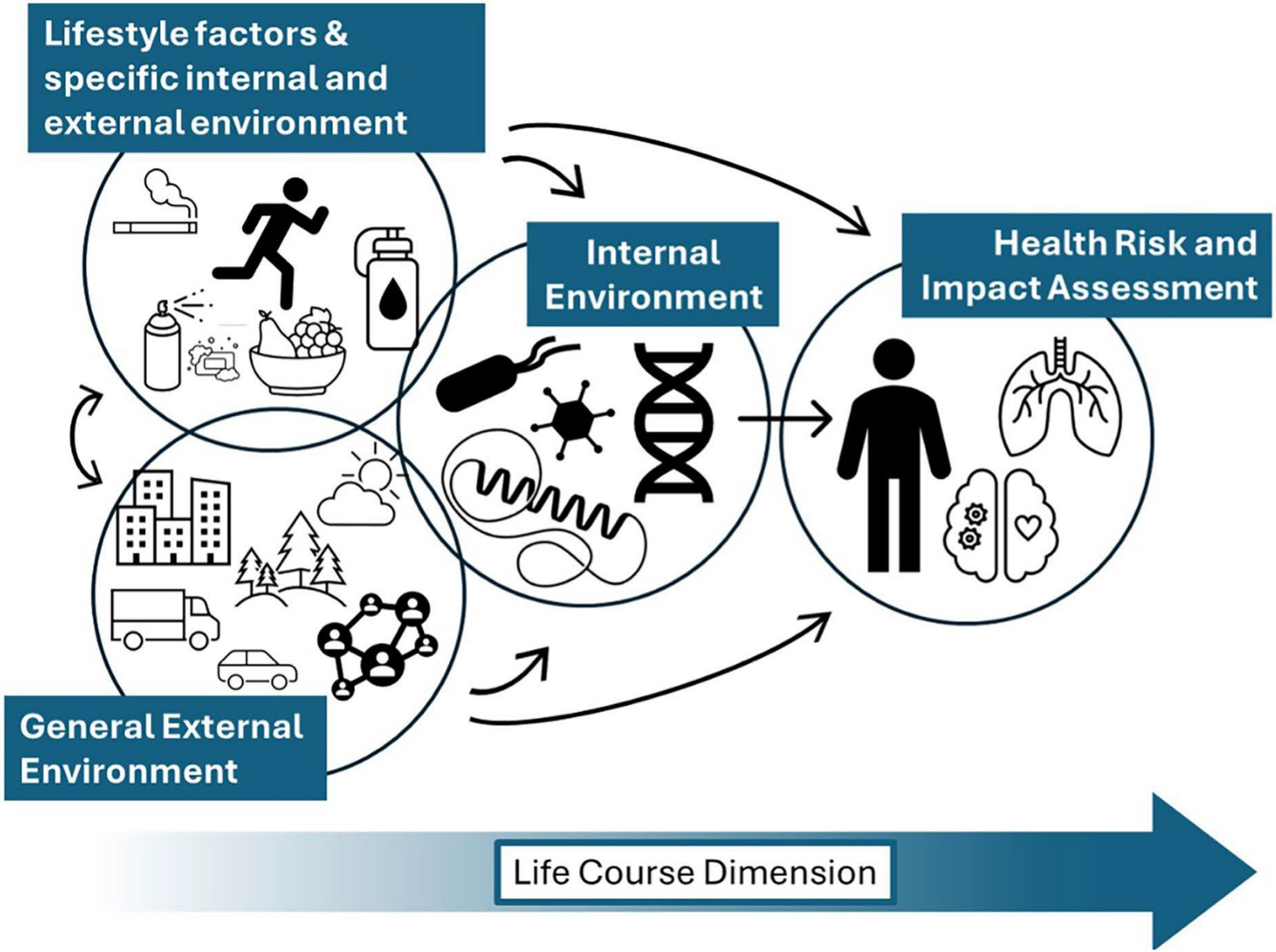
Opening Comments

Supported by
NIH: NIGMS U54GM115458, NIA RO1 AG17177

Exposome: Totality of chemical, physical, biological, behavioral, and social exposures throughout life.



Data are healthcare's lifeblood.

Exposome data from the IoT and other sources **interact** with genomics and-omics to shape:

- *Disease susceptibility* and resilience
- *Health and disease trajectories*
- Cognitive and functional phenotypes

Internal: microbiome, inflammation, metabolism)

External factors:

- **Lifestyle behaviors**: smoking, alcohol, diet, activity
- **Environmental exposures**: pollution, noise, climate
- **Social** : relationships, isolation, SES

References

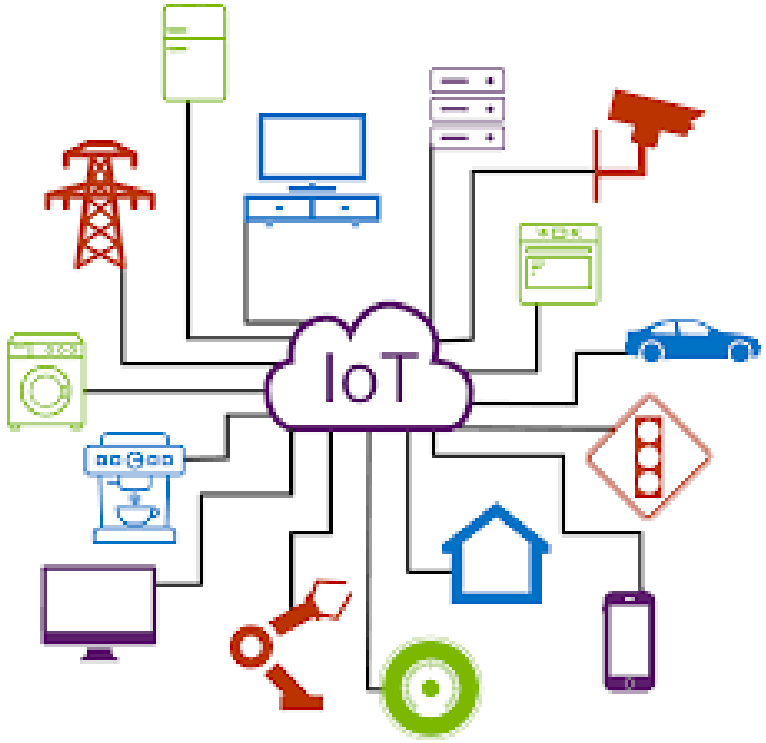
Wild (2012). Int JEpidemiol, 41(1):24–32.
Vermeulen et al. (2020). Science, 367(6476):392–396.

The exposome provides a comprehensive framework for advancing personalized, predictive, and preventive care, accelerating discovery, and supporting continuously learning health systems.

Digital IoT and Digital Biomarkers for dCOUNTS

Enabling Diagnosis, Treatment, and Monitoring beyond the Clinic

- **Sensor-Rich World-** Behavioral and **physiological tracking** from wearables, phones, vehicles, and homes.
- **Brain in the Wild-** Passive, real-time monitoring of cognition, emotion, volition, and physiology in natural contexts.
- **Enhanced Validity-** IoT + self-report/ EMA, extends testing beyond clinics.



Internet of Things (IoT)

- **RWD Insights-**New behavioral phenotypes; integrates with EMRs & exposome data.
- **Impact-** Advances CTR, clinical trials (NIH, FDA, industry), surveillance, precision health.
- **Access-** extends **care o**utside traditional settings.

The IoT provides infrastructure and evidence for actionable insights on the complex interplay between **environment, behavior, and brain health** in RW settings.

Linking Medicine and Technology In-The-Field

Aim 1. Real-world motor, non-motor, sleep, and driving digital biomarkers

Aim 2. Digital biomarkers of social connectedness with cohabiting partner

Aim 3. Integrate digital and biological markers with national cohort data to build predictive models and digital twins

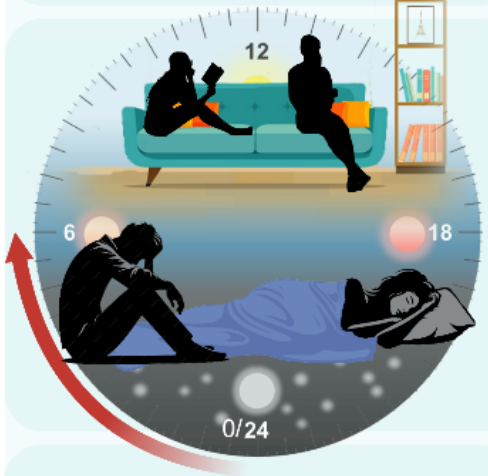
Methods

- Wearable device captures sleep, mobility, motor activity
- GPS captures driving behaviors
- 150 PD participants

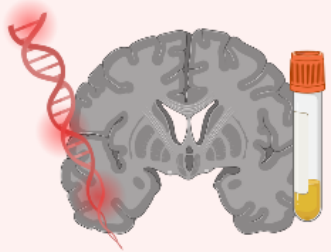
- Synchrony, derived from PD participant and partner's wearable devices, indexes social connectedness
- 150 dyads

- Biological markers from 150 PD participants [genetics, plasma markers (alpha-synuclein, Aβ, p-tau, NfL, GFAP), brain atrophy and white matter/ vascular disease]

Proposal concepts



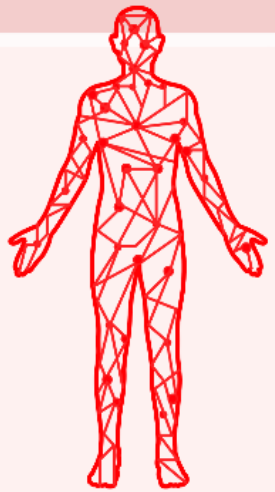
Biological markers from our PD cohort



Parkinson's Progression Markers Initiative (PPMI)

Longitudinal Research on Aging Drivers

LongROAD
Longitudinal Research on Aging Drivers



- ✓ Individualized prediction of cognitive decline
- ✓ Counterfactual simulation
- ✓ Biomarkers for future adaptive trials
- ✓ Advance personalized clinical care
- ✓ Enhance clinical trial outcomes

Anticipated proposal outcomes

Continuous real-world data monitoring identifies digital biomarkers to detect and predict cognitive decline in PD

Synchrony serves as real-world digital biomarker of social connectedness to detect cognitive decline in PD

Large national datasets (e.g., PPMI, LongROAD) support development of digital twins for personalized prediction of cognitive decline

Digital biomarkers of real-world behaviors + **Digital biomarkers of social connectedness** + **Biological markers & national cohort data** = **Predictive models Digital twins**

Synthetic data & counter-factuals

How do changes in medication timing or daily activity alter driving, sleep, or mobility trajectories?

How do reduced or enhanced caregiver interactions impact social connectedness and cognitive health?

How do new risk factors, e.g., REM sleep, diabetes, interact with genetic, plasma, or imaging biomarkers?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The Diagnosis of Parkinson's Disease

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Movement Disorders Division

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Today's Objectives

1. Define Parkinson's Disease (PD)
2. Talk about why it's so hard to define PD
3. Review the underlying causes of PD
4. Understand how your neurologist makes the diagnosis of PD
5. List the Movement Disorder Society (MDS) criteria
6. Look into the future of diagnosing PD
   - Imaging
   - Biomarkers
   - Artificial Intelligence

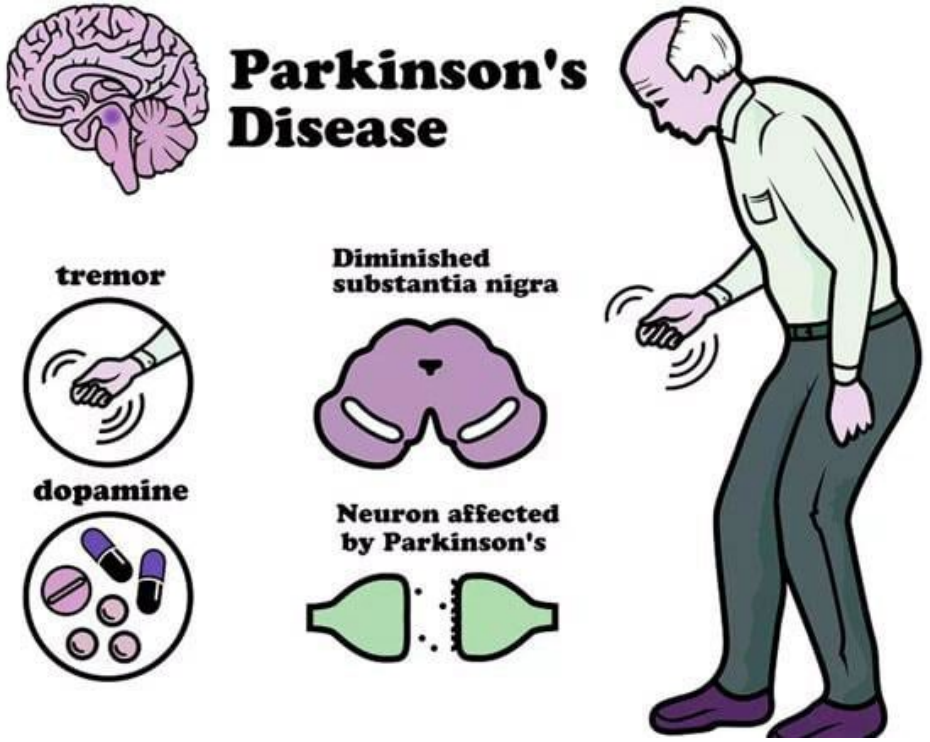
What is Parkinson's Disease (PD)?

Progressive neurological disease characterized by:

- Resting tremor
- Slowness ("bradykinesia")
- Rigidity / muscle stiffness
- Shuffling feet
- Stooped forward posture

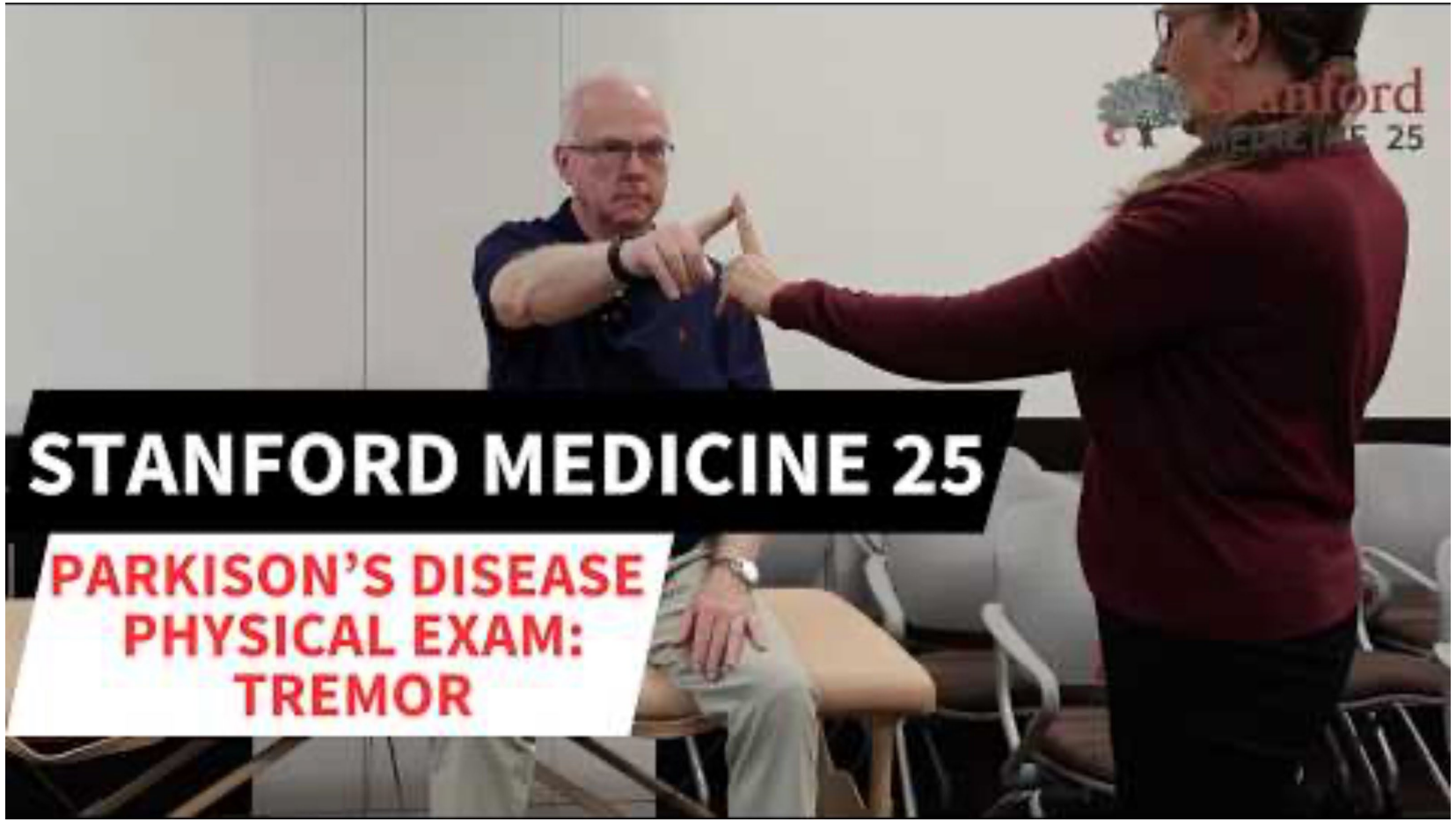
Starts on one side of the body first

Affects older persons (6-7th decade of life)



Resting Tremor

- Present when relaxed, distracted, or while walking
  - ➢ Goes away when using hands
- “Pill rolling” between fingers and thumb



Bradykinesia

- Essential feature!
- Movements get smaller and slower
  - Especially with repeating the same movement

Rigidity

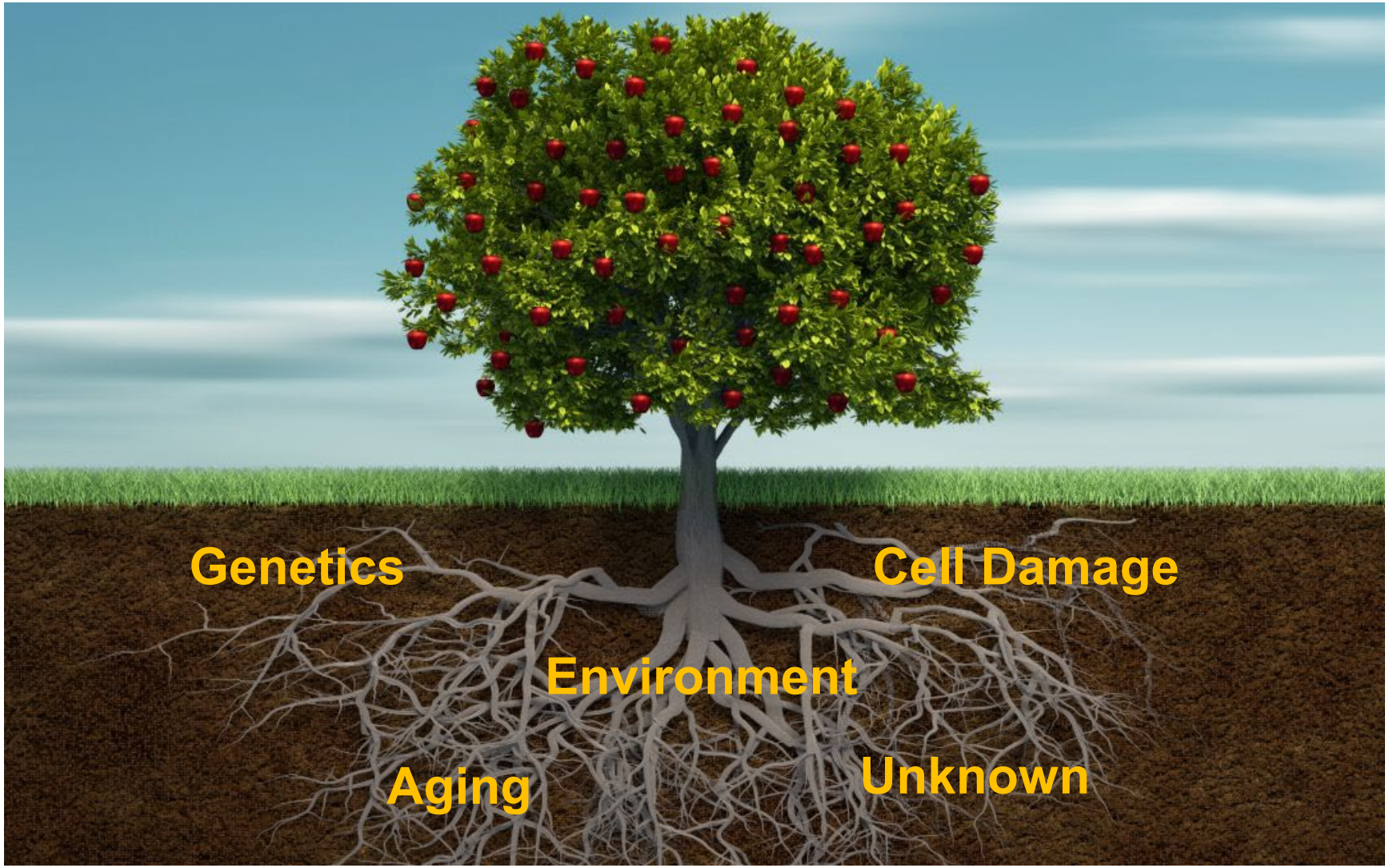
Tightness and stiffness in muscle

“Cogwheeling” = “notch-like” movements due to tremor

Shuffling Feet / Stooped Posture

- Smaller and shorter steps
  - Feet “shuffle”
- Arms do not swing as much
- Lean forward, “stooped”

What Causes Parkinson's Disease?



What Causes Parkinson's Disease?

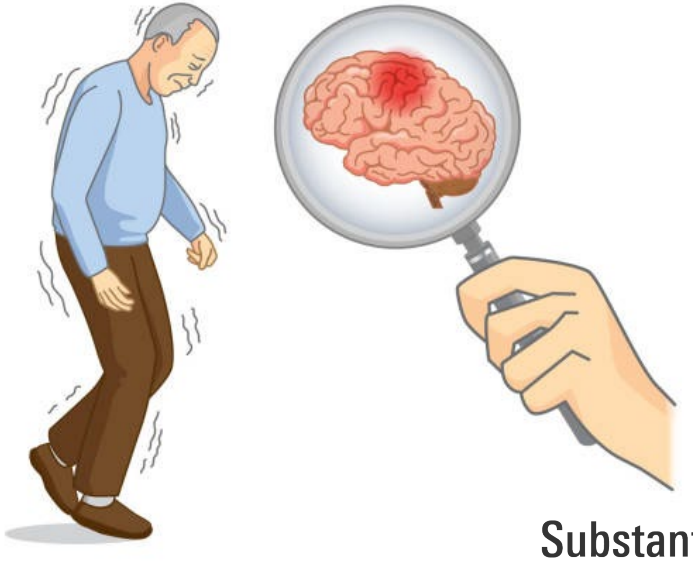
All of these combine in different amounts in every person…

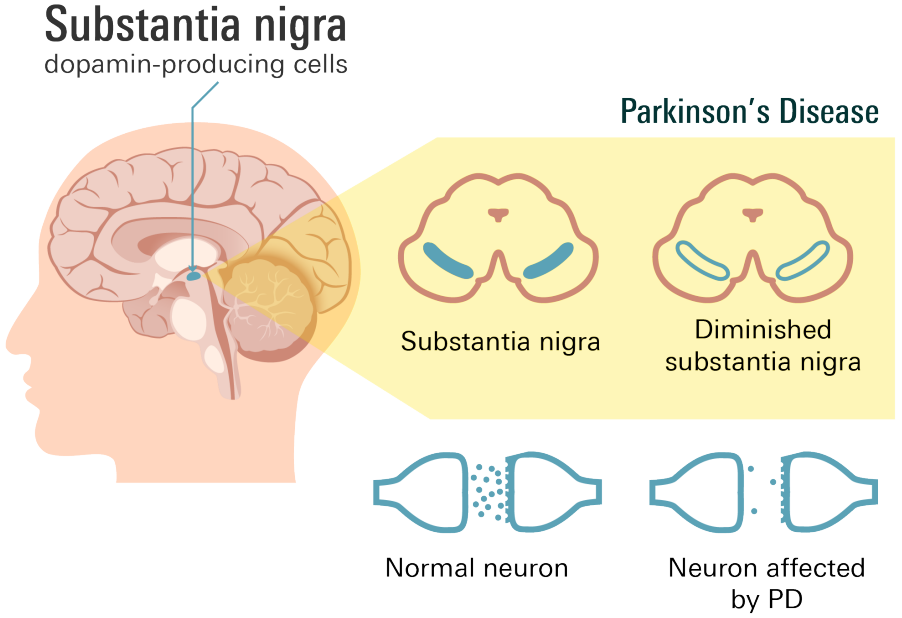
↓

Protein called **alpha synuclein** builds up into clumps

↓

Clumps kill off dopamine brain cells





How do we diagnose PD?

Clinical Diagnosis!

- Symptoms you describe
- Your neurological exam
- How things progress over time
- Response to treatment (Carbidopa/Levodopa)

How do we diagnose PD?

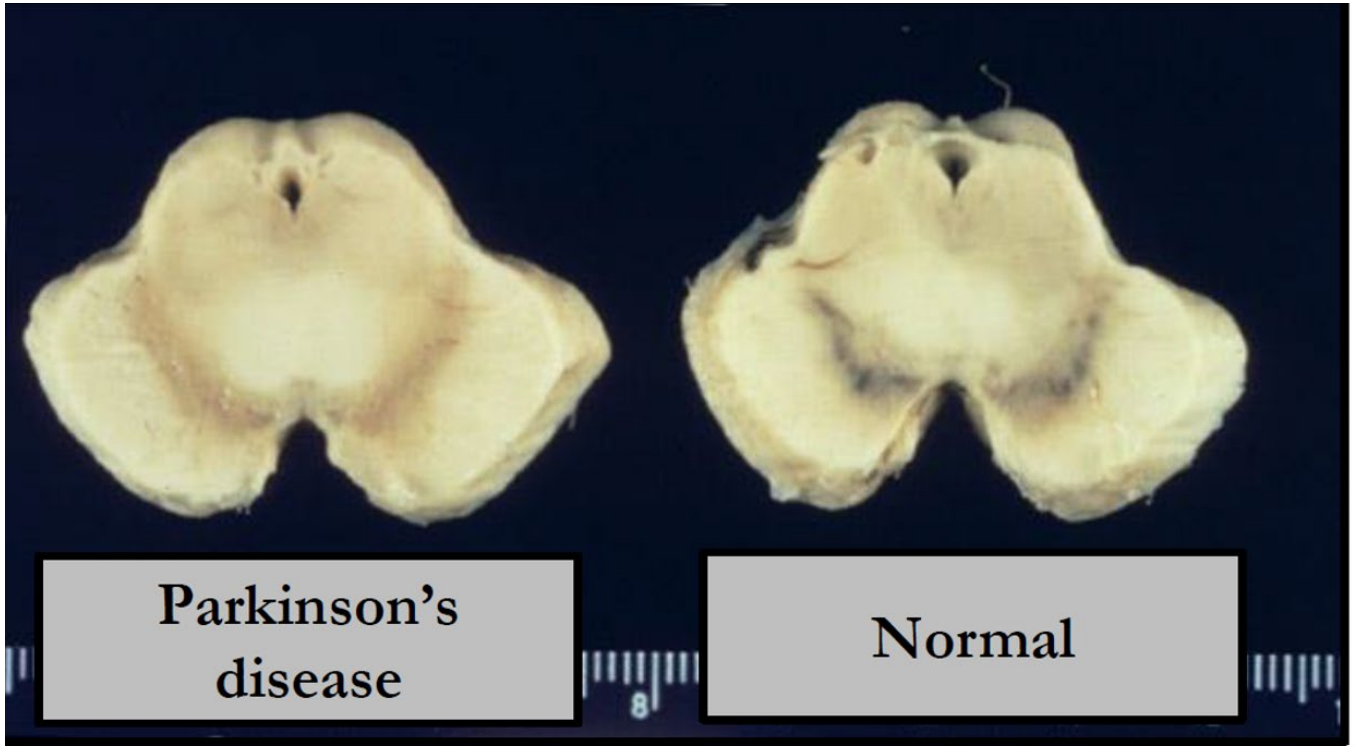
- No lab or imaging test can prove the diagnosis
- Some tests help support our suspicion

  → not required

Gold standard

(only way to know for sure):

Brain Autopsy



How do we diagnose PD?

- Your primary care doctor is on the front lines
- Diagnosis is best made by a Movement Disorders Neurologist
  - ***84% accurate (when compared to brain autopsies)***
  - Less accurate with a General Neurologist

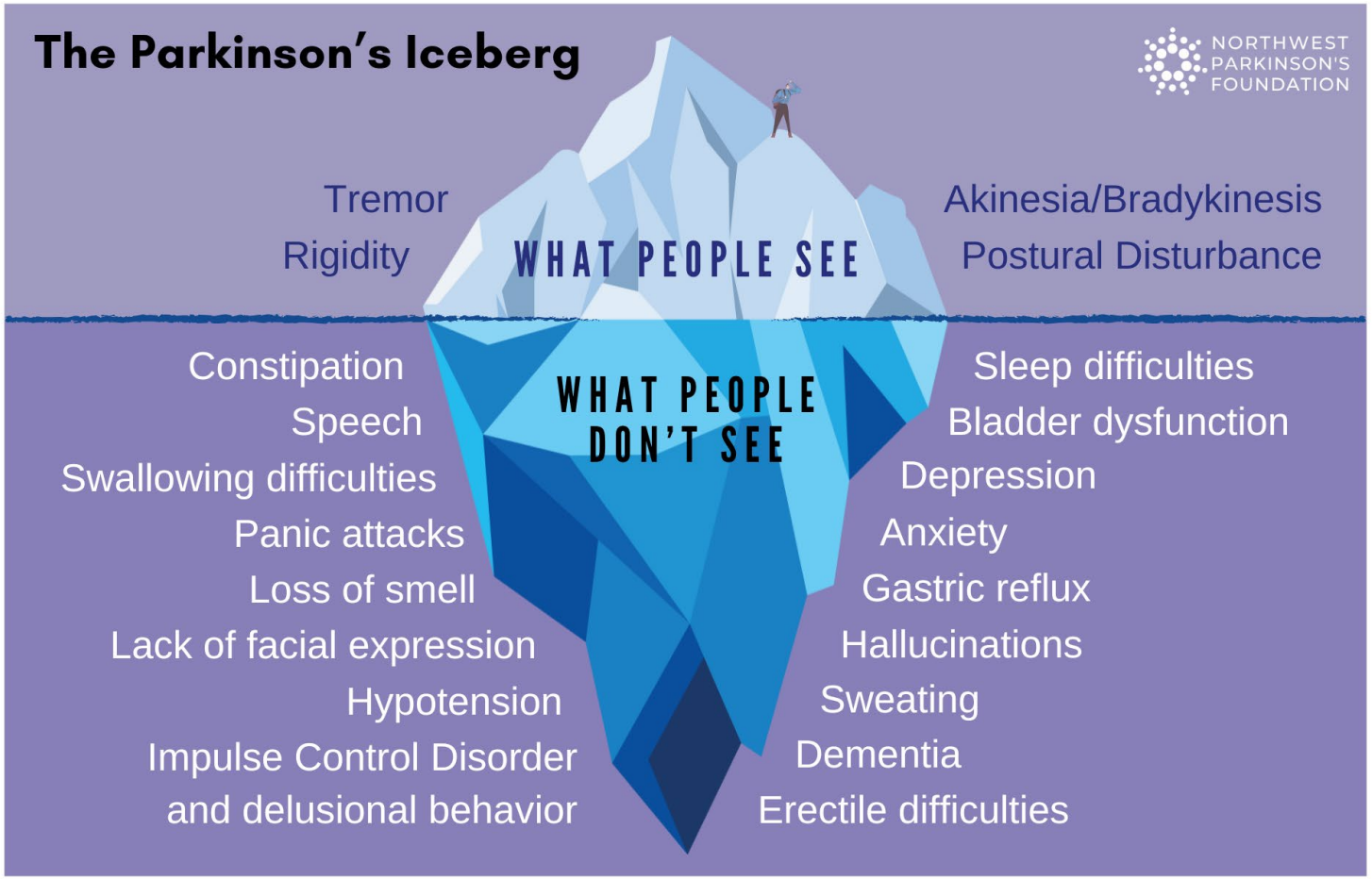
Quick Sidenote: What's a Movement Disorders Neurologist?

	Specialty Training	Fellowship Training	Diseases Seen	Procedures Offered
General Neurologist	4 years of medical school + 4 years of	None	Everything! Parkinson's Disease, Strokes, Epilepsy, Migraines, Neuropathy, and	Usually none for Parkinson's Some do Botox, may program DBS

Why is it so hard to diagnose?

PD is complicated!

- **Every patient has different symptoms**
- Every patient progresses at a difference pace
- Treatment response can be different



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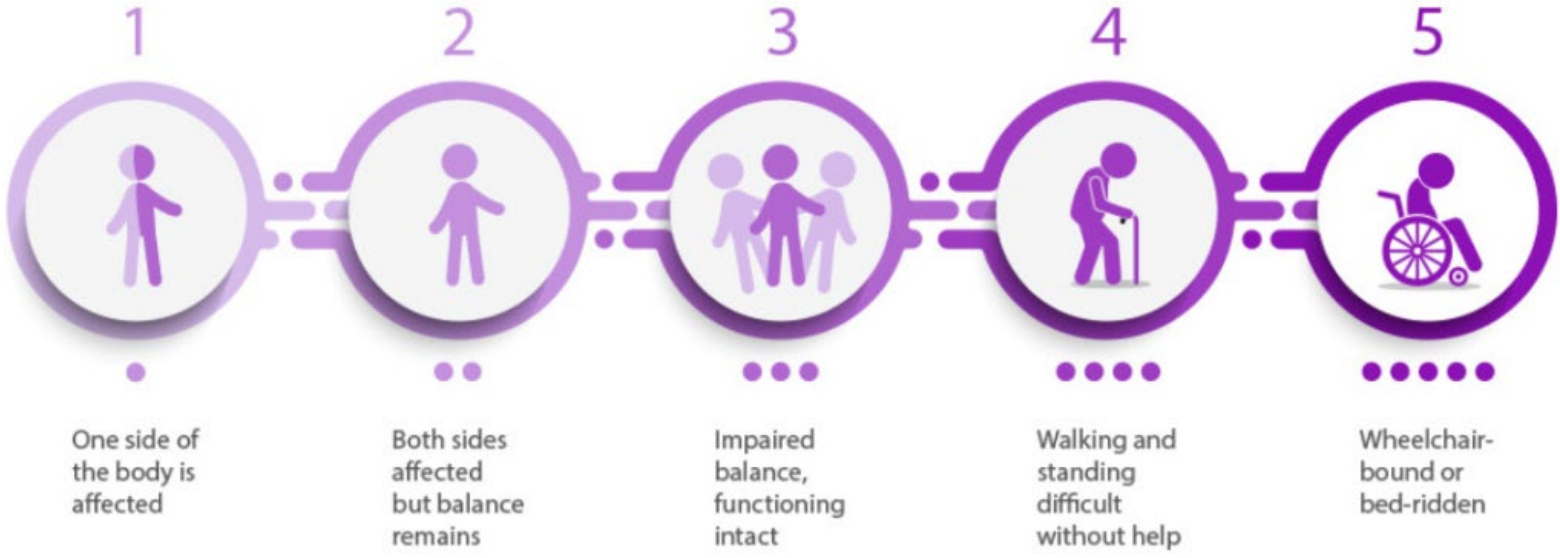
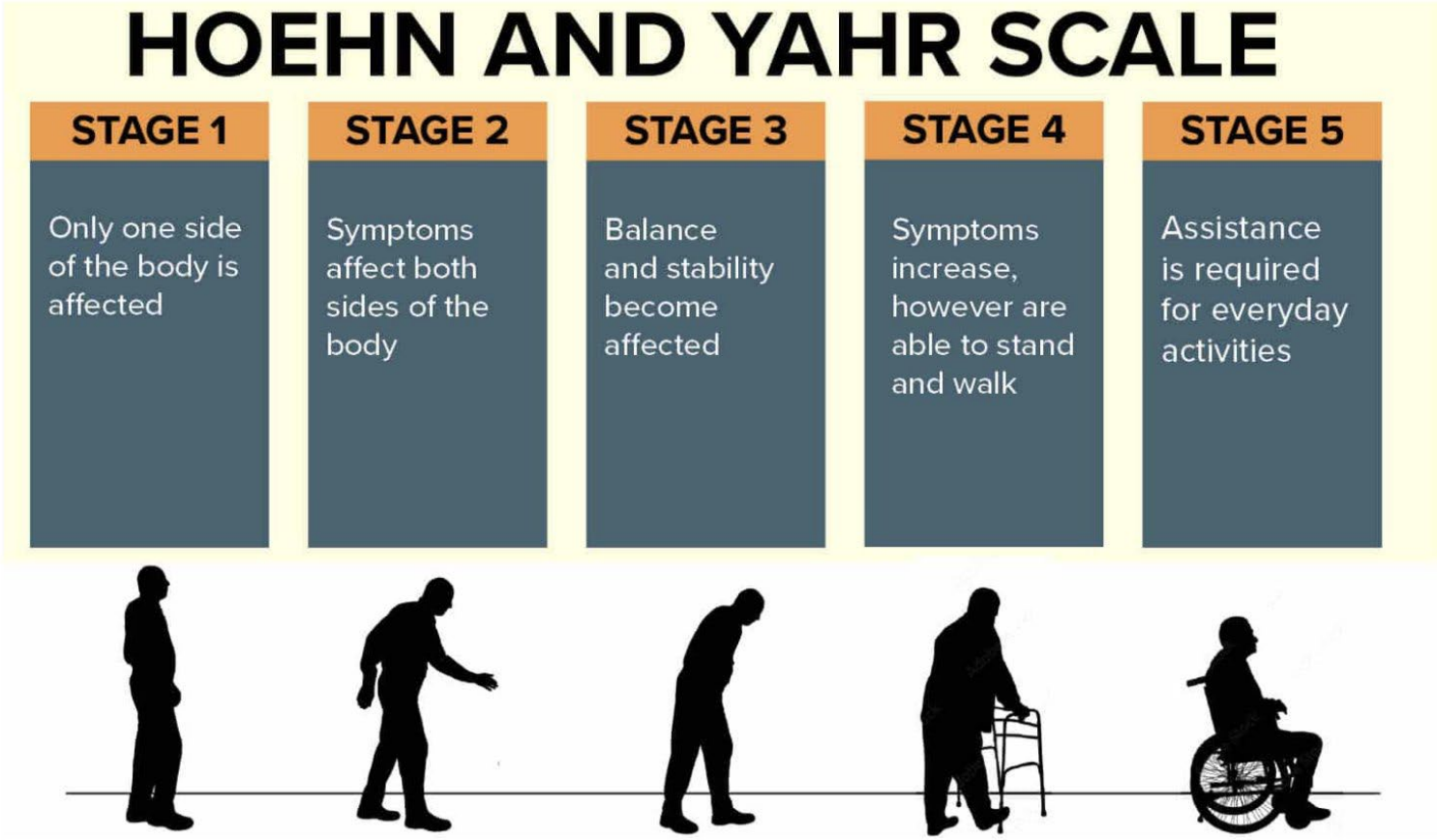


What Stage Am I?

- Used for motor (physical symptoms) only
- Progression is NOT linear
- It's different in every person

"Stage" is best used for research purposes



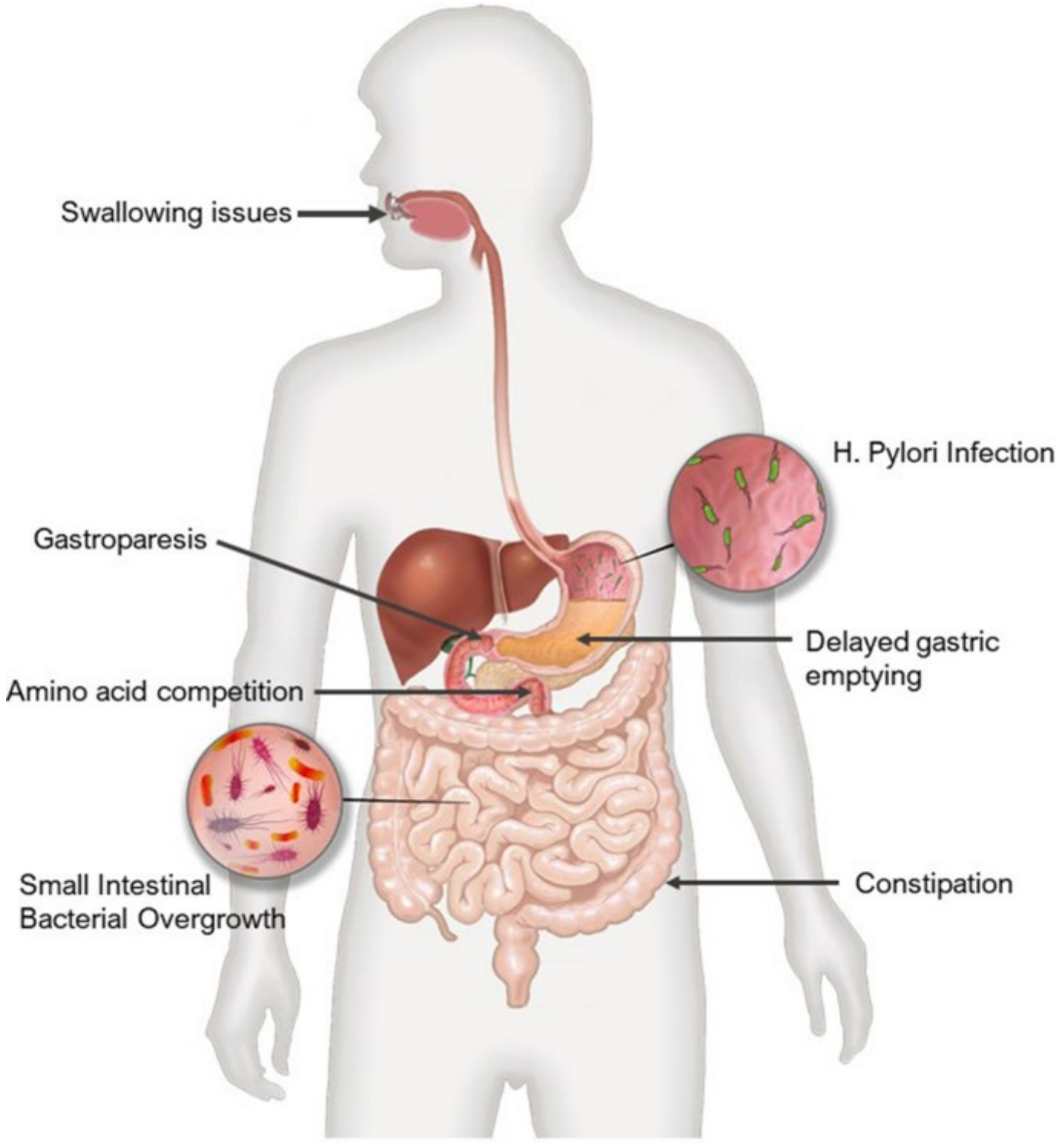
You set your own pace with PD!

Don’t forget:
EXERCISE SLOWS PD DOWN!

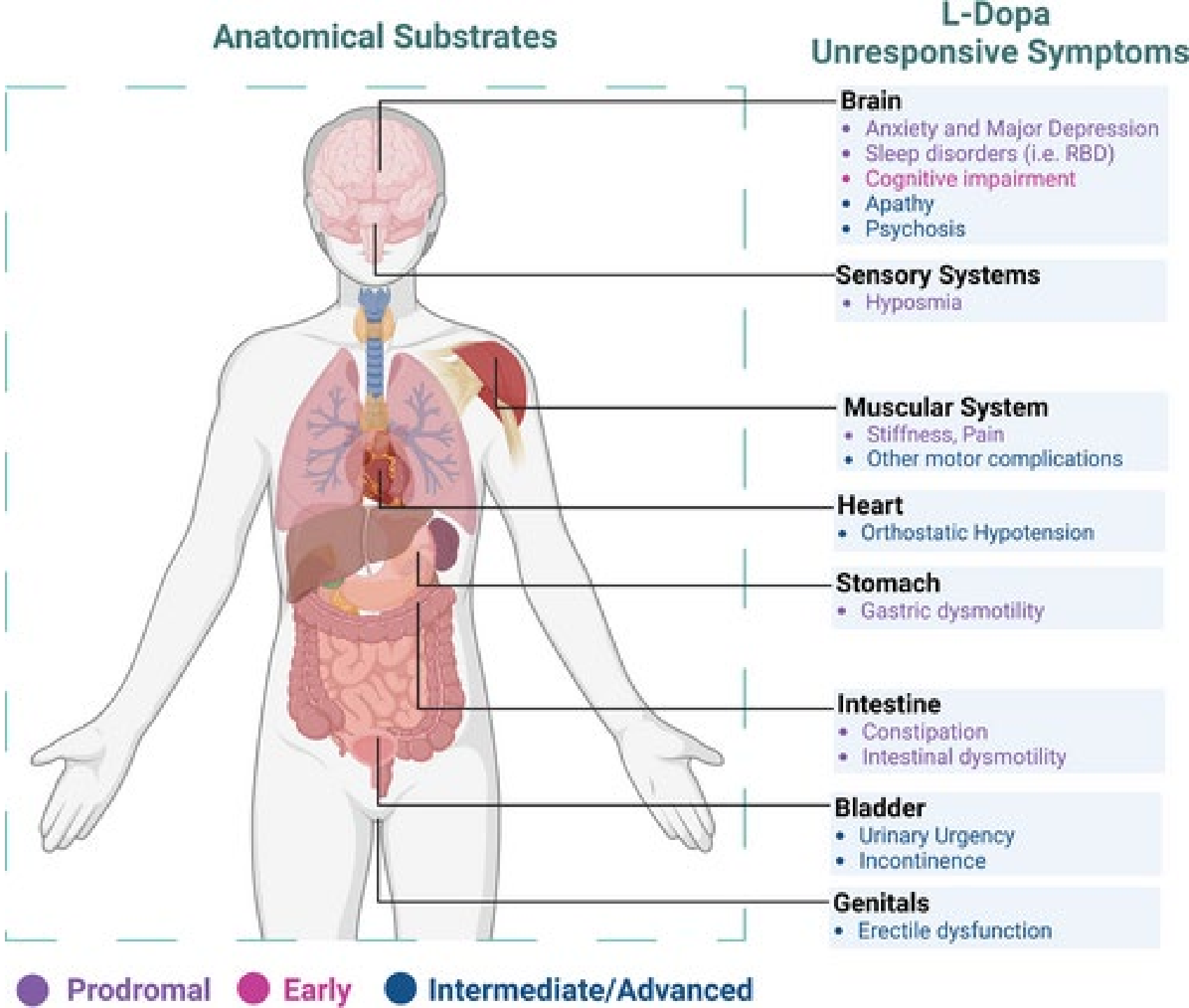
Why is it so hard to diagnose?

PD is complicated!

- Every patient has different symptoms
- Every patient progresses at a difference pace
- **Treatment response can be different**



- Different dose needs
- Swallowing problems
- Slowed gut movement
- Absorption problems
- Nausea
- Low blood pressure



Diagnostic Criteria

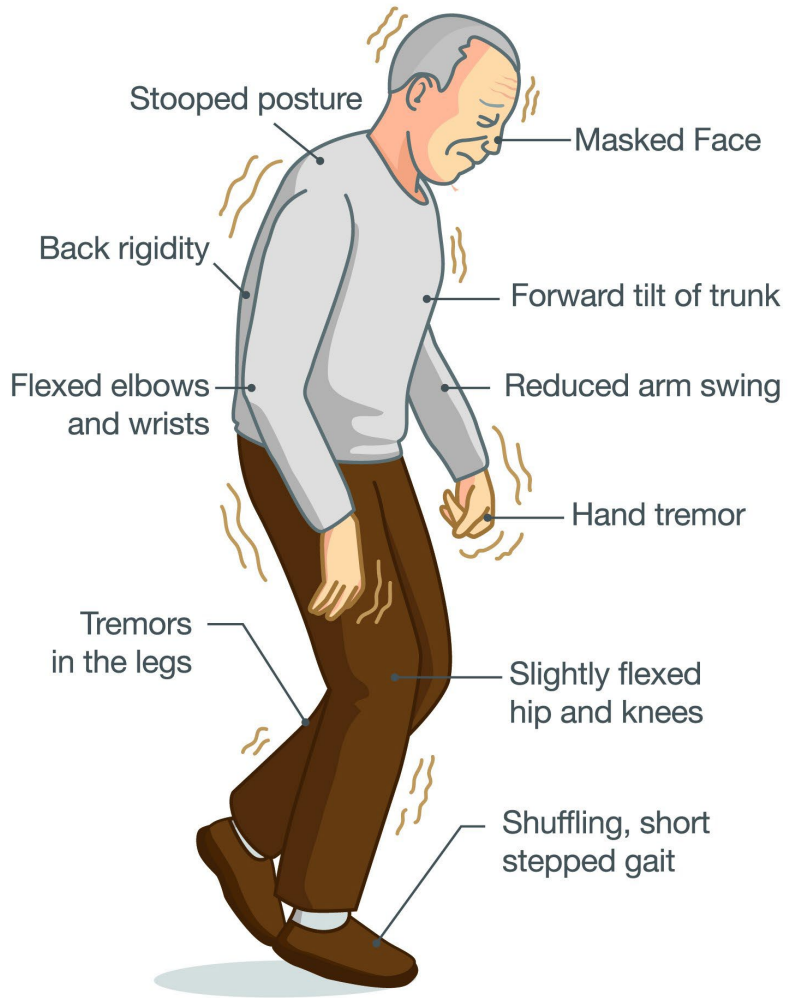
Movement Disorders Society (MDS) 2015:

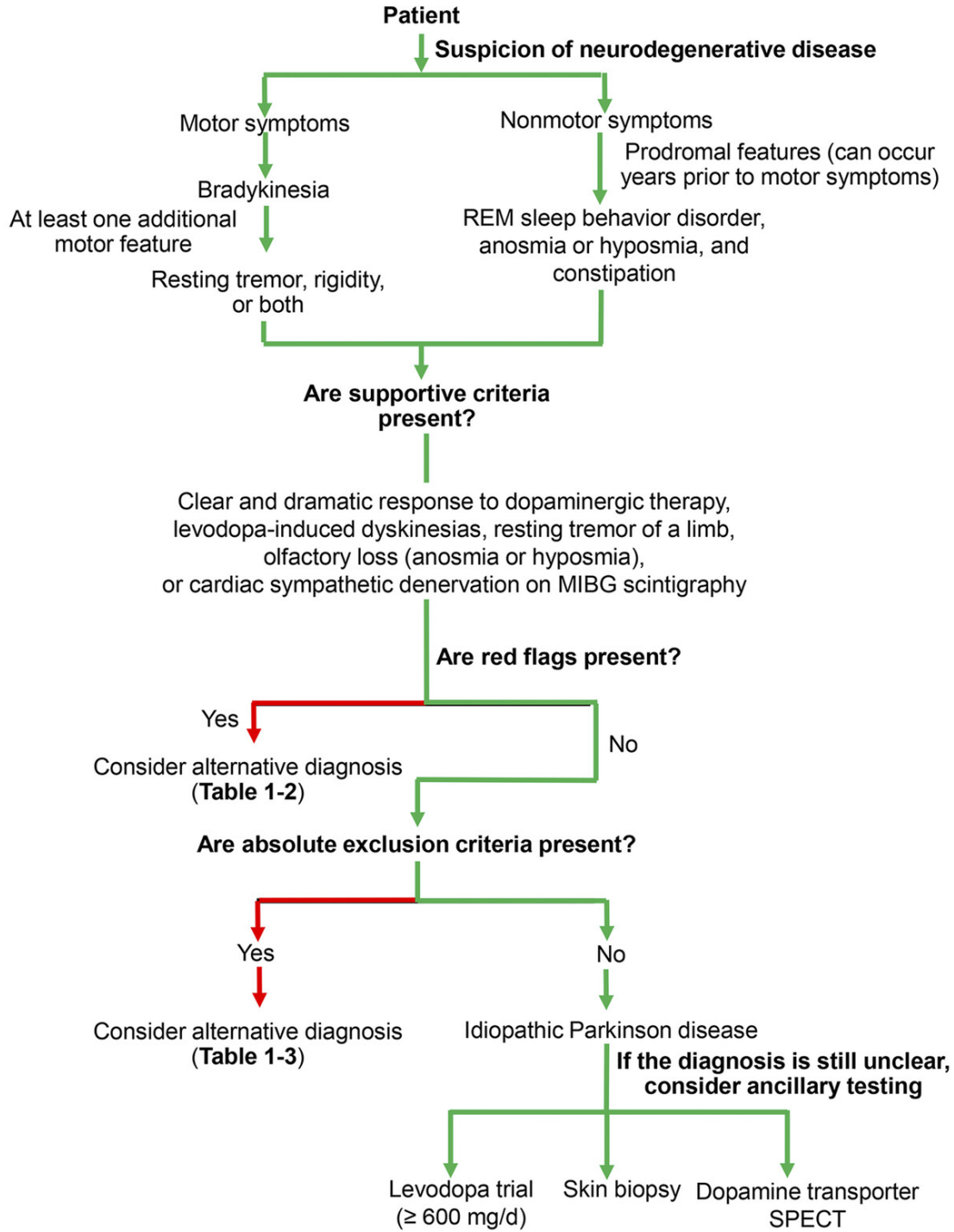
Bradykinesia PLUS
Tremor AND/OR Rigidity

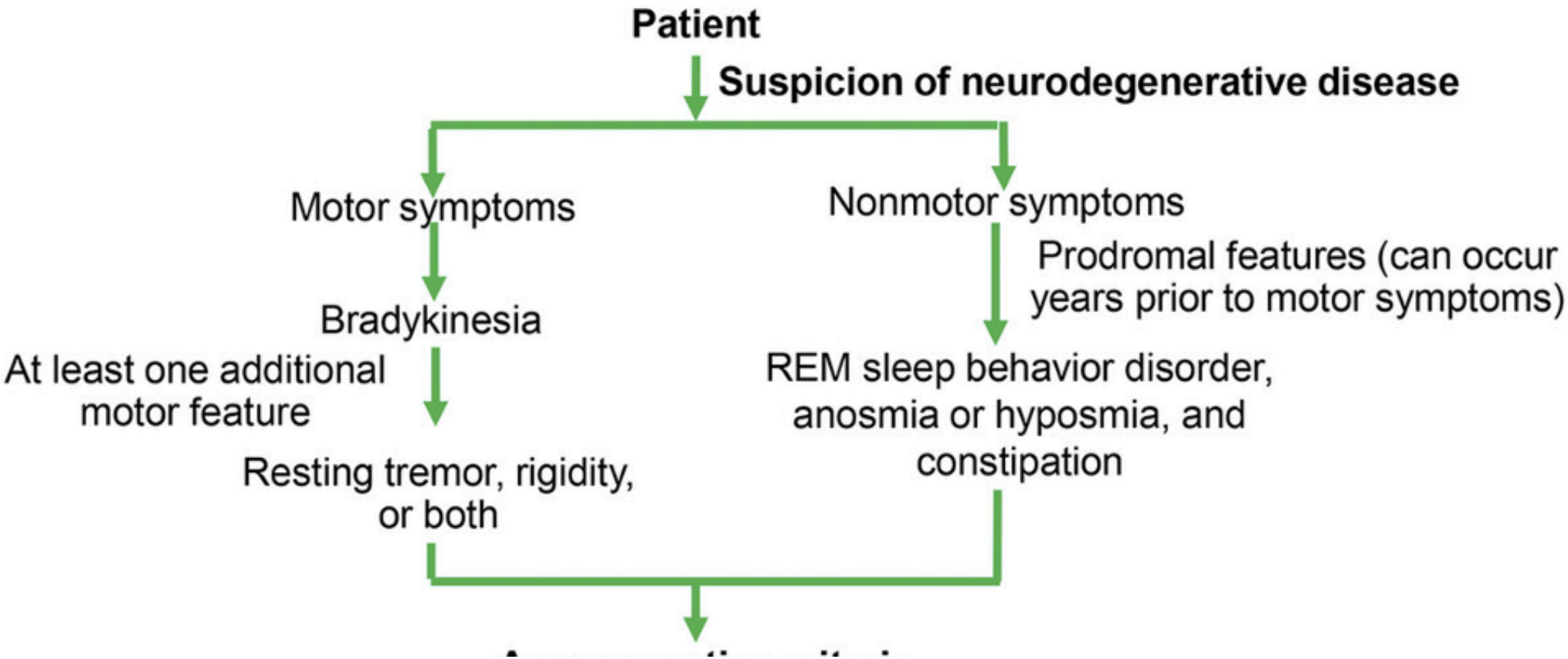
+/- Early “non-motor” signs: REM Behavior Disorder (RBD), change in sense of smell, constipation

Supportive features:

- Response to levodopa
- Dyskinesias (!!)
- Loss of sense of smell




Patient
Suspicion of neurodegenerative disease
Motor symptoms
Nonmotor symptoms
Prodromal features (can occur years prior to motor symptoms)
Bradykinesia
At least one additional motor feature
REM sleep behavior disorder, anosmia or hyposmia, and constipation
Resting tremor, rigidity, or both
Are supportive criteria present?
Clear and dramatic response to dopaminergic therapy, levodopa-induced dyskinesias, resting tremor of a limb, olfactory loss (anosmia or hyposmia), or cardiac sympathetic denervation on MIBG scintigraphy
Are red flags present?
Yes
No
Consider alternative diagnosis (Table 1-2)
Are absolute exclusion criteria present?
Yes
No
Consider alternative diagnosis (Table 1-3)
Idiopathic Parkinson disease
If the diagnosis is still unclear, consider ancillary testing
Levodopa trial (≥ 600 mg/d)
Skin biopsy
Dopamine transporter SPECT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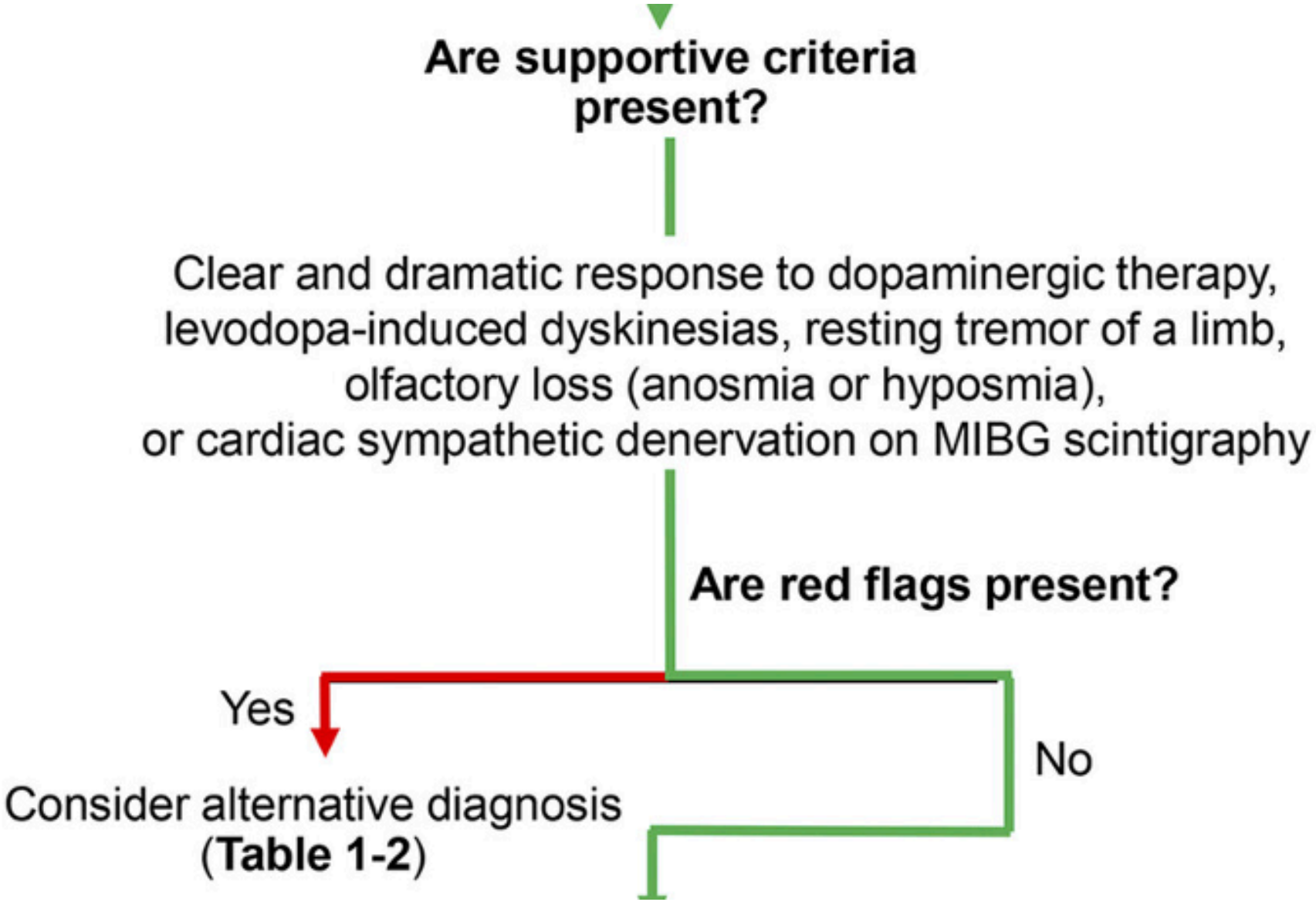
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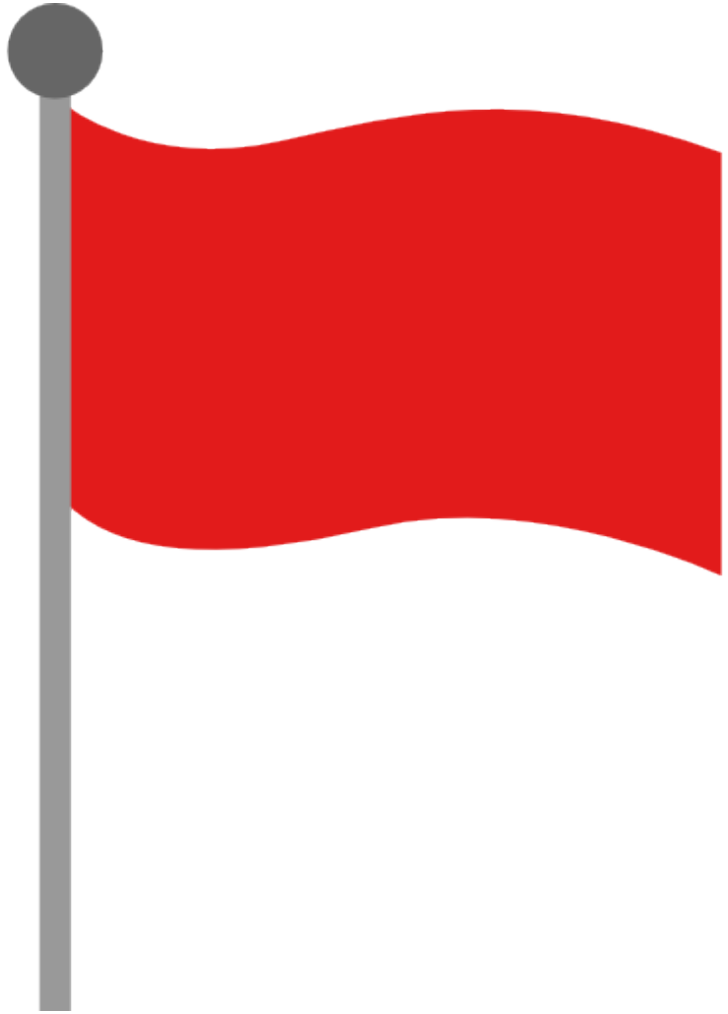
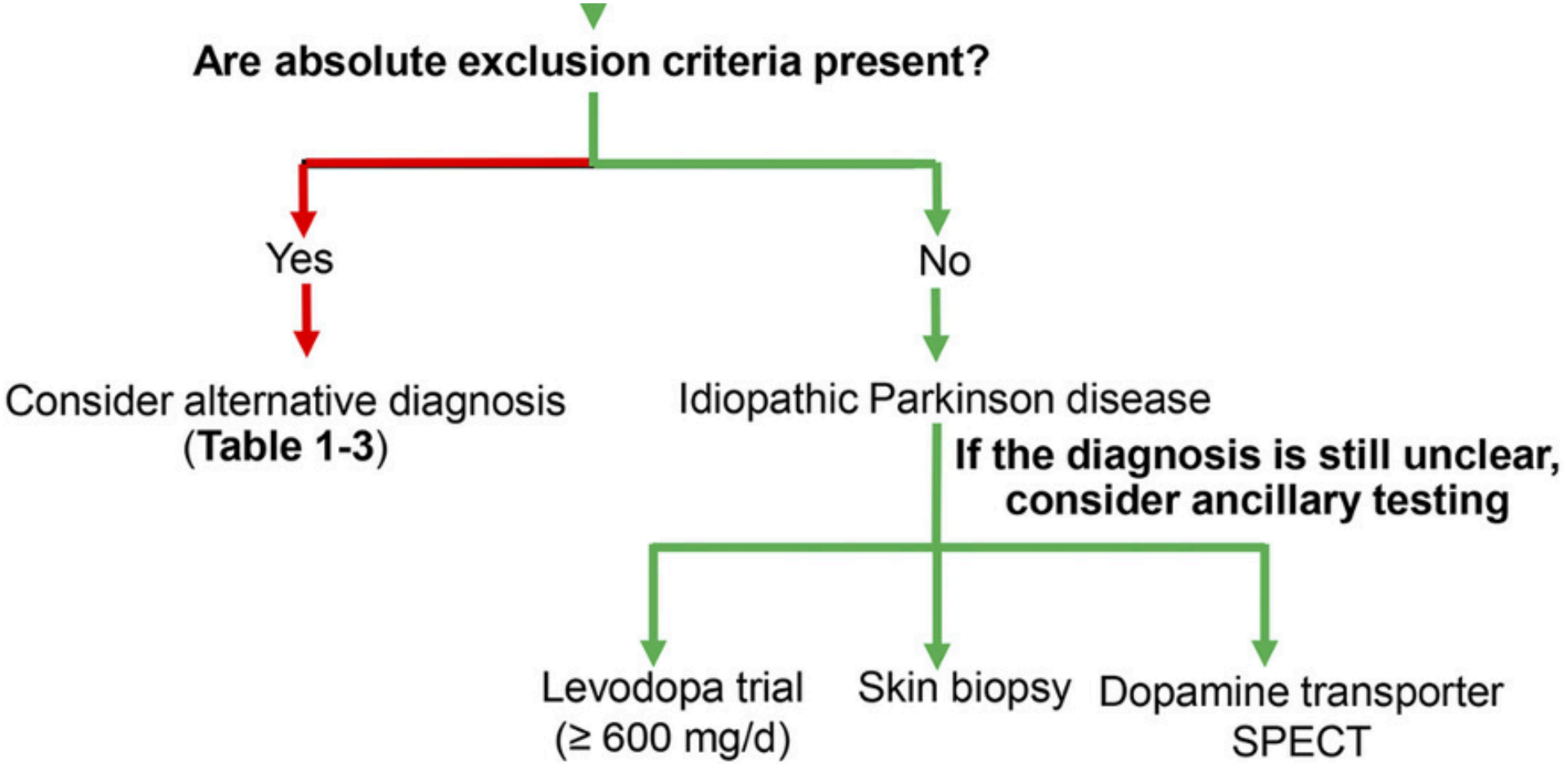
What are the “Red Flags”??

Features that make us consider a different diagnosis



Red Flag Examples:
Rapid progression
Needing a wheelchair within 5 years
Early slurred speech or trouble swallowing
Severe blood pressure issues within 5 years
Repeated falls within 3 years
Absence of nonmotor symptoms
Symptoms on both sides right away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(≥ 600 mg/d)
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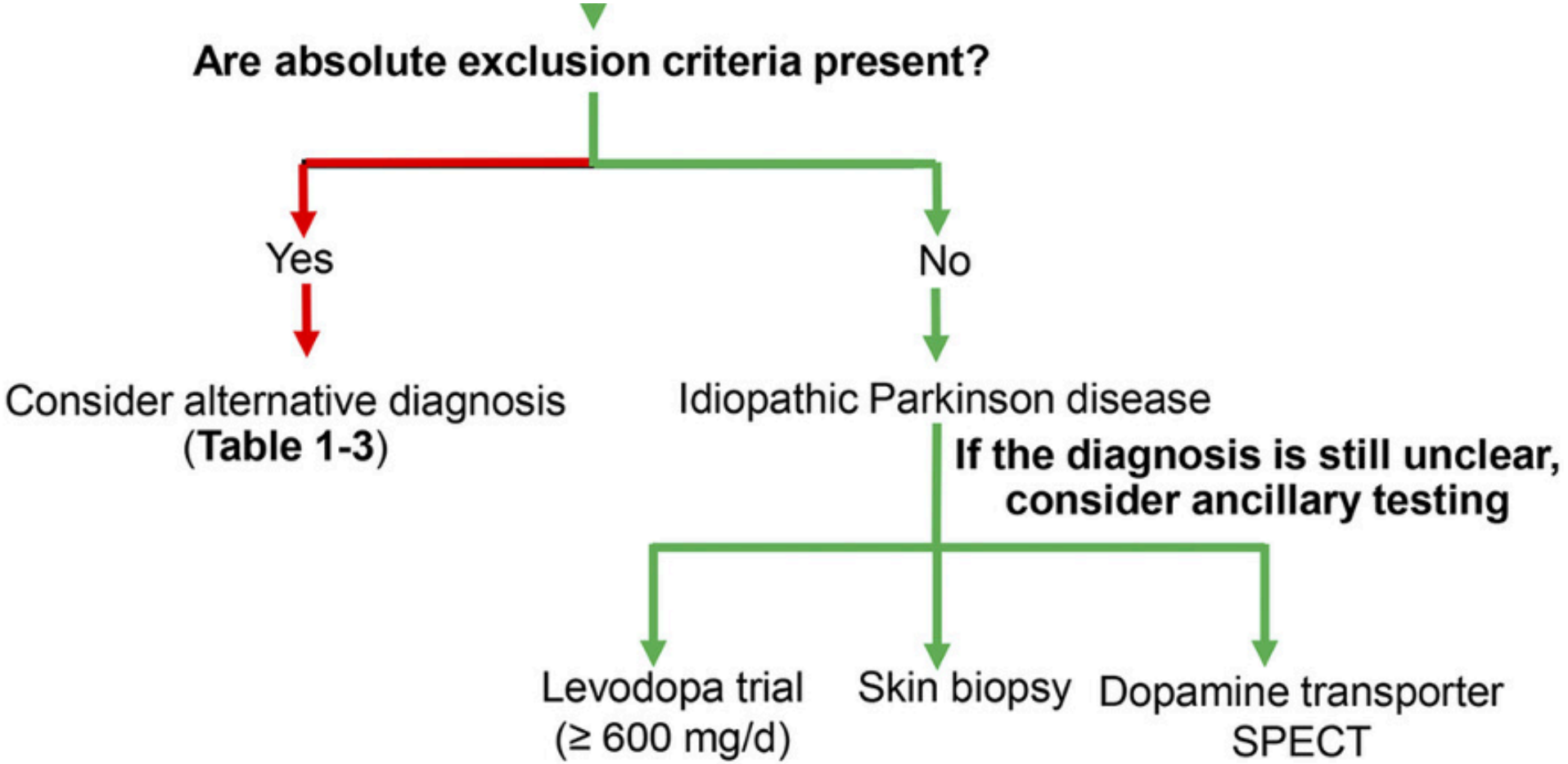
Absolute Exclusion Criteria (ie, who does NOT have PD?)

Exclusion Criteria	Other Possible Diagnosis
Unexplained coordination issues (ataxia)	Multiple System Atrophy (MSA), ataxia caused by something else
Eye movement problems	Progressive Supranuclear Palsy (PSP)
Early behavioral changes or language issues within 5 years	Frontotemporal Dementia (FTD), Alzheimer's Dementia
Use of a dopamine-blocking drug known to mimic Parkinson's	Drug-induced Parkinsonism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”Testing for PD”: Levodopa Trial

- Safe for most people
- Cost effective

Requirement: > 600 mg
(that’s > 6 tablets a day!)

Caveat: Some people still need higher doses than this

How do I know if levodopa is working?

Common benefits:

- Less tremor
- Less stiffness
- Less slowness
- Easier to walk

Less common benefits:

- Easier swallowing
- Faster thinking
- Improved mood & sleep

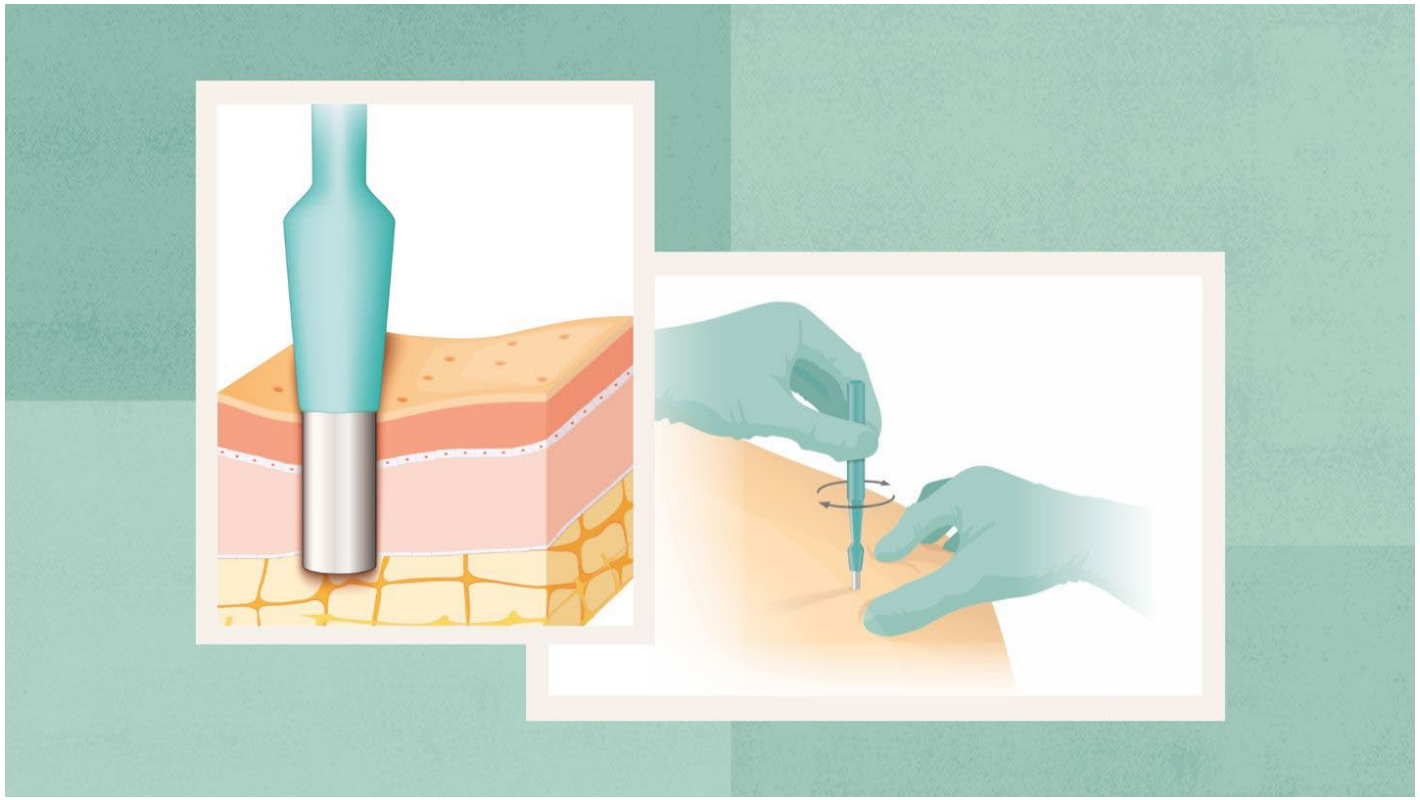
Levodopa Trial Limitations

- Side effects limit dose
  - Nausea
  - Low blood pressures
  - Hallucinations
- ”Better” is hard to measure
- Expectations vary

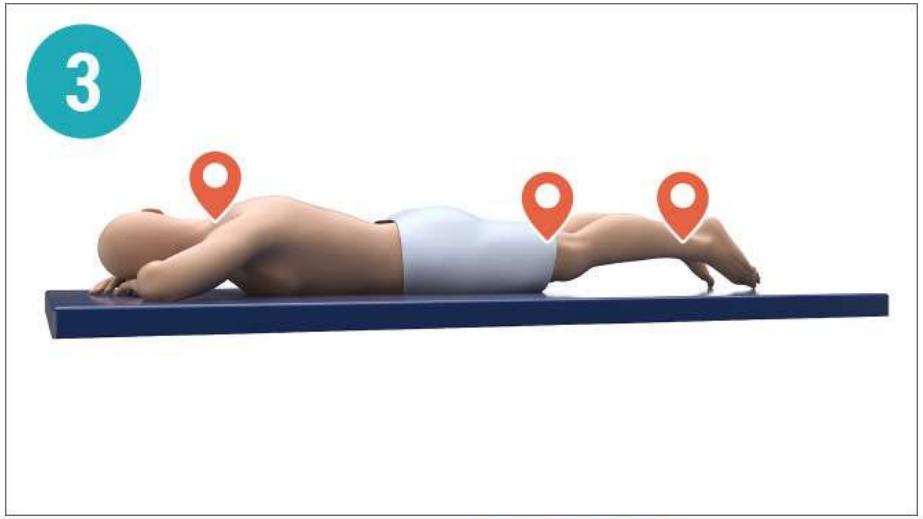
Supportive Tests: Skin Biopsy

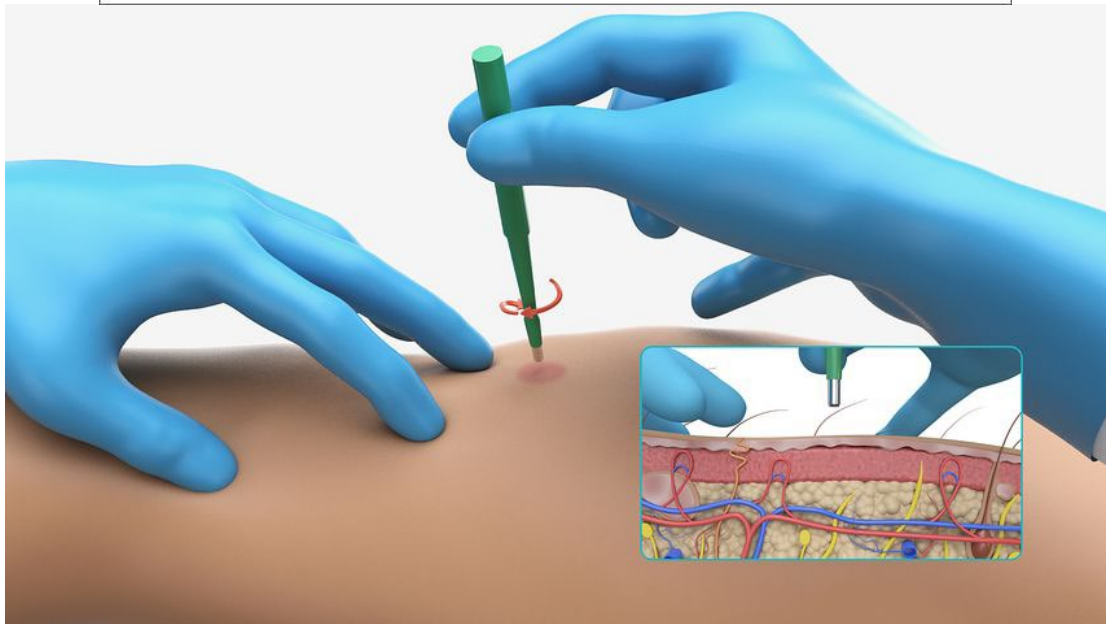
Concept:

- Alpha synuclein clumps can be seen in places besides the brain
  - Skin, cerebral spinal fluid (CSF), intestines, spit glands
- Skin samples are easy to get



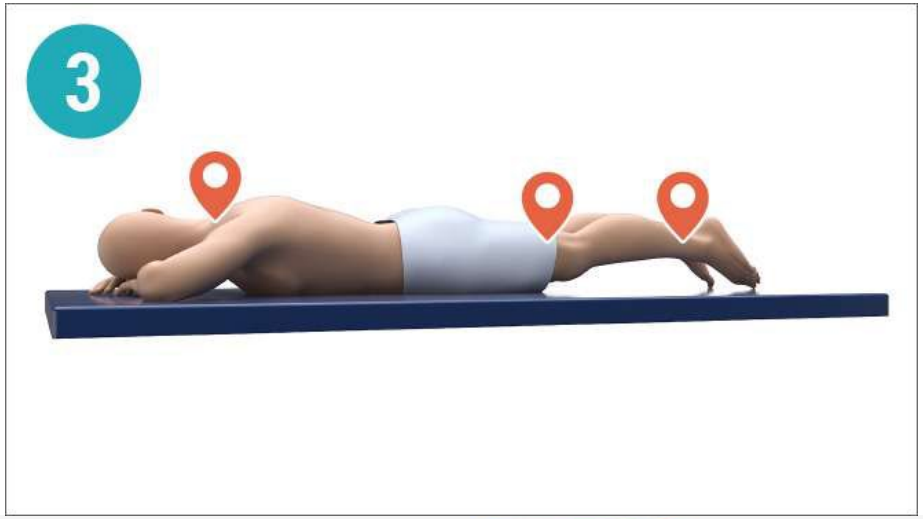
Supportive Tests: Skin Biopsy

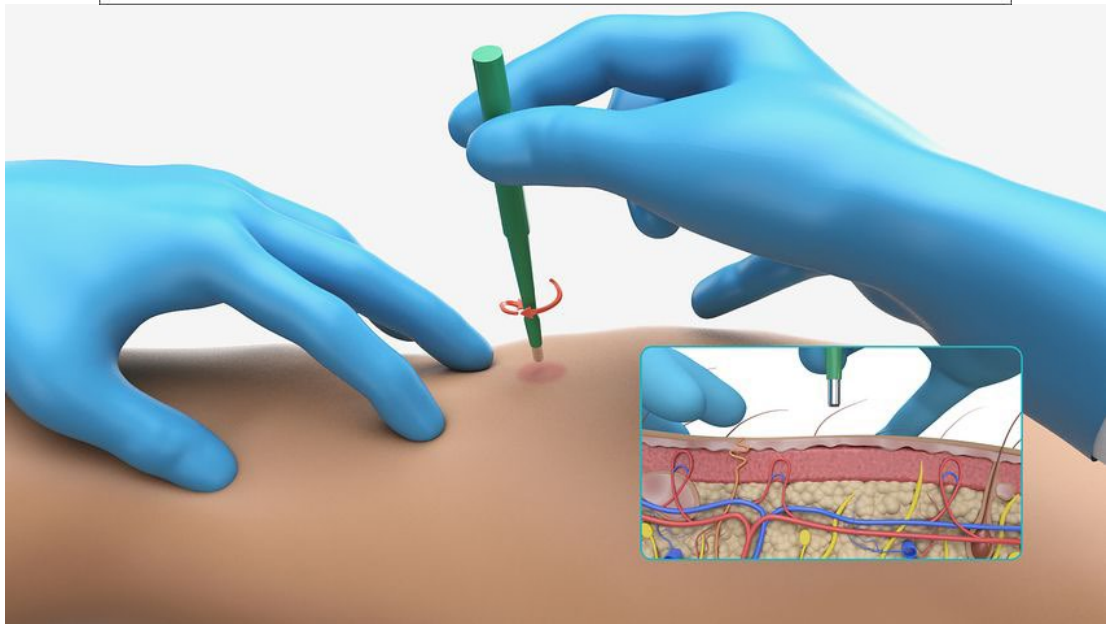




- Three Sites:
  - Shoulder (close to neck)
  - Above knee
  - Above ankle
- Collected in vials
  - Shipped to company
- 4-6 weeks for results

Supportive Tests: Skin Biopsy





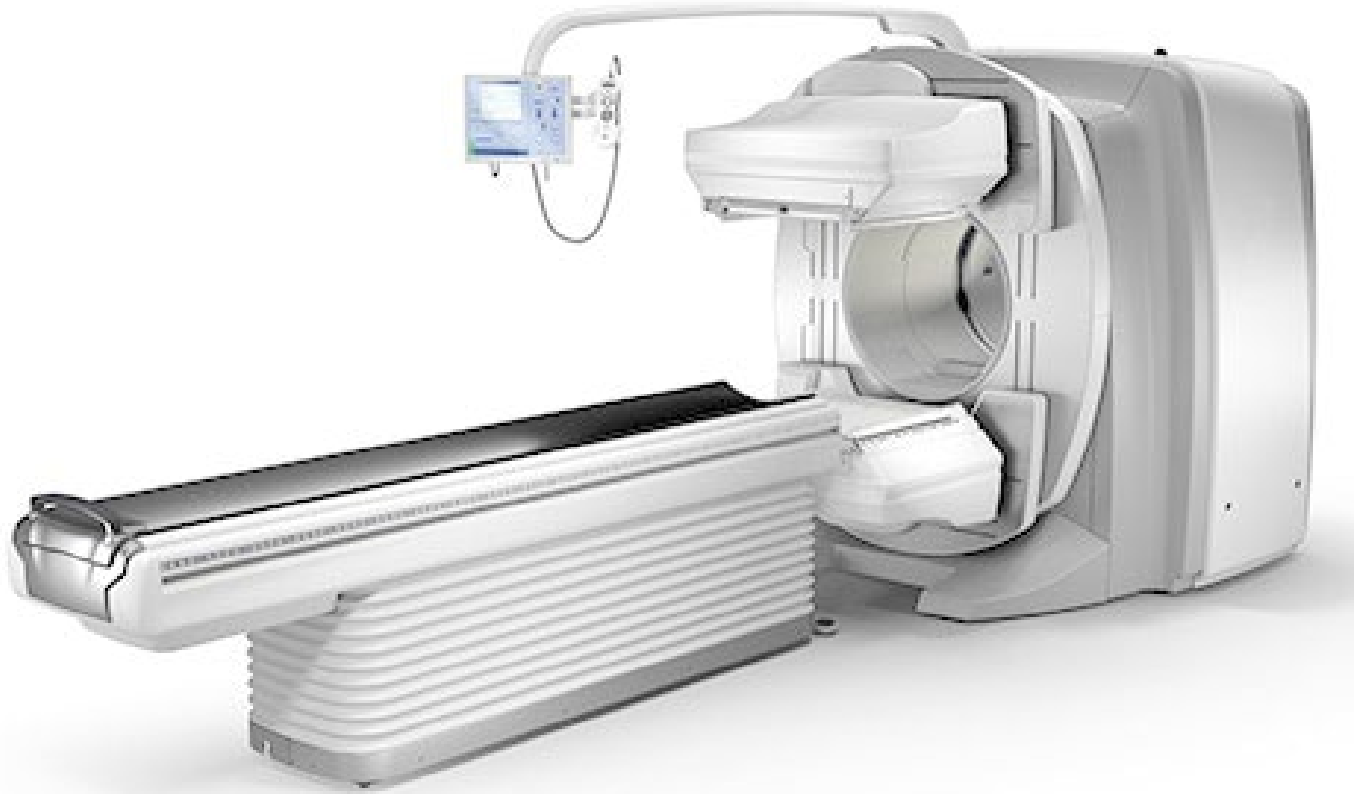
Good at <u>supporting</u> PD

- **Rare false positives**
- **Could have false negatives**

Support Tests: Dopamine Transporter (DAT) Scans

- Nuclear scan
  - *CAT scans and MRIs don't show PD!*

- Tracer injected through IV
  - ➢ Attaches to dopamine transporters in brain
  - ➢ Takes 3-4 hours

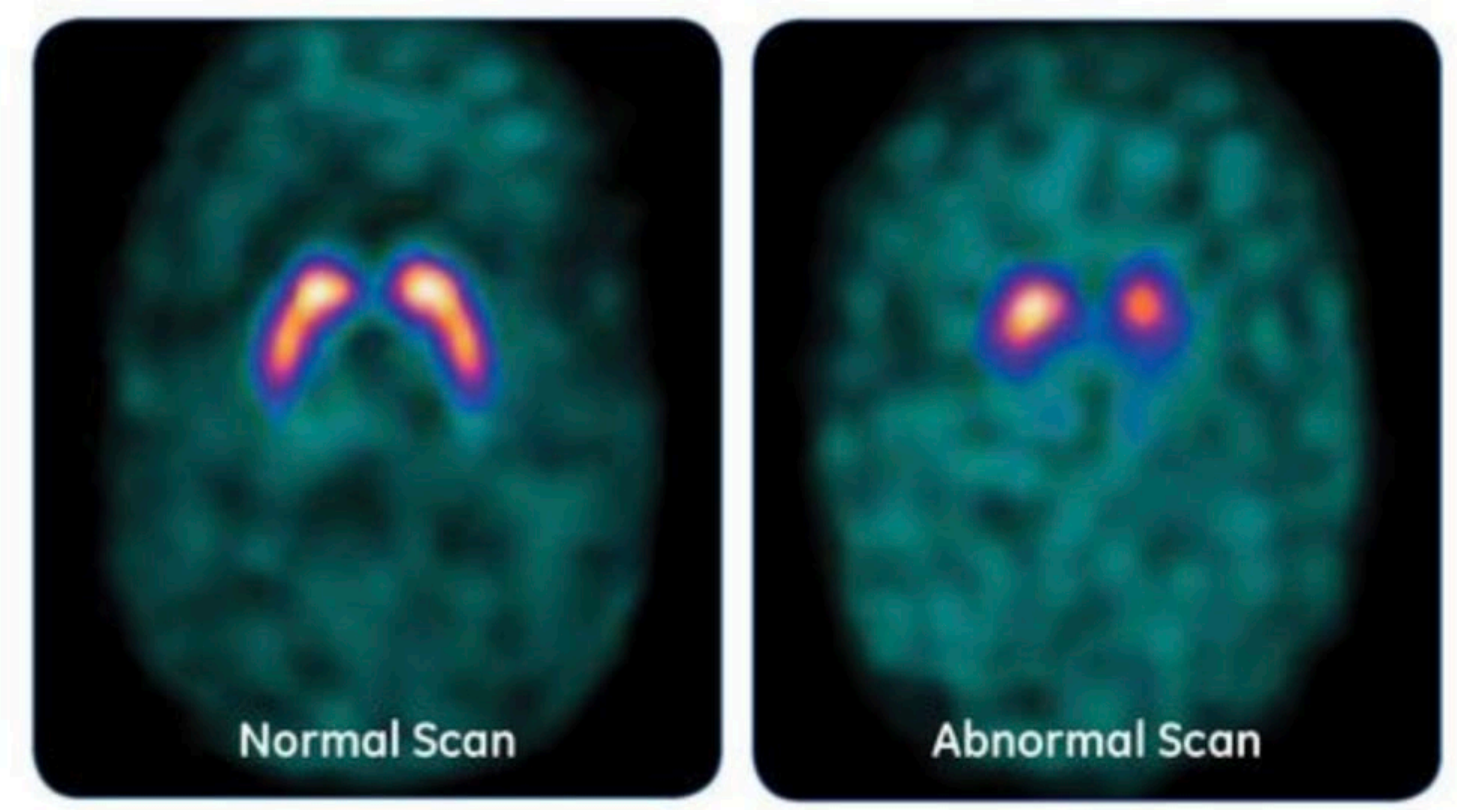


Support Tests: Dopamine Transporter (DAT) Scans

Parkinson's brains have weaker signals

Either abnormal or not:

- Doesn't help stage PD
- Can't measure:
  - progression
  - treatment response



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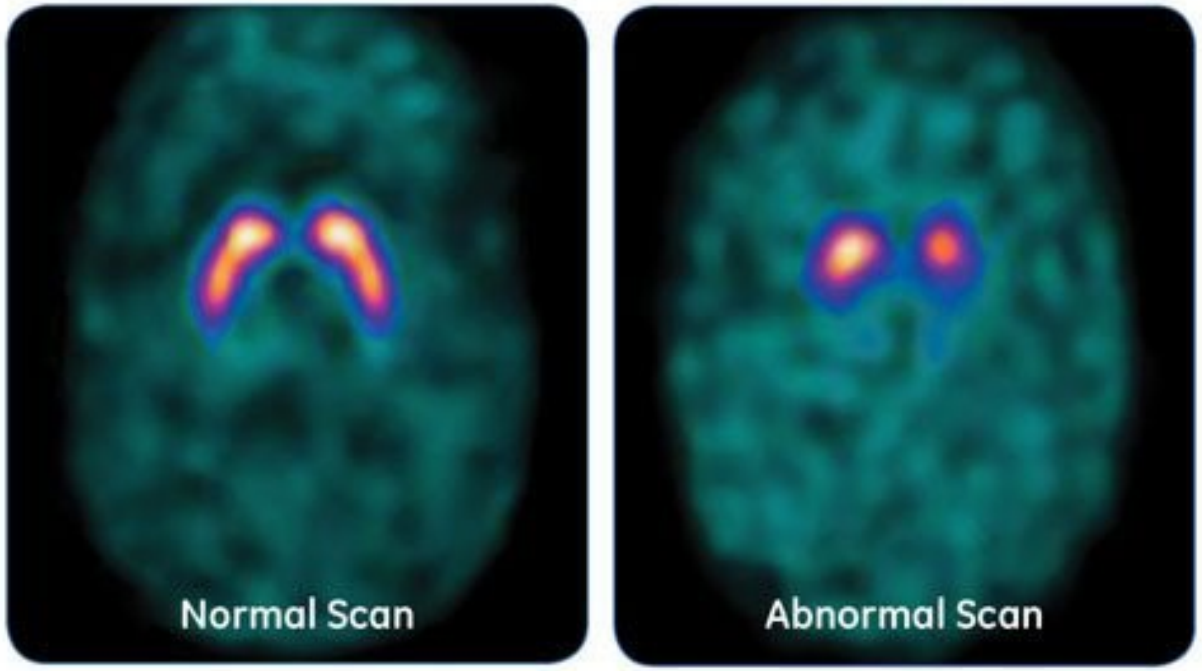


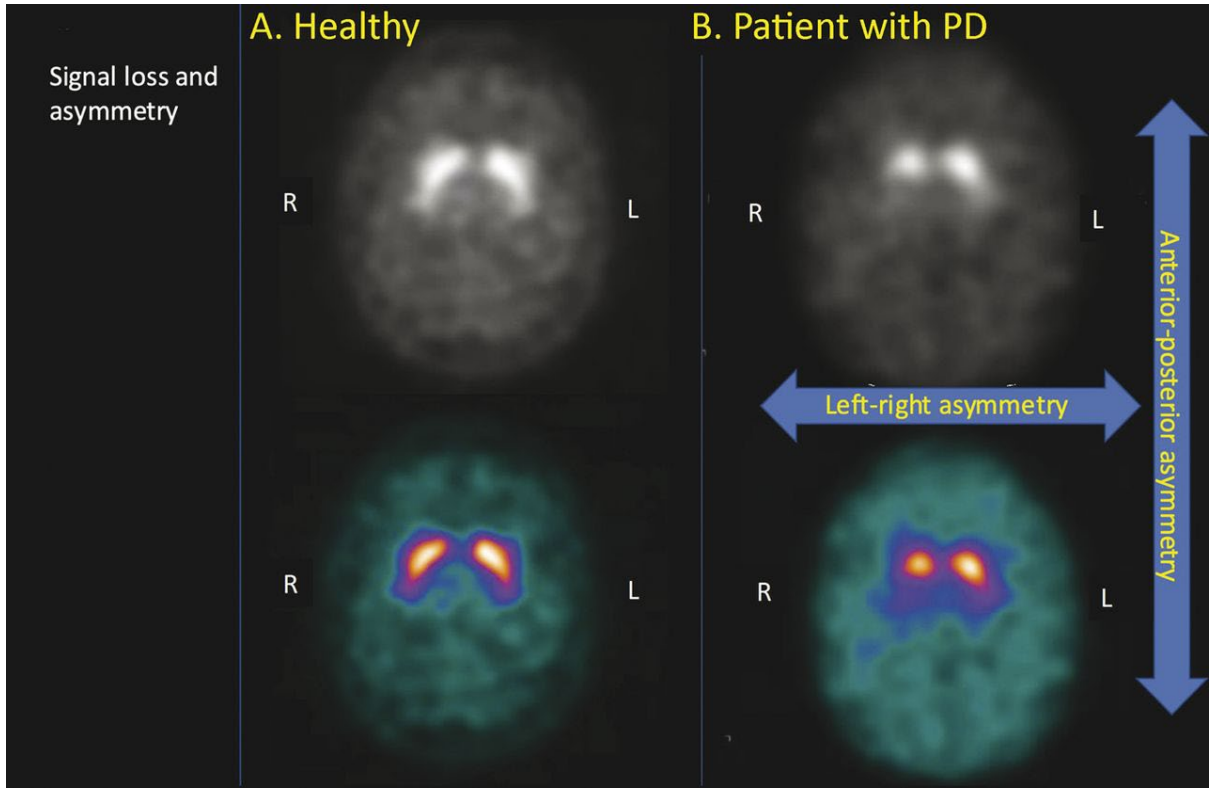
"Comma"-shaped
Possible essential tremor

"Period"-shaped
Possible parkinsonian syndrome

Pitfalls:

- Accuracy not much better than clinical exam
- Other diseases have positive DAT scans
  - ➢ "Parkinson's Plus Syndromes," Dementia with Lewy Bodies

Support Tests: Dopamine Transporter (DAT) Scans



Best Uses for a DAT Scan:

- Presentations with “red flags”
- Lack of progression
- Separate PD from similar tremors
  - Essential Tremor
- Check for PD in people on dopamine blocking drugs that mimic PD

The Future of Diagnosing Parkinson's Disease

Artificial Intelligence (AI)

Potential Roles:

- Predict early signs and symptoms
- Assess disease progression and/or treatment response
- Close geographical barriers (allowing remote exams)

J Parkinsons Dis. 2021; 11(Suppl 1): S117–S122. PMCID: PMC8385515
Published online 2021 Jul 16. Prepublished online 2021 Jun 28. doi: 10.3233/JPD-212545 PMID: 34219671

Will Artificial Intelligence Replace the Movement Disorders Specialist for Diagnosing and Managing Parkinson's Disease?

Matt Landers,[a,*] Suchi Saria,[b,c,d] and Alberto J. Espay[e,*]

Using AI to Diagnose PD

250 patients (PD & controls)

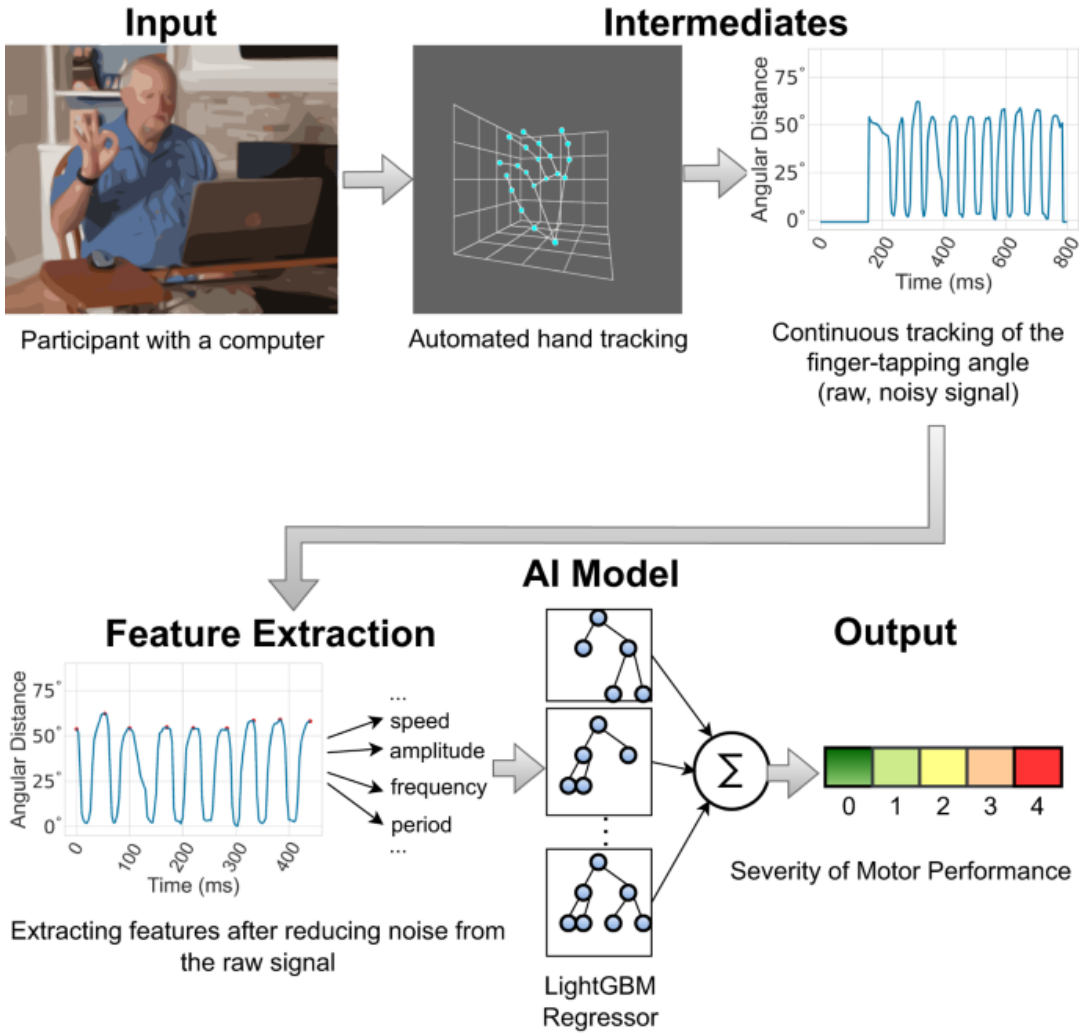
Performed finger tapping in front of a webcam

Compared:

- Expert neurologists
- Non-neurologists
- Computer generated score

Using AI to Diagnose PD

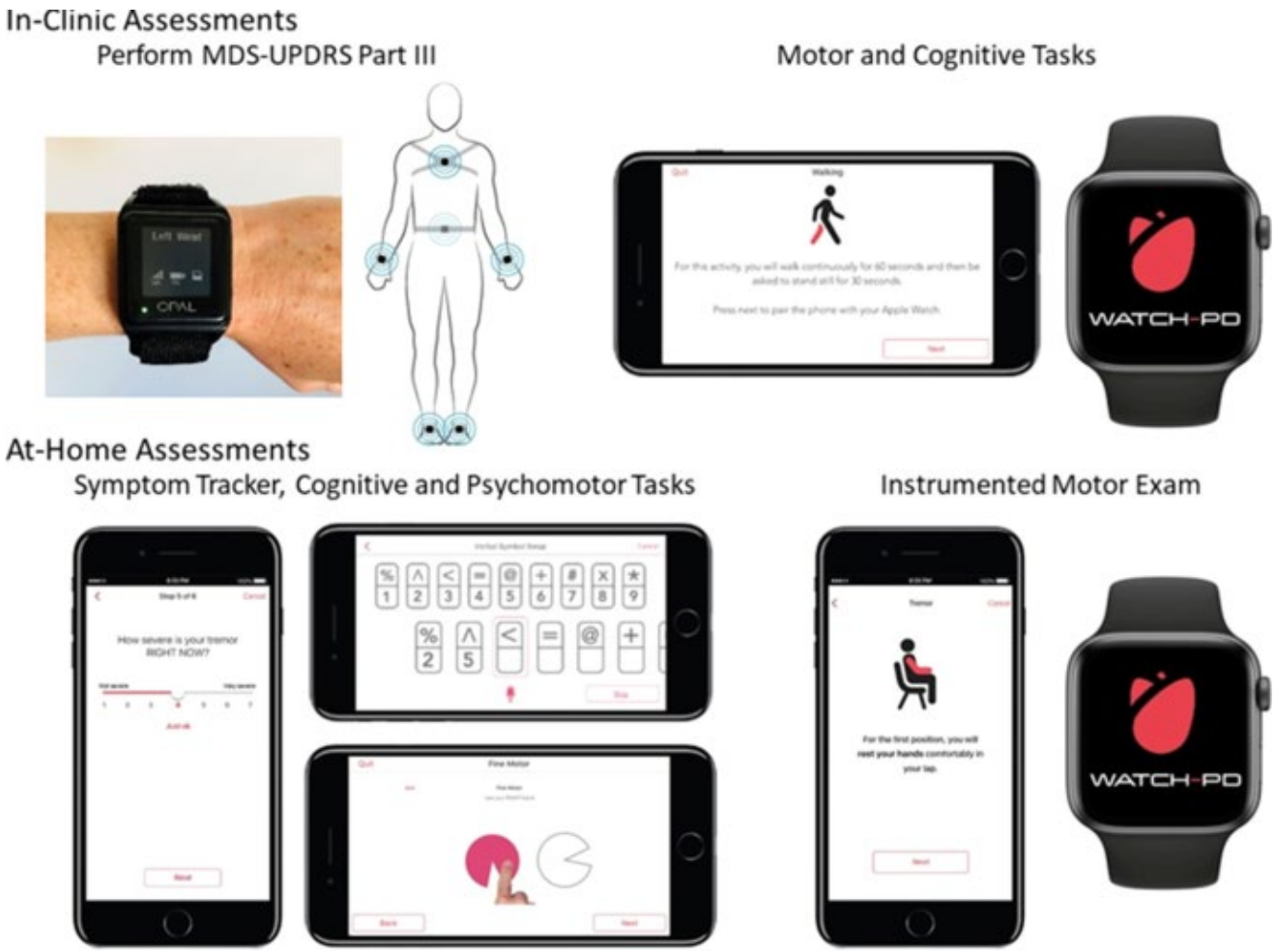
- Neurologists were still the most accurate
- AI outperformed non-neurologists

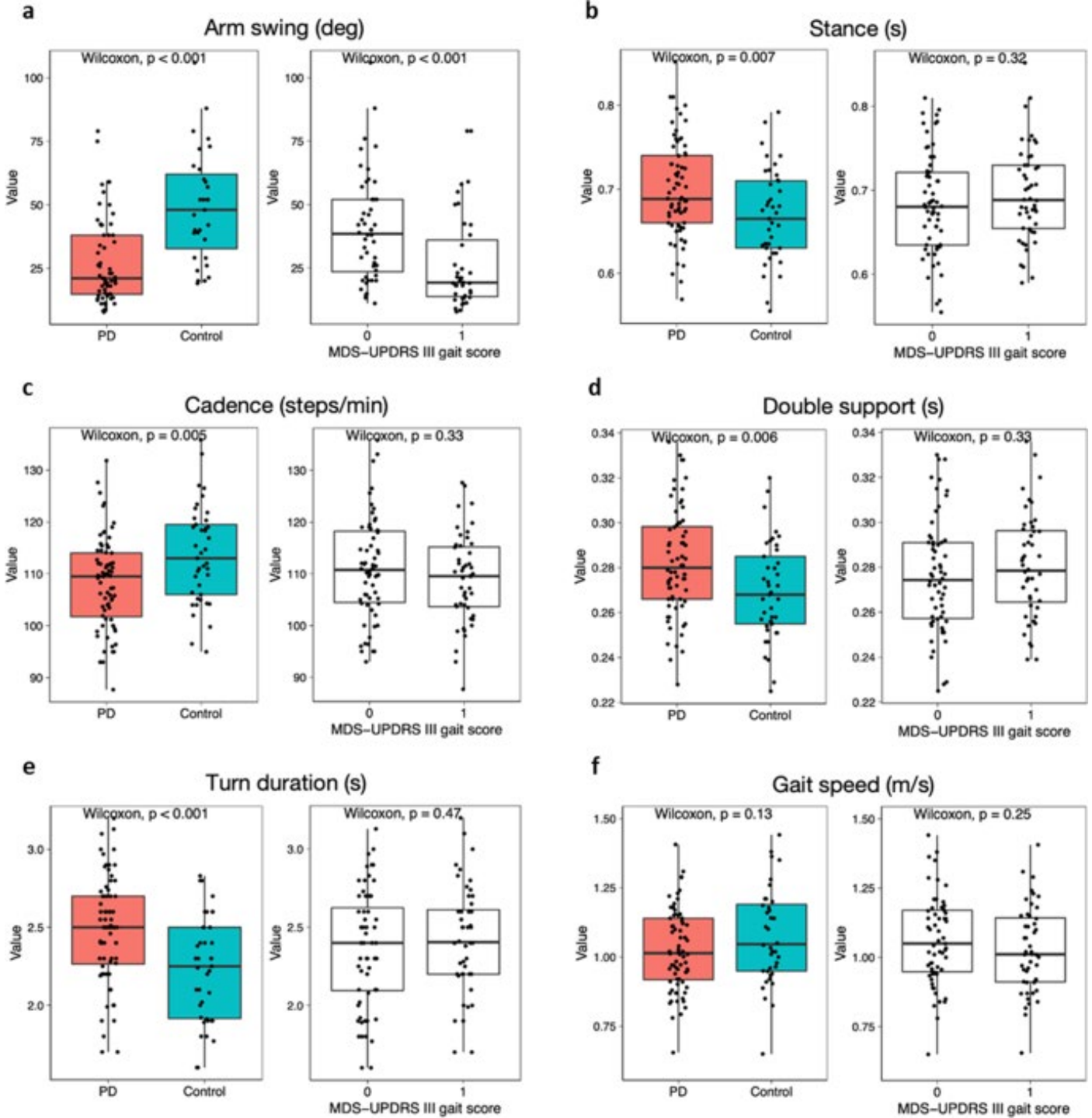


Other Uses of AI

Smartwatch & other wearable devices

- Track symptoms
- Memory exercises
- In-home (remote) exams





Wearable devices can detect subtle motor changes:

- Arm swing
- Walking speed
- Turning speed

Adams, J.L., Kangarloo, T., Tracey, B. *et al.* Using a smartwatch and smartphone to assess early Parkinson's disease in the WATCH-PD study. *npj Parkinsons Dis.* **9**, 64 (2023). https://doi.org/10.1038/s41531-023-00497-x

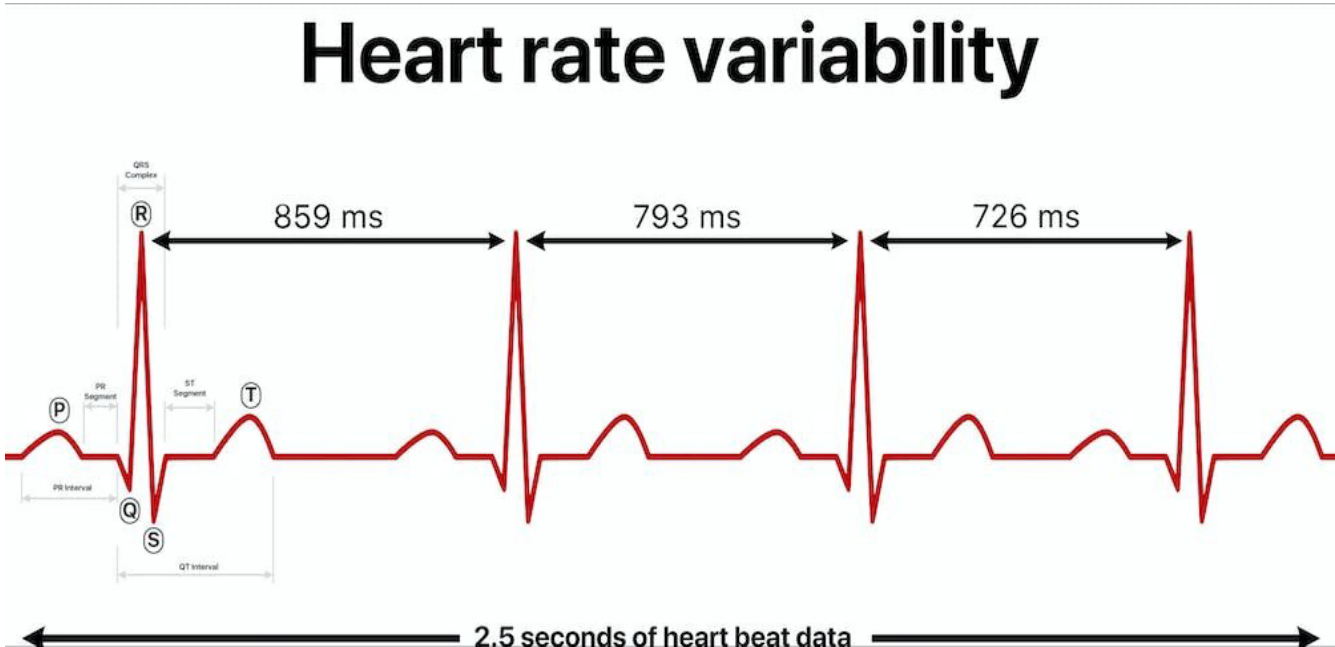
Can an EKG Detect Early PD?

Heart Rate Variability (HRV)

- Difference in time between heart beats
  - High HRV is good
- HRV is reduced in PD
  - Means there is a **problem with the nervous system's control of heart function**
  - Called autonomic dysfunction

Low HRV associated with

2-3x increased PD risk



Karabayir, I., Gunturkun, F., Butler, L. *et al.* Externally validated deep learning model to identify prodromal Parkinson's disease from electrocardiogram. *Sci Rep* **13**, 12290 (2023). https://doi.org/10.1038/s41598-023-38782-7

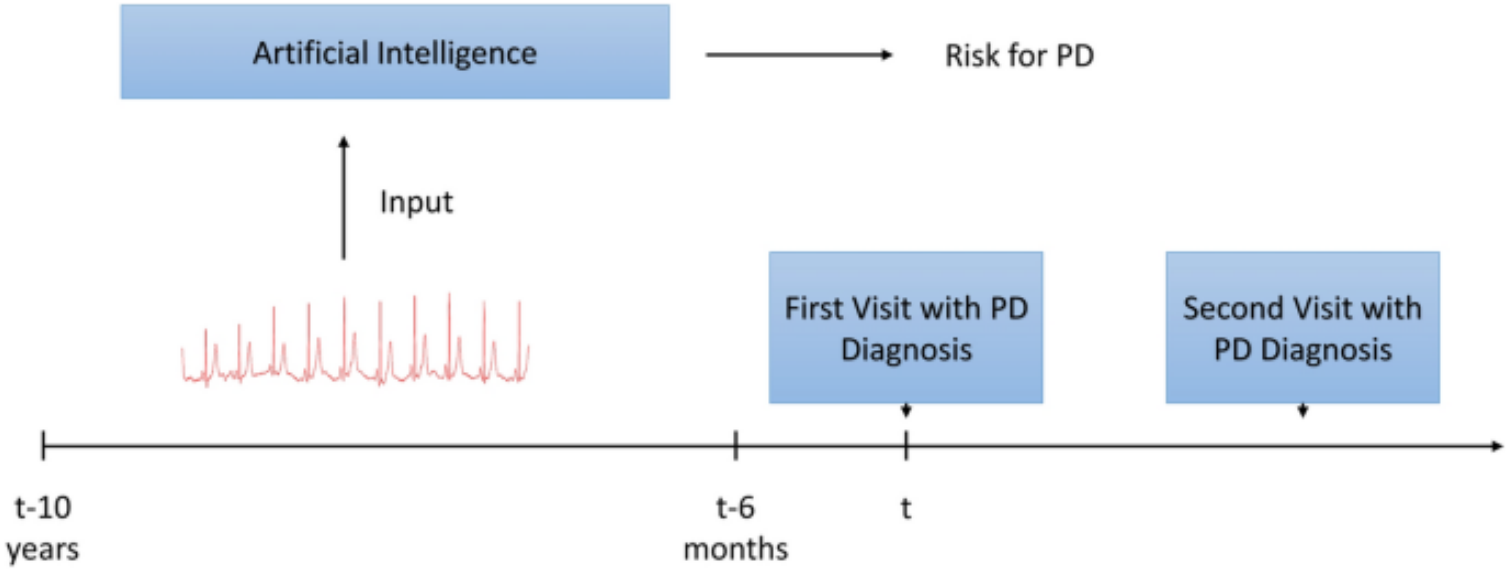
Can an EKG Detect Prodromal PD?

EKGs obtained at least 6 months before PD symptoms started

AI was more accurate when the EKG was done closer to PD diagnosis

AI could predict how soon a patient would develop PD:

1. 6 months–1 year
2. 6 months–3 years
3. 6 months–5 years



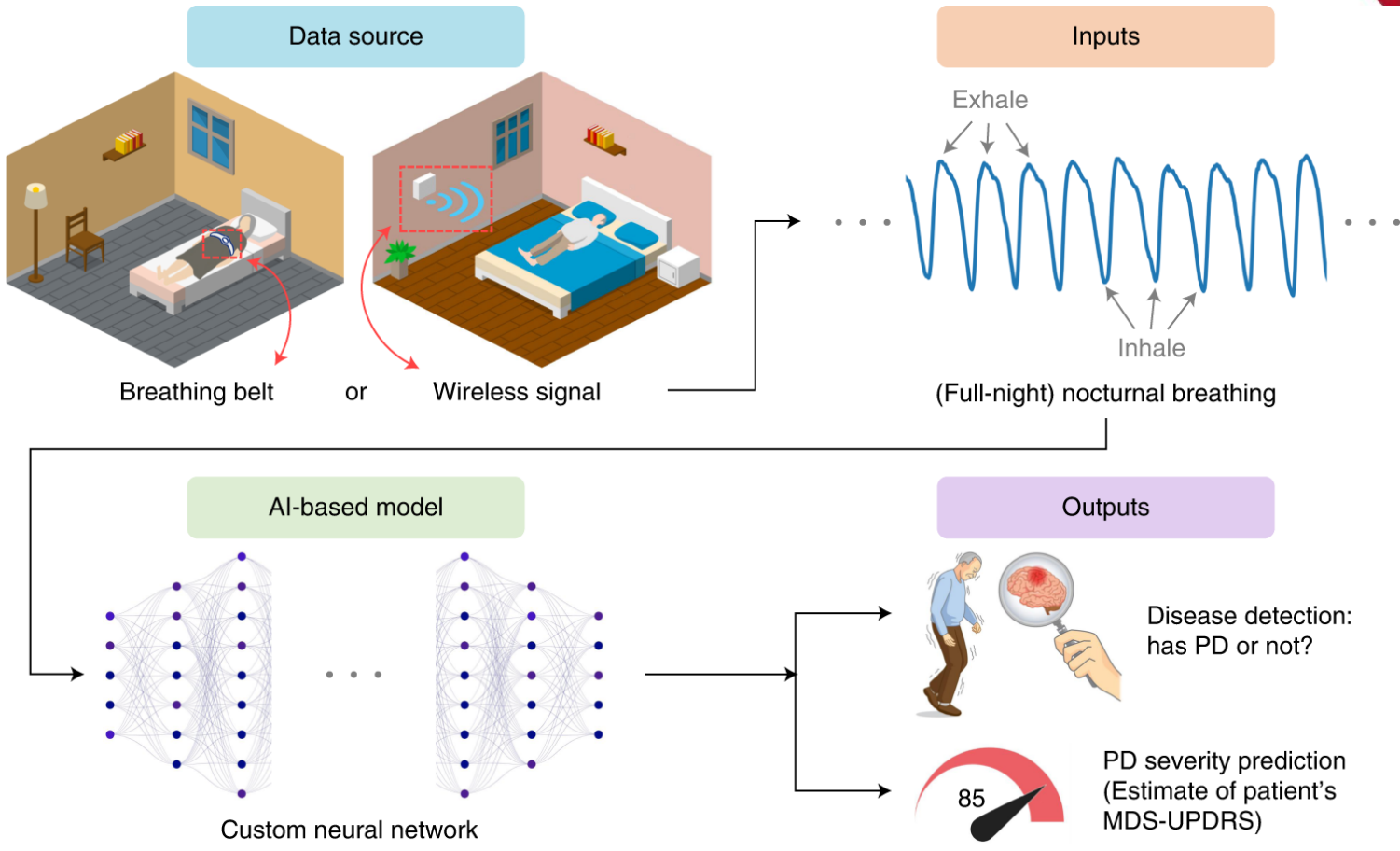
Karabayir, I., Gunturkun, F., Butler, L. *et al.* Externally validated deep learning model to identify prodromal Parkinson's disease from electrocardiogram. *Sci Rep* **13**, 12290 (2023). https://doi.org/10.1038/s41598-023-38782-7

“Nighttime Breathing” to predict PD

Looked at over 7,000 sleep studies

AI could predict:

- PD vs non-PD breathing patterns
- Disease severity
- Disease progression



Today's Objectives

1. Define Parkinson's Disease (PD)
2. Talk about why it's so hard to define PD
3. Review the underlying causes of PD
4. Understand how your neurologist makes the diagnosis of PD
5. List the Movement Disorder Society (MDS) criteria
6. Look into the future of diagnosing PD
   - Imaging
   - Biomarkers
   - Artificial Intelligence

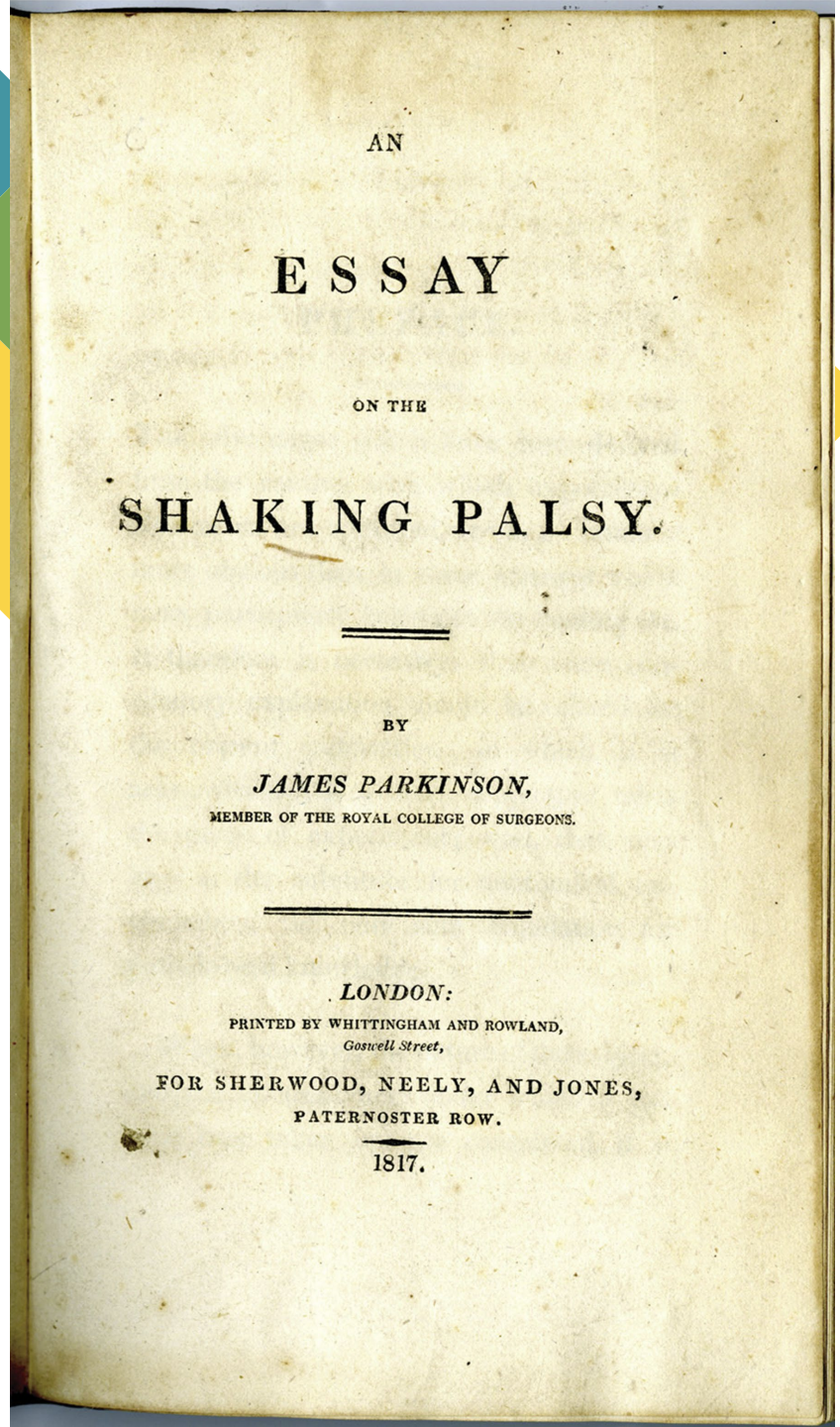
University of Nebraska Medical Center

The Story of Levodopa: Past, Present and Future

Mara Seier, MD
Associate Professor
UNMC Neurological Sciences
Movement Disorder Division

“The Shaking Palsy”

- Parkinson’s disease was initially described in the medical literature in 1817 in “An Essay on the Shaking Palsy”
  - James Parkinson, an English physician, described 6 people: 3 of them his patients; the other 3 were people he observed on the streets of London
  - Resting tremor, slowness of movement, shuffling gait, flexed posture, falls, soft speech, drooling, constipation, swallowing issues, difficulty with handwriting, festination of gait



AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

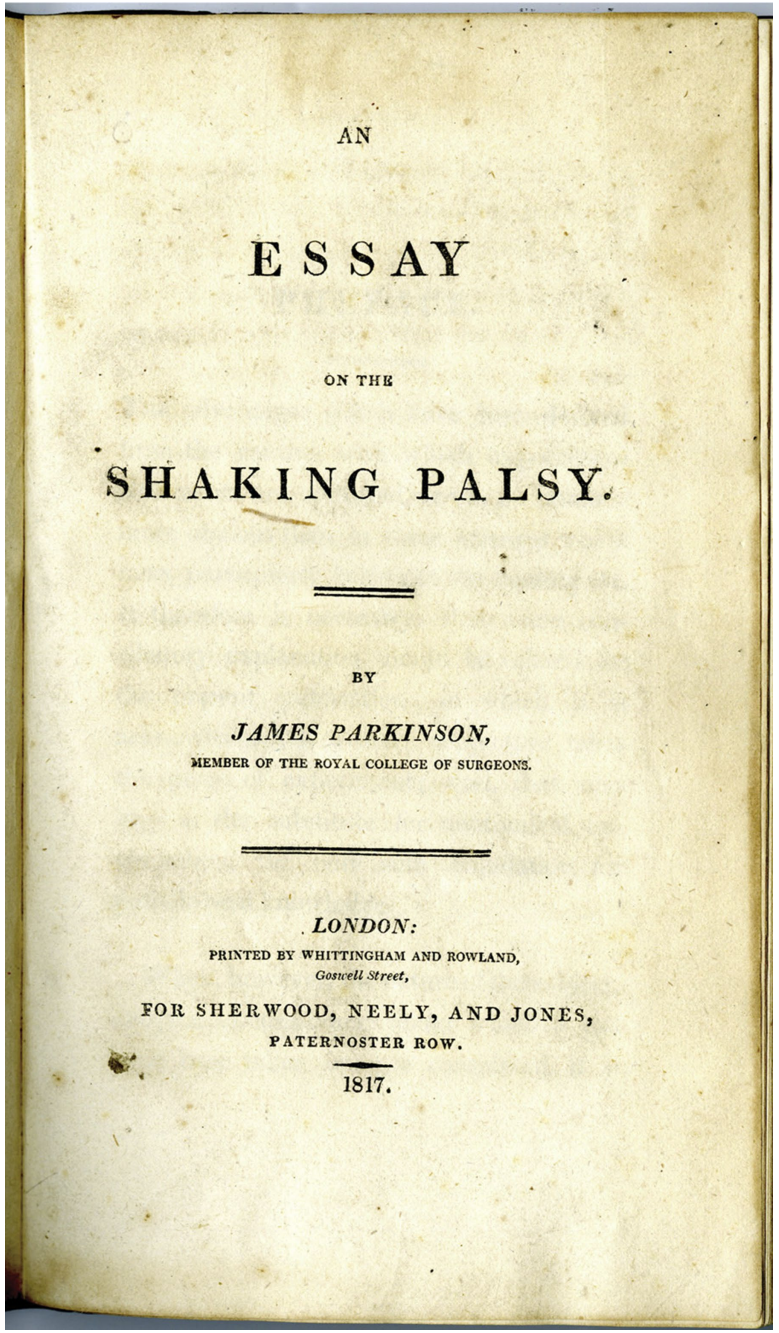
MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:

PRINTED BY WHITTINGHAM AND ROWLAND,
Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,
PATERNOSTER ROW.

1817.



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1817.

- Parkinson hypothesized that the disease may be coming from a “disordered state in the medulla”
  - His name for these symptoms: “Paralysis agitans”
- Essay does offer potential treatments:
  - Mercury
  - Removal of blood from the “upper part of the neck” followed by application of blistering agents and subsequent drainage of the blisters

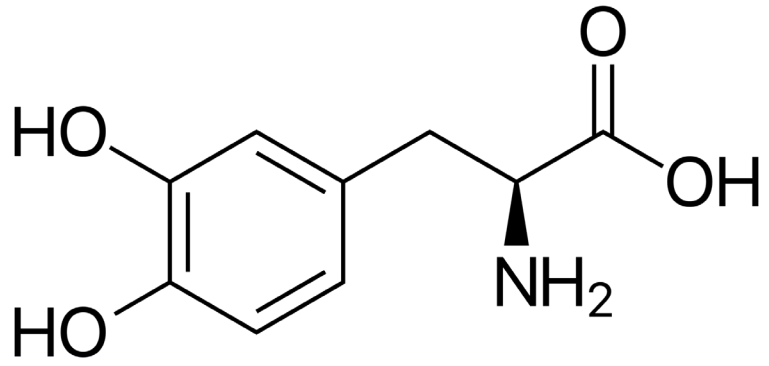
Early Treatment of PD

- The term **Parkinson's Disease** was coined by a famous French neurologist, Jean-Martin Charcot, in the 1860's after reading Parkinson's work

- **Other treatments tried:**
  - Iron, ergot of rye, belladonna, chloroform, strychnine, phosphorus, arsenic, cannabis, galvanism (application of electrical current)
  - 1868: Charcot advocated use of **vibratory chair** and later a device that vibrated the brain
  - *"Everything, or almost everything, has been tried against this disease. Among the medicinal substances that have been extolled and which I have myself administered to no avail"*

Discovery of Levodopa

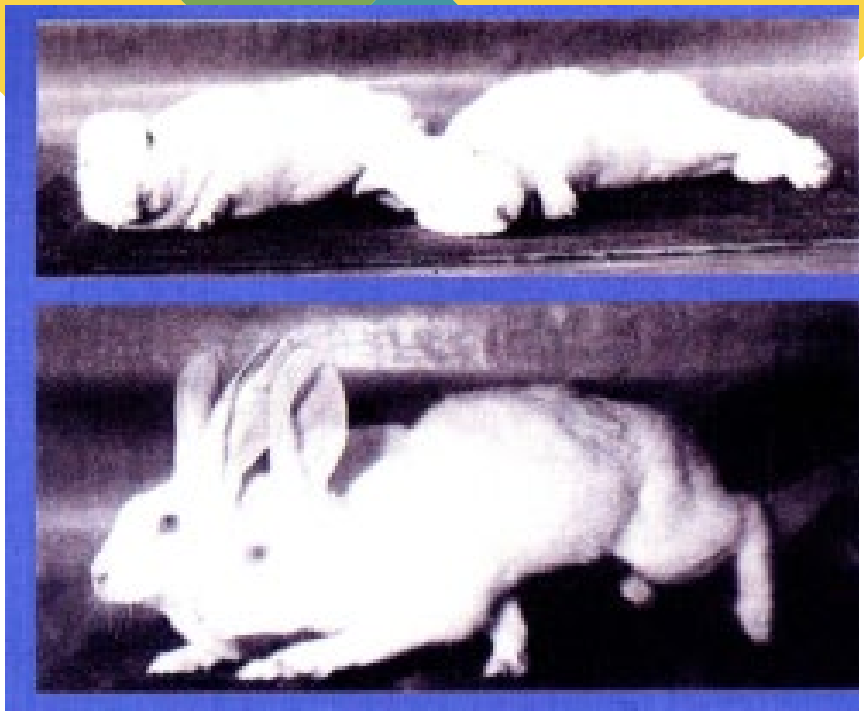
- D,L- Dopa was first synthesized in 1911 by a Polish biochemist, Casimir Funk.
  - Also famous for coining the term “vitamin”
- 1913, Marcus Guggenheim, another biochemist from Switzerland, isolated the pure L-Dopa or Levodopa
  - From the bean plant *Vicia Faba* – Fava bean
  - Guggenheim ingested it and was reported to have “violently” vomited; thus viewed as a toxic substance
  - Later discovered that **Levodopa is converted to Dopamine** (an emetic) in the body



Levodopa

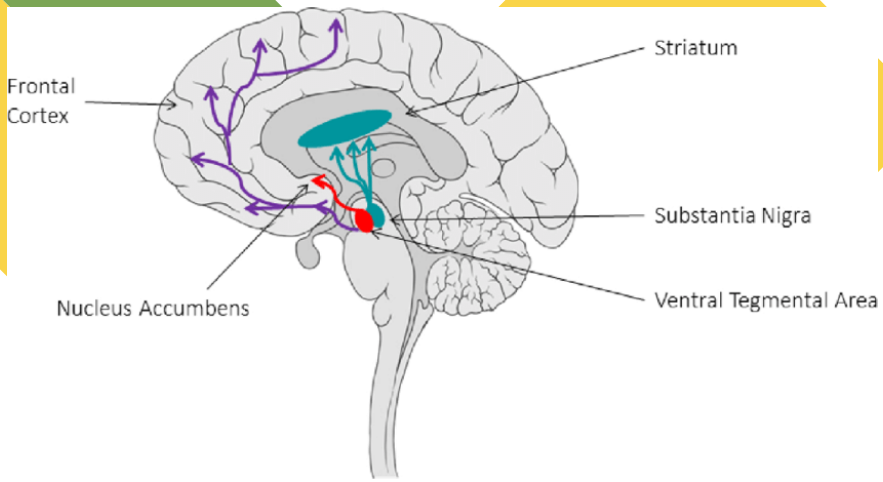
Reserpine and Bunnies!

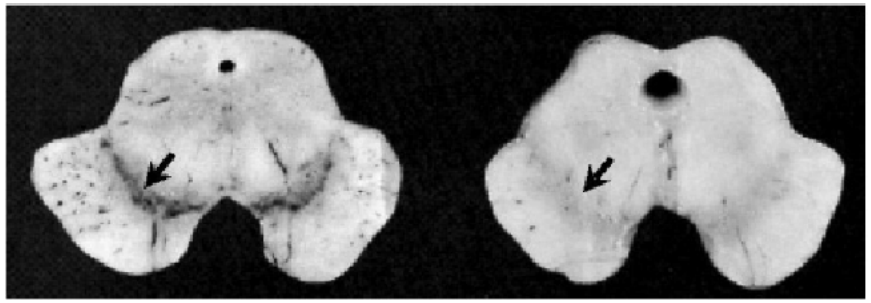
- 1950's: Arvid Carlsson, a Swedish pharmacologist and researcher, began to investigate reserpine's effects on dopamine and brain function:
  - Reserpine depletes neurotransmitters to treat schizophrenia
  - Rabbits give reserpine become catatonic
  - He reversed this effect by giving levodopa and thus increasing dopamine levels
  - He then postulated the dopamine was a very important neurotransmitter involved in movement regulation and thus likely responsible for PD
- He excitedly presented his work at international conferences → with poor reception and skepticism



Work in the 1960's

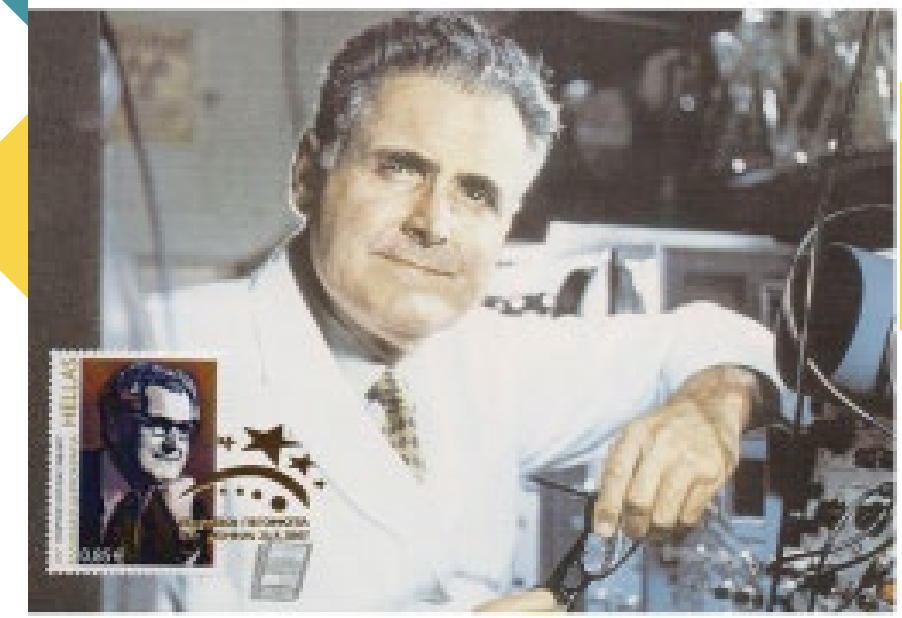
- Oleh Hornykiewicz, Austrian physician-scientist, reviewed Carlsson's work and started to study post-mortem brain material in people with PD
  - Parkinson's brains: consistent loss of dopamine in the areas responsible for controlling movement (striatum)
    - Especially in the pars compacta of the substantia nigra
  - Luckily, other researchers were developing ways to label neurotransmitters like dopamine; and view these structures and projections to help prove that cause of PD
- He was able to show that a group of cells in a lower part of the brain had impact and projections to a distant part of the brain





Levodopa works!

- Early attempts at use of Levodopa failed in the early 1960's
- George Costzias, a Greek-American physician, discovered a breakthrough with levodopa in 1967
- Followed up by another paper in 1969 and 1972 of levodopa given WITH carbidopa
  - He spoke at an international conference; showing the success with videos of his patients
  - Prompted further placebo-controlled studies and carbidopa/levodopa was FDA approved and **became available in 1975**

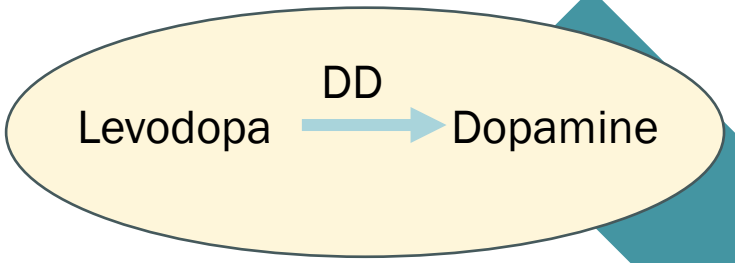


Revolutionary treatment

1) Treatment of a formerly untreatable, neurodegenerative disease

2) Use of "replacement therapy" to supplement a deficient neurotransmitter

Ever wondered why you take Carbidopa and Levodopa?

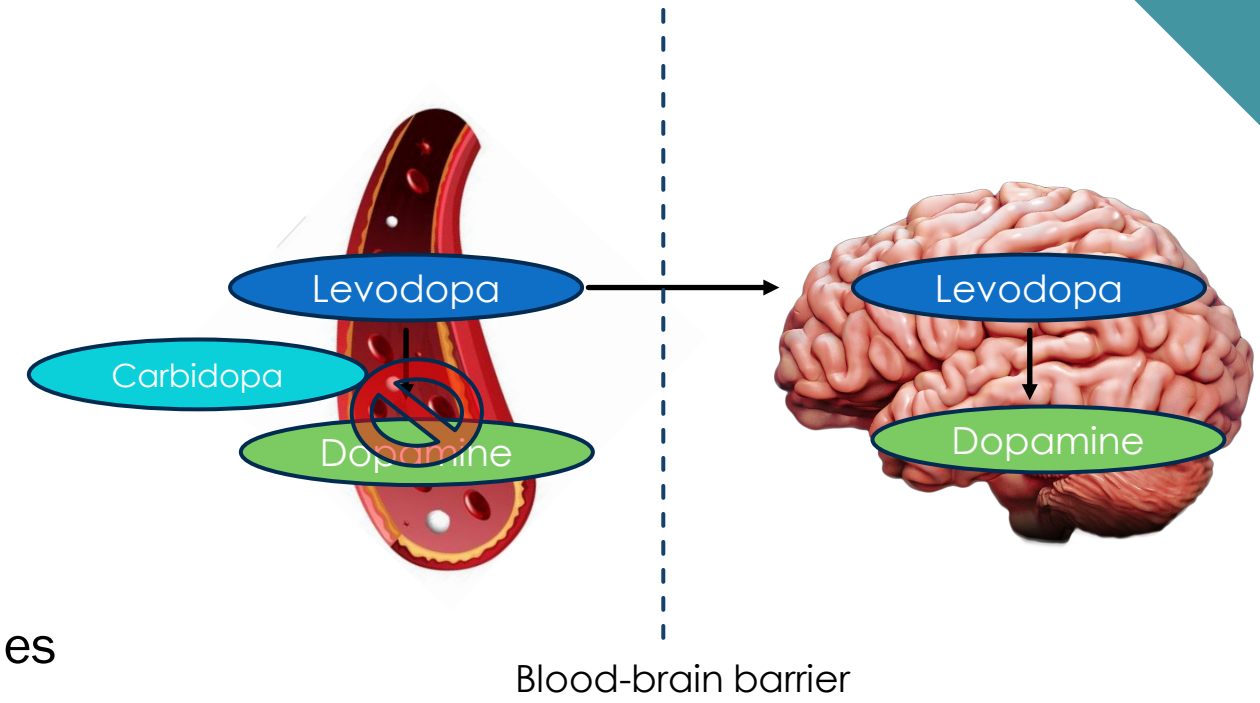


Dopamine decarboxylase (DD): Enzyme responsible for converting levodopa into dopamine

- Good in the brain!
- Not so great in the GI tract or bloodstream

Carbidopa does not cross the blood brain barrier

Carbidopa is **ALWAYS** given with Levodopa (sometimes bonus is given to help with nausea)



What does Levodopa Help With?

Chief motor symptoms of Parkinson's Disease

-Bradykinesia (slowness of movement)

-Rigidity (Stiff muscles)

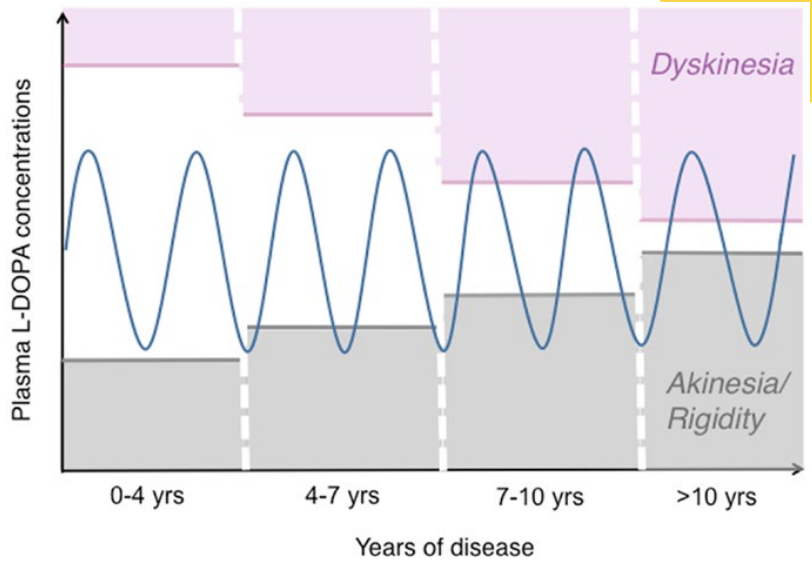
-Tremors *

Is not a cure for PD

-But there was significantly higher mortality rates (3x) in PD patients prior to the 1970's

-In the post-Levodopa era, survival rates closer to the general population

Levodopa Timeline



"Honeymoon" Period

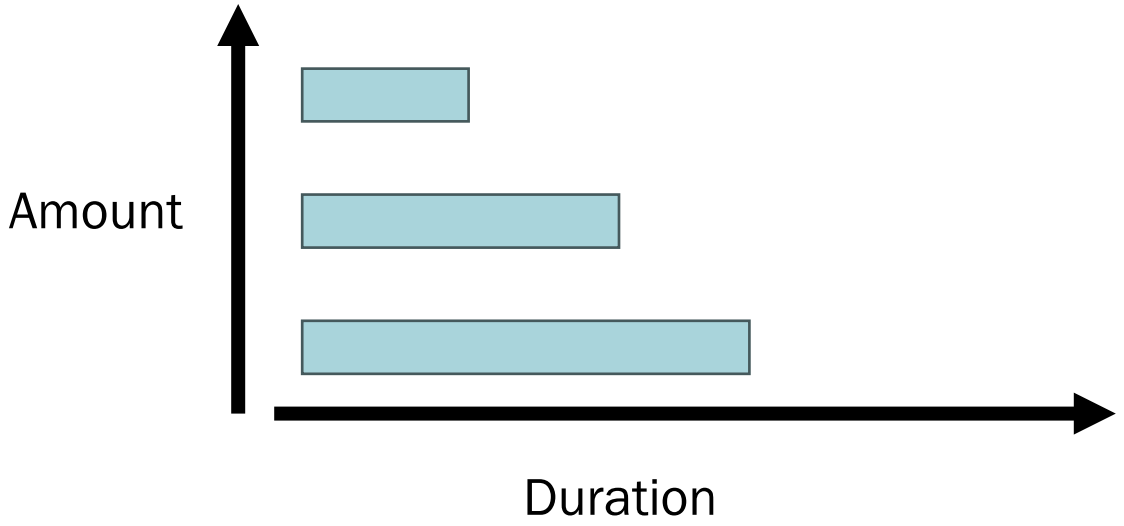
- Nausea

→ Wearing Off
(AKA Motor Fluctuations)

↔ Abnormal Movement
(Dyskinesia)

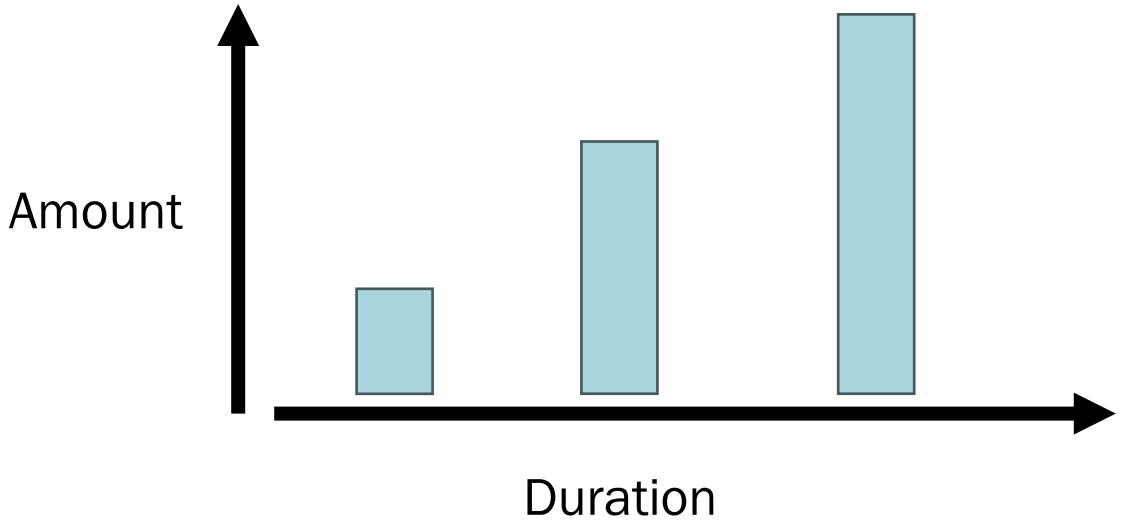
Levodopa Timeline

"Honeymoon" Period → Wearing Off (AKA Motor Fluctuations) ↔ Abnormal Movement (Dyskinesia) → Dose Increase



Levodopa Timeline

"Honeymoon" Period → Wearing Off (AKA Motor Fluctuations) ↔ Abnormal Movement (Dyskinesia) → Dose Increase



What is causing this need to change dose?

1) The progression of the Disease; **NOT** tolerance!

2) Factors related to the Gastrointestinal Tract (GI) or AKA the“Gut”

1) Small area of absorption in the small bowel
2) Competition for absorption (food – especially protein!)
3) Enzymes that degrade it in the gut before it gets to the brain
4) Factors within the gut itself (including slow transit –ie constipation)

What is causing this need to change dose?

1) The progression of the Disease; **NOT** tolerance!

Effect of Early Levodopa use versus Late use

Levodopa in **EA**rly **P**arkinson's: **LEAP** study

- Early start versus Delayed start (started at 40 weeks) levodopa groups
  - 2019 results: no disease modifying effect of levodopa at 80 weeks
  - 5-year follow-up study; there was no significant difference between groups:
    - Prevalence of motor fluctuations
    - Prevalence of dyskinesia
    - Symptoms of autonomic dysfunction
    - Cognition
    - Levodopa (other dopaminergic medication) dosage

This is in keeping with other studies including a retrospective study: 2 groups compared – patients started on levodopa early in the course of the disease and another patient population with late access to the medication (due to lack of access) → **motor complications were NOT associated with timing of levodopa use but seem to be associated with disease duration!**

Death + Disability and Levodopa use

Effect of early levodopa treatment on mortality in people with PD

- Early levodopa (use within 2 years) = 25,000
- Late levodopa (use >2 year or never) = 5,000

- **No difference in mortality or PD-related complications**

"Early L-dopa initiation in PD does not postpone mortality or PD-related complications, nor does it lead to earlier occurrence of PD-related complications or death."

Another population-based study with over 20 years of follow-up:

Investigated the impact of L-dopa initiation timing on the survival of people with PD

- **Early L-dopa treatment was associated with higher life expectancy** compared to delayed treatment
  - Highlighting the detrimental effect of delaying L-dopa to more advanced stages of the disease

“Levodopa phobia”

Misperception of medical data (perceived/anticipated onset and severity of side effects; occurrence of severe dyskinesia)

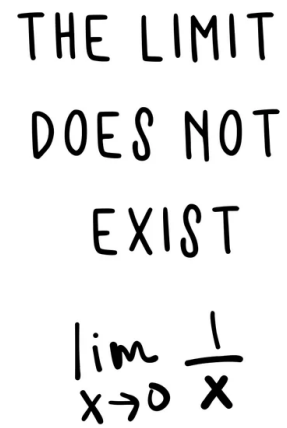
“Saving it for when I need it” or employment of strict levodopa-sparing strategies despite severe symptoms

Early discontinuation; inadequate dose (ie: patient stopping after few days or weeks)

Primary care or neurologist concern about LID; over-reliance on animal models showing toxic affects of levodopa

Patient fear of taking medications as disease marker

How much Levodopa can I take?



There is no true limit on dosing; except…

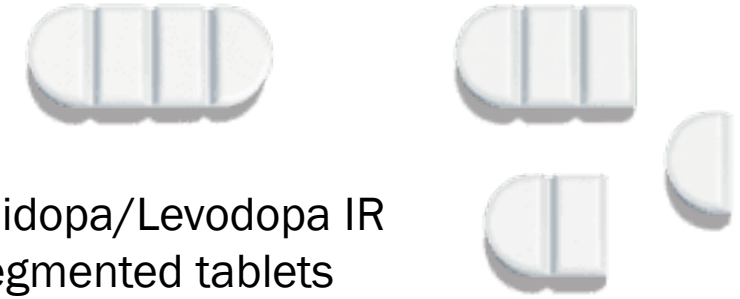
The “BIG 4” limitations:

1. Nausea
2. Blood pressure drops (PD can also causes this!)
3. Dyskinesia
4. Hallucinations (PD can also cause this!)

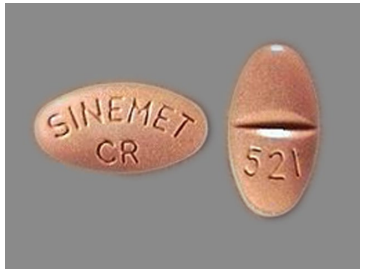
- 5th side effect less commonly encountered: effects on sleep: both drowsiness and insomnia reported; vivid dreams
- 6th side effect also to mention: impulse control issues; more common with dopamine agonists

Levodopa Formulations Available

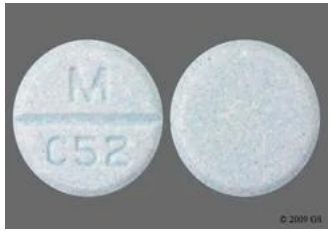
Carbidopa/Levodopa IR tablets



Carbidopa/Levodopa IR segmented tablets (Dhivy)

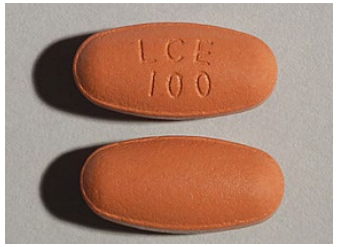


Carbidopa/Levodopa CR tablets

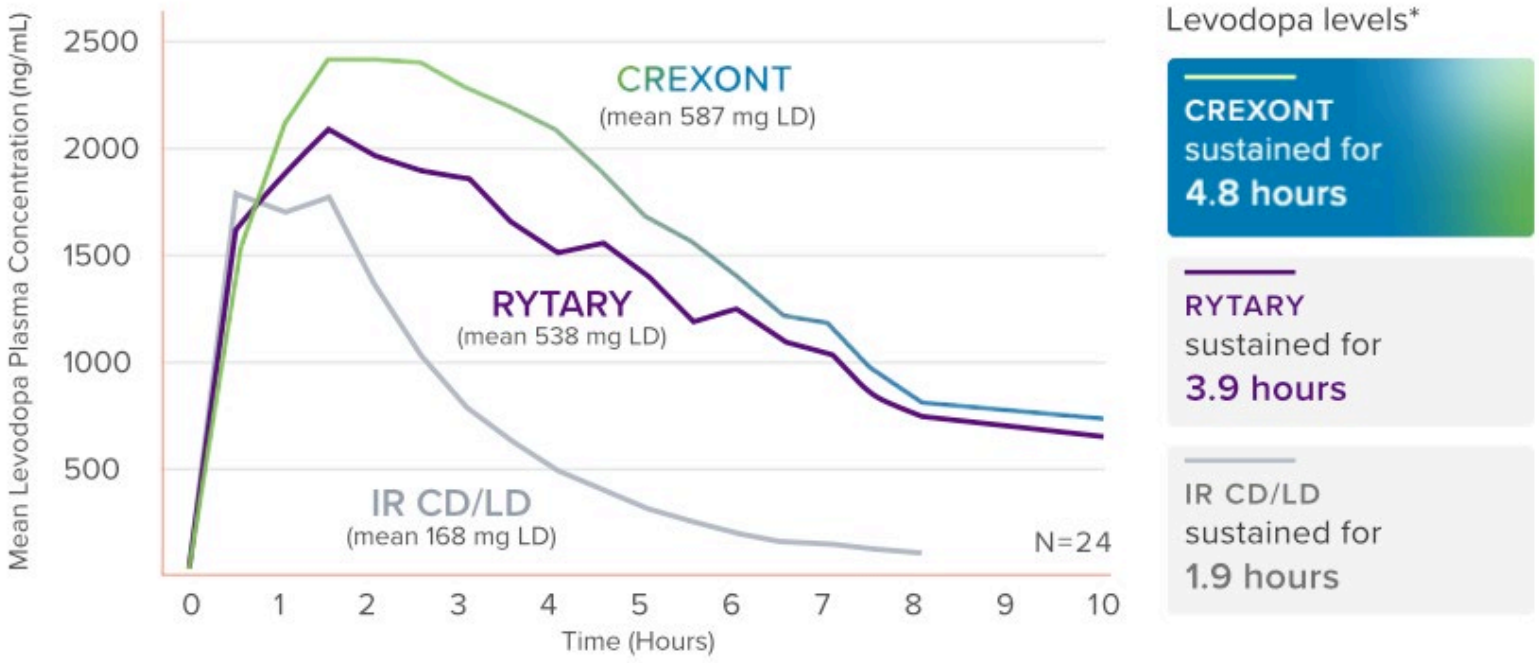


Carbidopa/Levodopa orally disintegrating tablets (Parcopa)

Levodopa Formulations - Wearing Off



Carbidopa/Levodopa/Entacapone (Stalevo)



Levodopa Formulations – Wearing Off

Carbidopa/Levodopa intestinal infusion
(Duopa)

- **Continuous dosing**
- **Up to 16 hours per day**
- **Surgically implanted tube**

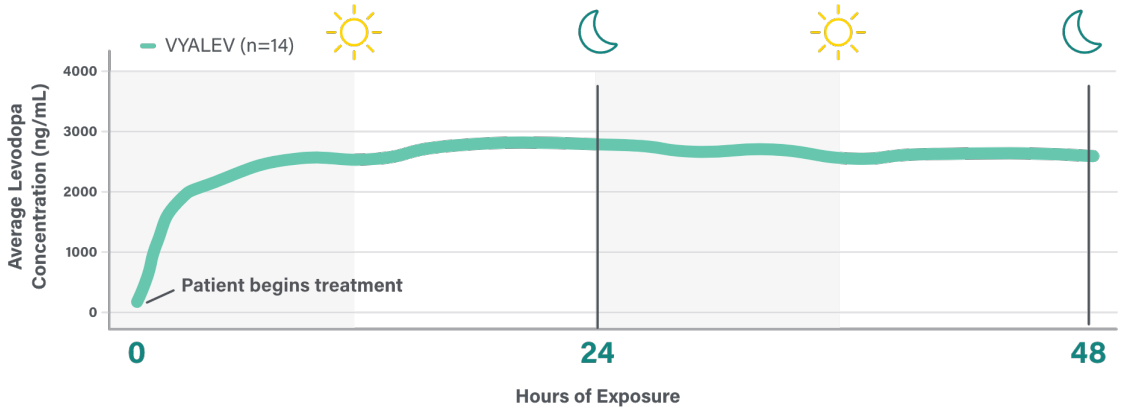
Levodopa Inhaled
(Inbrija)

- **Rescue therapy for Off time, as needed**
- **Quicker onset that oral**

Foscarbidopa/Foslevodopa subcutaneous infusion
(Vyalev)

- **Continuous dosing**
- **24 hours a day**
- **Directly into skin**


Foslevodopa/
foscarbidopa
Motor effects:
Increased good on
Decreased off period
Efficacy maintained at 52 weeks
Abstract data:
Improved nocturia
Useful in "early advanced PD"
Abstract data:
Beneficial in cost benefit analysis
Improved freezing of gait
Monotherapy in approximately 30%
Decreased troublesome dyskinesias
Improved sleep (decreased off, improved QoL)
Decreased early morning akinesia and off


VYALEV (n=14)
Average Levodopa Concentration (ng/mL)
4000
3000
2000
1000
0
Patient begins treatment
0
24
48
Hours of Exposure

Future of Levodopa

- **Two other subcutaneous carbidopa/levodopa pumps**:
  - ND0612: Under review with the FDA as of this spring
  - DIZ102: Under early investigation
- **Intravenous carbidopa/levodopa form**: DIZ101
- **Another intestinal infusion option**: carbidopa/levodopa/entacapone
  - Not yet approved in US; available in Europe since 2021
- **Intraoral System**: Continuous levodopa delivery with an intraoral micropump system
  - Still in early research phase

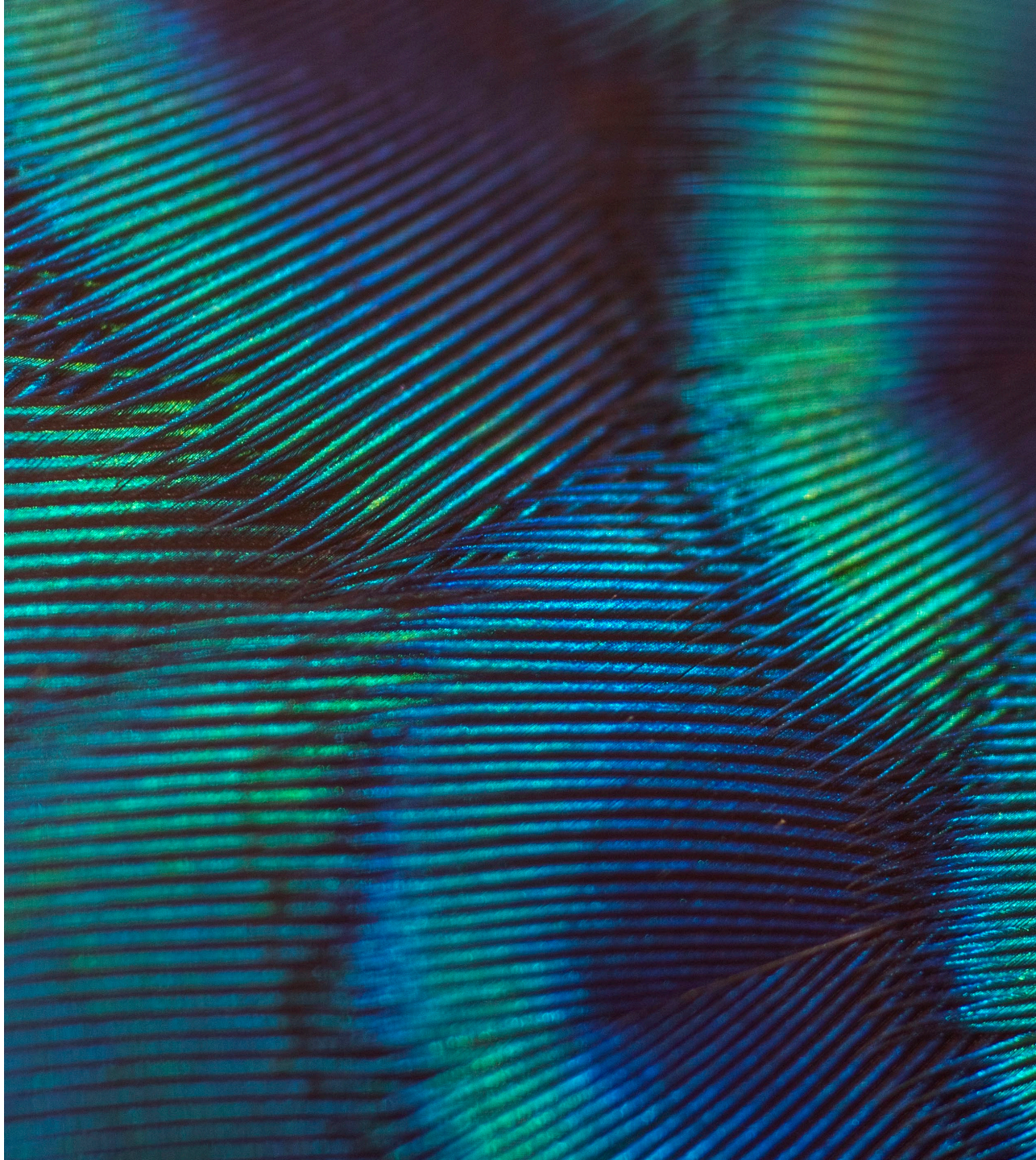
Thank you

Cognitive Changes in Parkinson's Disease (PD)

Nicholas Kavish, PhD

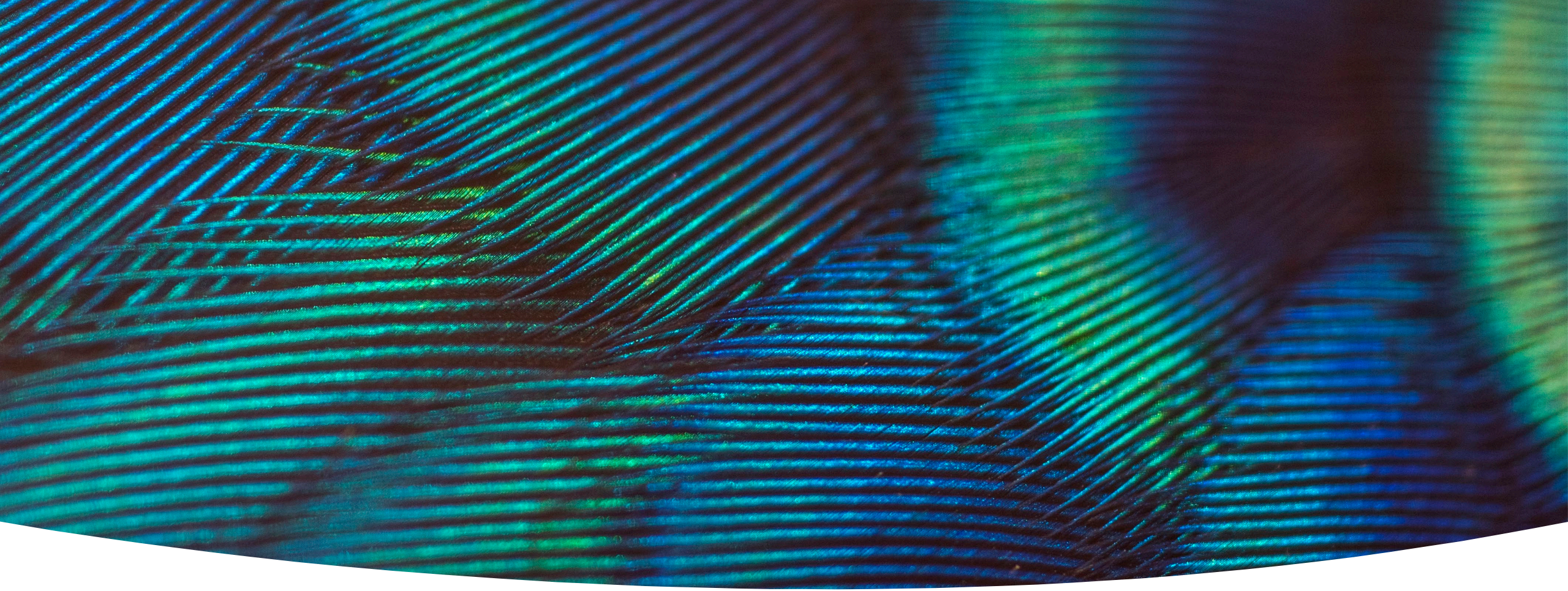
Clinical Neuropsychologist, Assistant Professor

Dept. of Neurological Sciences, UNMC



I have no financial disclosures.

Presentation is for informational purposes only,
not for diagnosis or treatment



What is Cognition?

What is Cognition?

- Mental speed
- Attention
- Learning
- Memory
- Language
- Visuospatial skills
- Executive functions

What Affects Cognition?

- Age
- Psychiatric symptoms
- Sleep, fatigue
- Nutritional status, vitamin deficiencies
- Pain
- Vision, hearing
- Infections
- Thyroid functions
- Blood sugar levels
- Medication side effects

…among other factors, including diseases such as PD

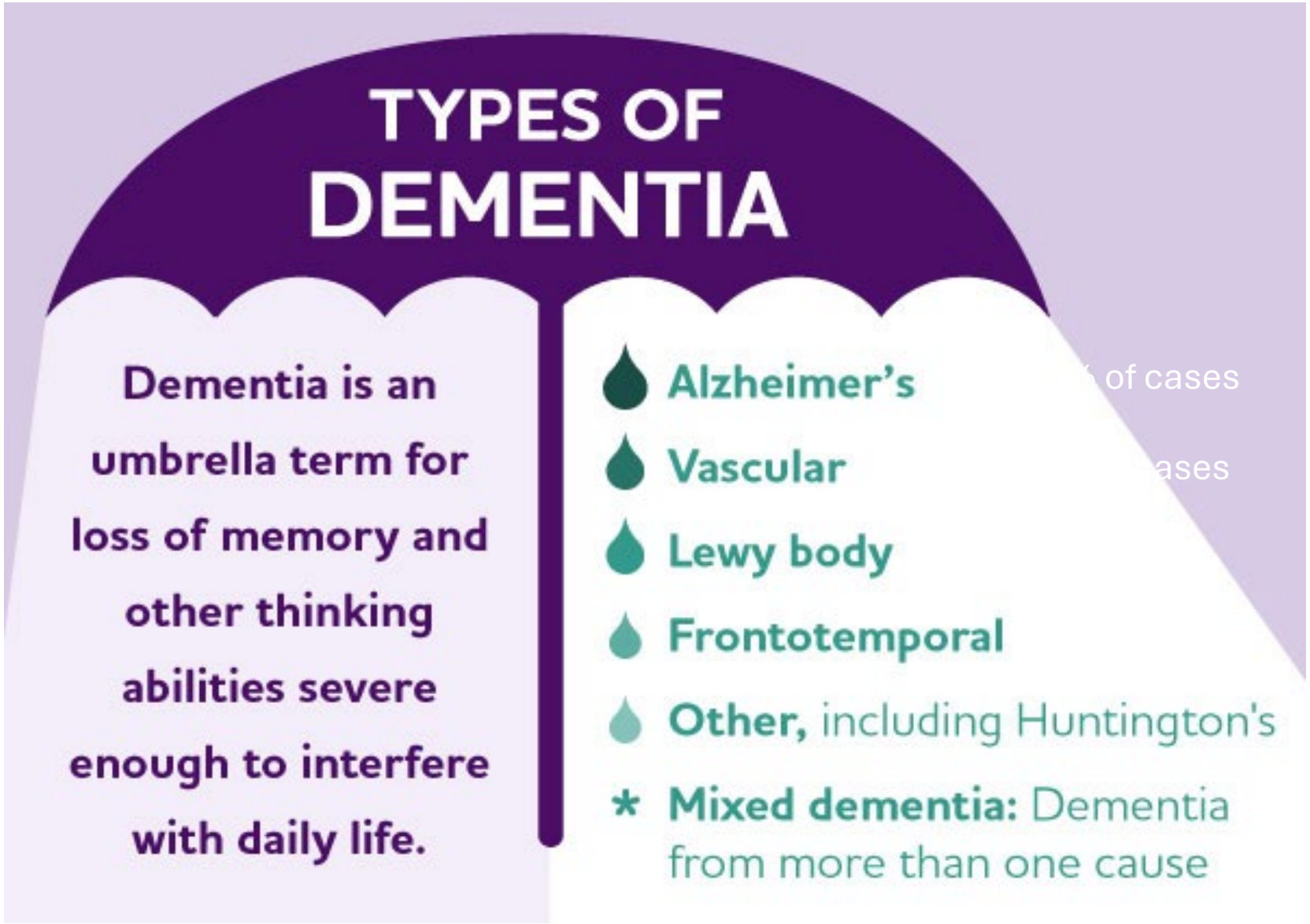
Cognitive Trajectories

Cognitive Changes: Functional Impact

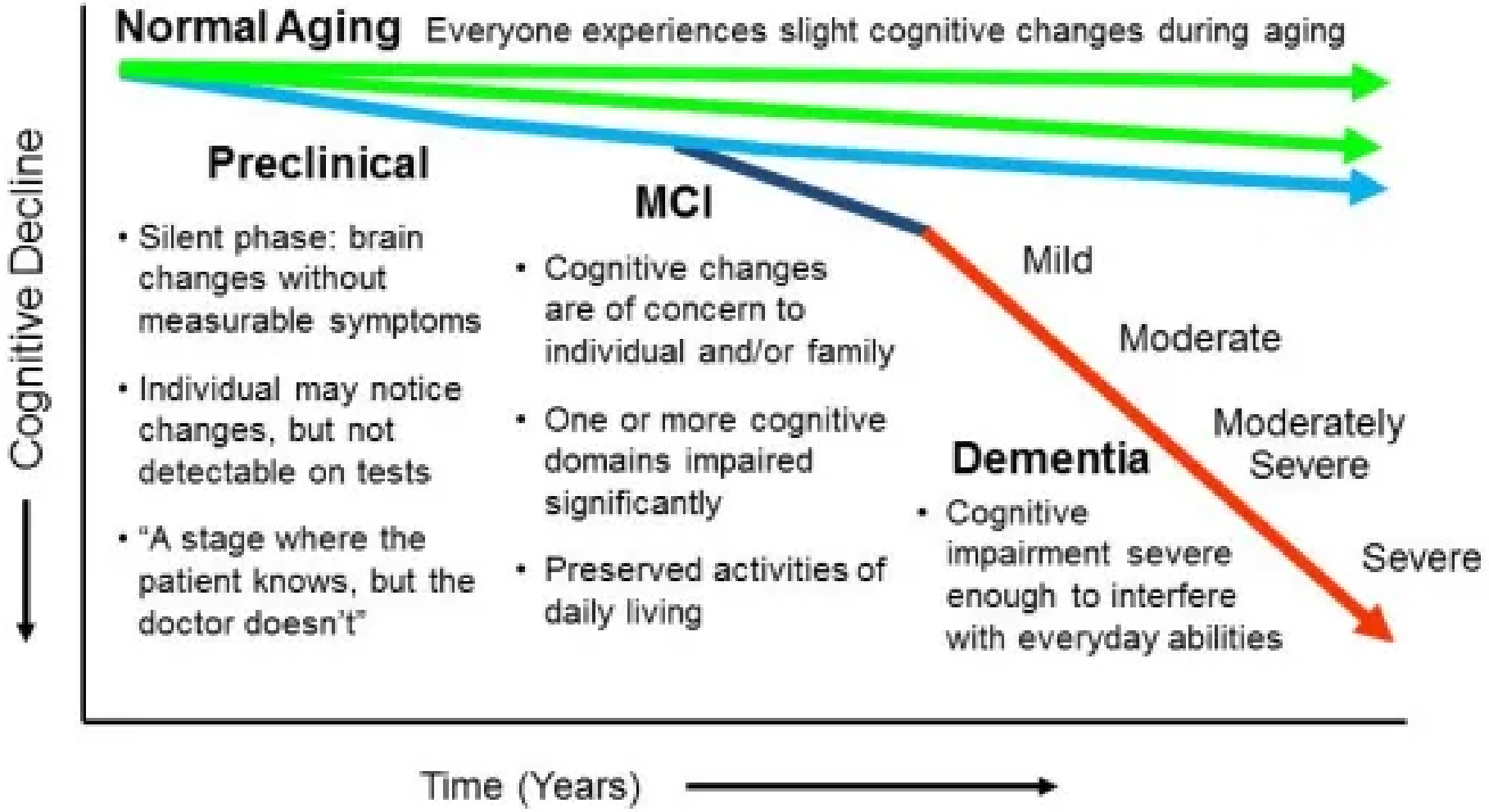
- "Mild Cognitive Impairment" (MCI) and "Dementia"

Normal Aging		Mild Cognitive Impairment (MCI)		Major Neurocognitive Disorder (Dementia)	
✓	Cognition (On testing)	⇩	Cognition (On testing)	⇩	Cognition (On testing)
✓	Daily Functioning	✓	Daily Functioning	⇩	Daily Functioning

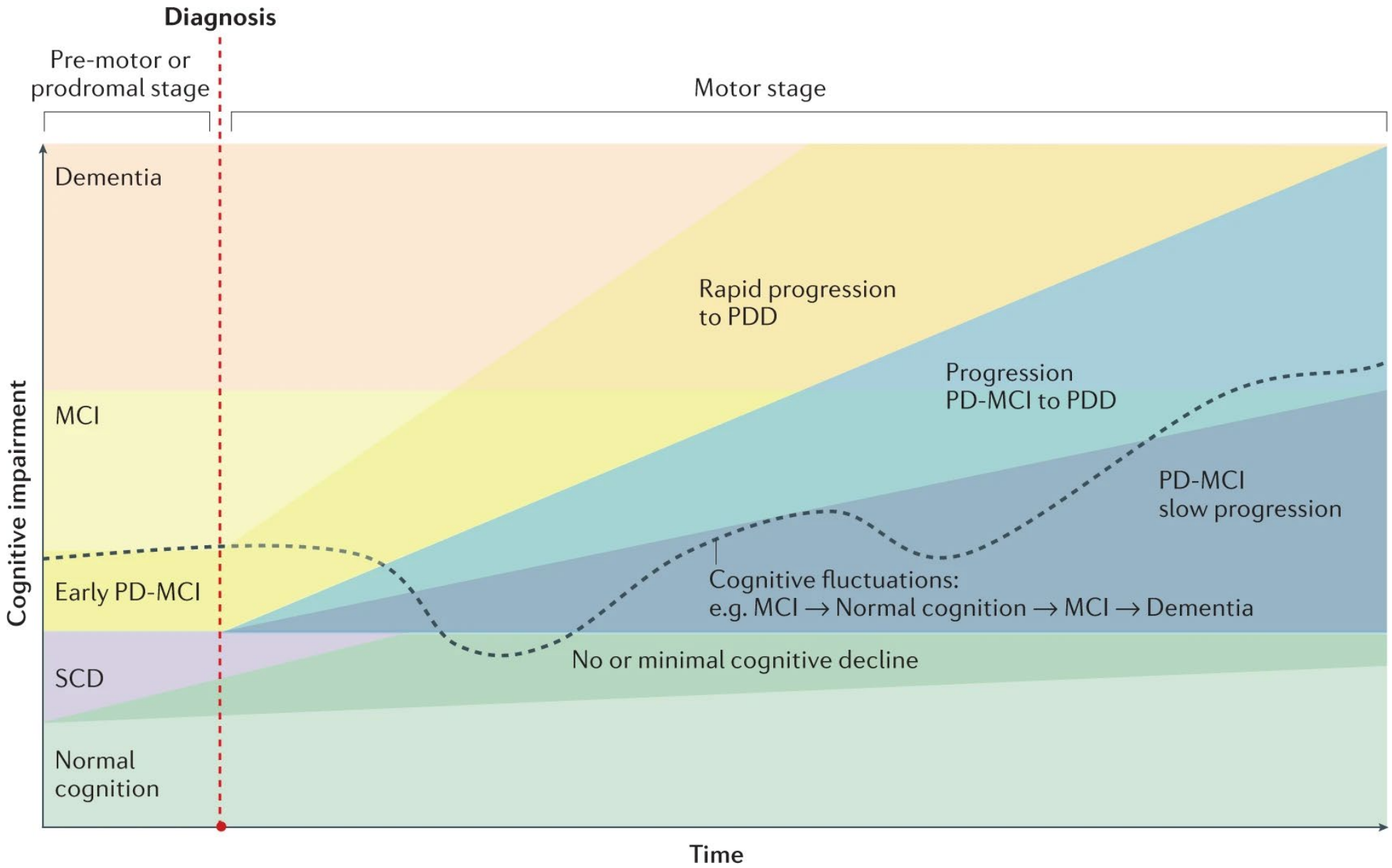
Image Credit: https://www.mccare.com/education/mcidementia.html



https://www.alz.org/alzheimers-dementia/what-is-dementia

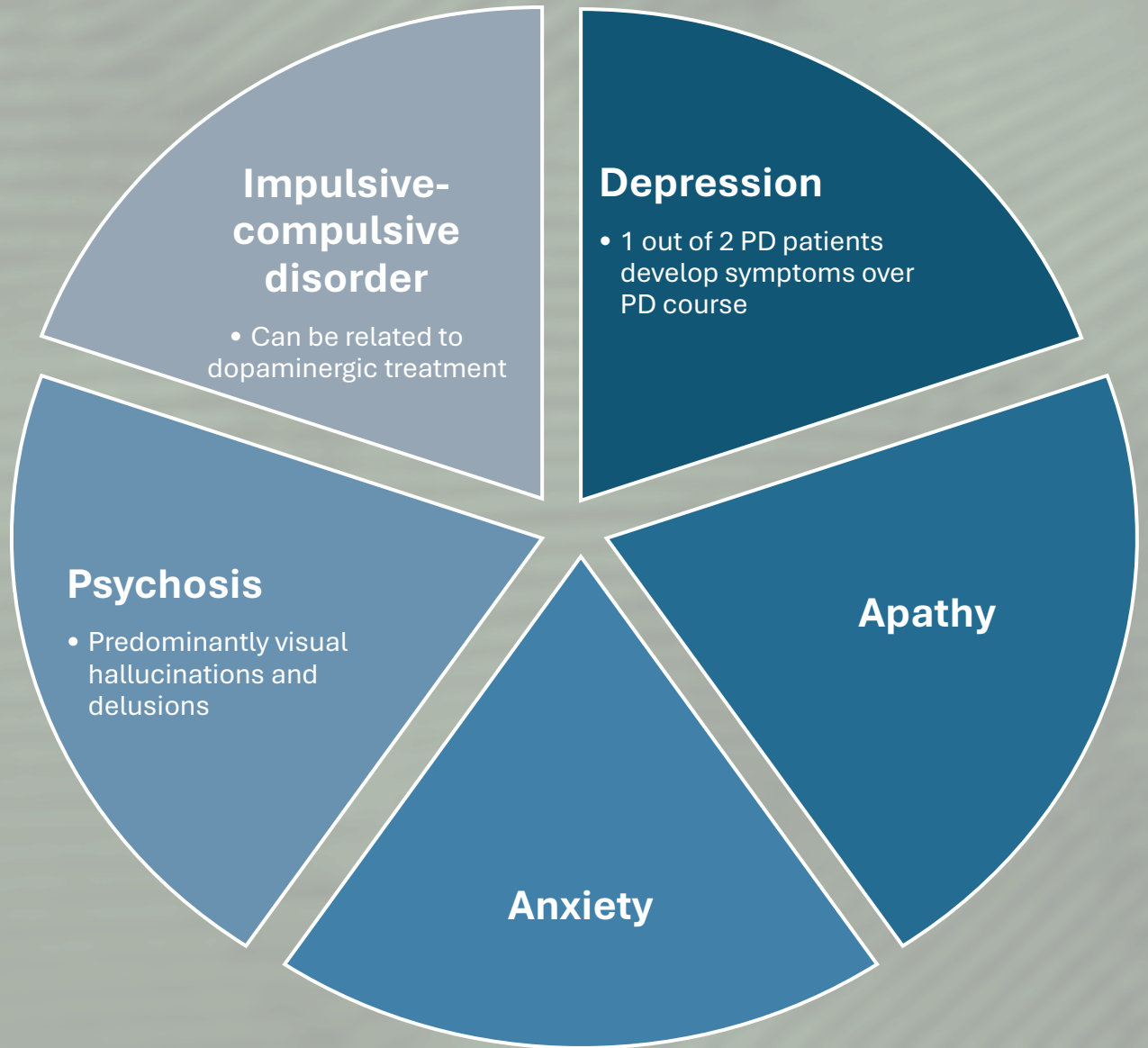


https://mind.uci.edu/dementia/mild-cognitive-impairment/



Aarsland et al. (2021). Parkinson disease-associated cognitive impairment

PD as a *Neuropsychiatric* Presentation



Cognitive Changes

Early in PD course, subtle changes in:

- Retrieval memory and planning, organizing, and other executive functions

With mild cognitive impairment, difficulties may arise in:

- Attention: sustaining attention, shifting attention, completing multi-step processes
- Executive functions, including inhibition and regulation
- Mental speed (increased time to register, retrieve, and respond to information)
- Language (word-finding)
- Retrieval of recent memories (yet benefiting from cues, reminders)
- Visual perception

With dementia, additional difficulties may arise in:

- Comprehension
- Naming
- Memory (benefiting less from cueing, reminders)

Clinical Neuropsychology and Cognitive Neurology of PD and Other Movement Disorders (2015). Edited by Tröster.

Recognizing Emotions

More difficult for people with PD to identify others' emotions

- Particular difficulties with identifying or making sense of negative emotions, such as anger, disgust, fear, and sadness, of others' facial expressions and voices

People with PD may have difficulties identifying their own emotions

- Otherwise known as "alexithymia"
- Independent of depression
- People with PD and cognitive decline may not be aware that they are depressed

Weng-Rang Ho et al. (2020). Impairments in face discrimination and emotion recognition are related to aging and cognitive dysfunctions in Parkinson's disease with dementia

General Risk Factors Associated with Developing PD Dementia

Demographic factors:

- Older age
- Male sex
- Later age of PD onset

Potentially modifiable factors:

- Depression
- Head injuries
- Tobacco use
- Hypertension

Disease variables:

- Olfactory dysfunction
- Visual hallucinations
- REM sleep behavior disorder (RBD)
- Non-tremor/akinetic rigid predominant PD
- ApoE4
- Longer duration of PD symptoms
- Mild Cognitive Impairment

in *Clinical Neuropsychology and Cognitive Neurology of PD and Other Movement Disorders* (2015). Edited by Tröster.

Risk of Developing PD Dementia

People with PD have a more than three-fold increased risk of developing dementia versus people without PD

Annual risk of developing dementia in PD is approximately 3.1%

- Cumulative risk of about 30% at 10-years
- Varies significantly by age/age-of-onset

Aarsland et al., (2005) A systematic review of prevalence studies of dementia in PD
Aarsland et al., (2003) Prevalence and characteristics of dementia in PD: An 8-year prospective study

What to Do?

- Talk to your doctor. Can be helpful to bring a loved one to this visit to discuss their observations
- Cognitive screen in office
- Comprehensive neuropsychological evaluation

What is a Neuropsychological Evaluation?

- Record review and test selection based on history / referral question
- Interview
- Gather additional information from collaterals, outside medical records
- Cognitive and psychological testing / scoring
- Written report
- Feedback to patient of results, diagnosis, and recommendations

Recommendations

Modifications to Complex Tasks

- Work accommodations
- Driving evaluation by occupational therapist
- Medication management
- Financial oversight
- Communication habits
- Discuss surrogate decision maker

Cognitive Compensatory Strategies

- Develop a routine and good habits, to make procedures “muscle memory”
- Use calendars, reminders on smartphone, and other visual and auditory cues for memory and planning
- Inform others when providing information too quickly or when something needs to be repeated. Ask others to write information down.
- Reduce distractions when possible (e.g., turn off the television or radio while you’re having a conversation)
- Avoid shifting back and forth between tasks
- Divide tasks into individual steps that are easier to complete
- Keep rooms well-lit to reduce issues with visual misperception

Stay Engaged!

- Exercise to the extent it is safe
- Stimulate the mind with novel, cognitive activities (attend a lecture, read a book, learn a new hobby)
- Be social. Stay connected to friends and family

Healthy Habits

- Diet (e.g., Mediterranean diet, MIND diet, adequate fluid intake)
- Sleep
- Avoiding toxins to the brain

Medications

- Consideration of whether there are any offending medications that might contribute
- Optimizing “on” time, reducing “off” time
- Treating providers may offer medications for people with memory impairment

Prevent Delirium

- Delirium is a state of confusion that comes on very suddenly and lasts hours to days. It looks like trouble thinking clearly, trouble paying attention, and being less aware of your environment.
- Delirium is one of the most common complications of surgery (of any type)
- Risk factors for postoperative delirium
  - Older age
  - Cognitive impairment prior to surgery
  - Parkinson's disease WITH OR WITHOUT cognitive impairment
- Postoperative delirium is a risk factor for dementia and can accelerate cognitive decline and disease progression
- Talk to your doctors – there are steps that can be taken to reduce your risk!


UNMC
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BUFFETT
CANCER CENTER
DURHAM RESEARCH CENTER

Autonomic Dysfunction in Parkinson's Disease

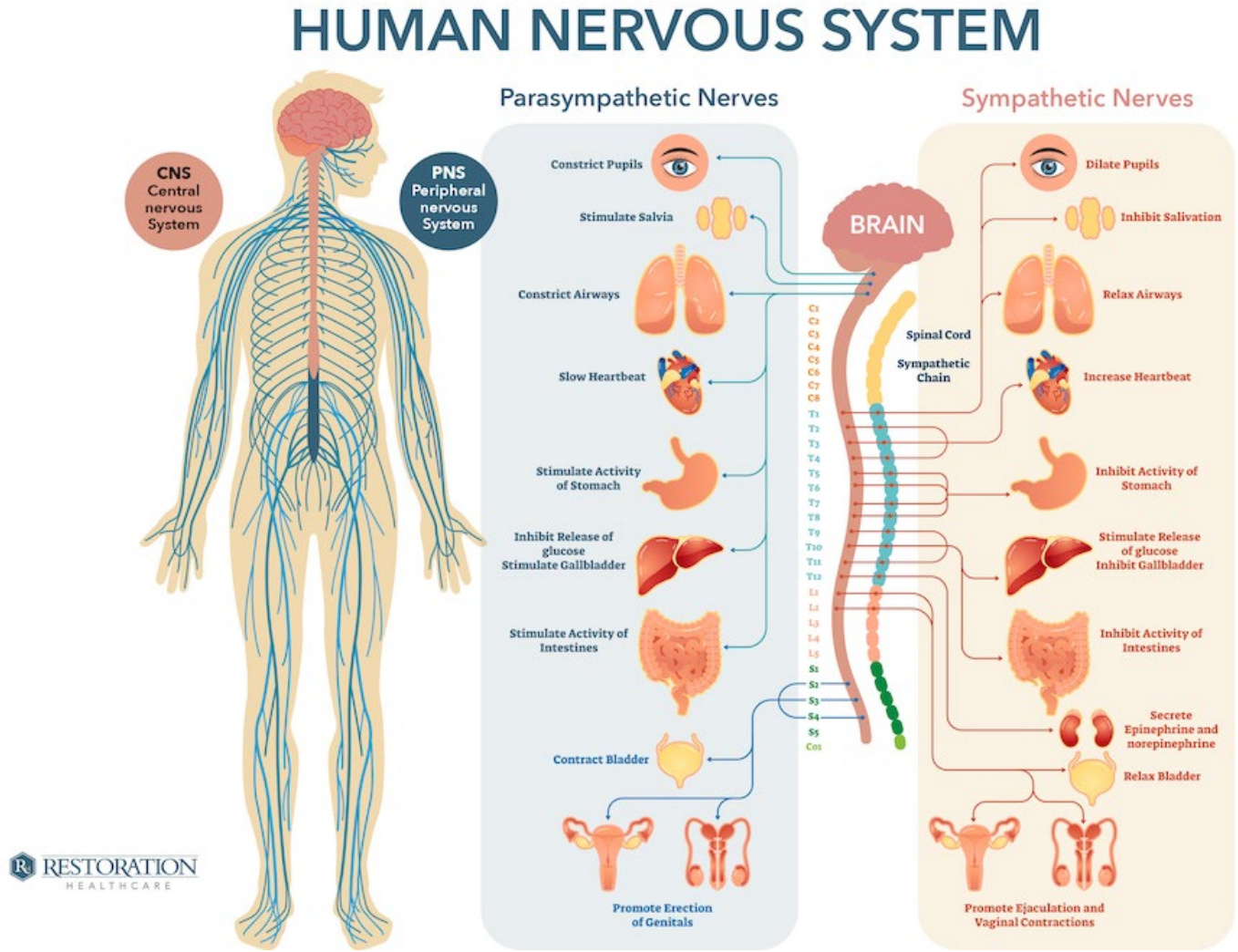
Kiel Woodward, MD

Assistant Professor UNMC Neurological Sciences

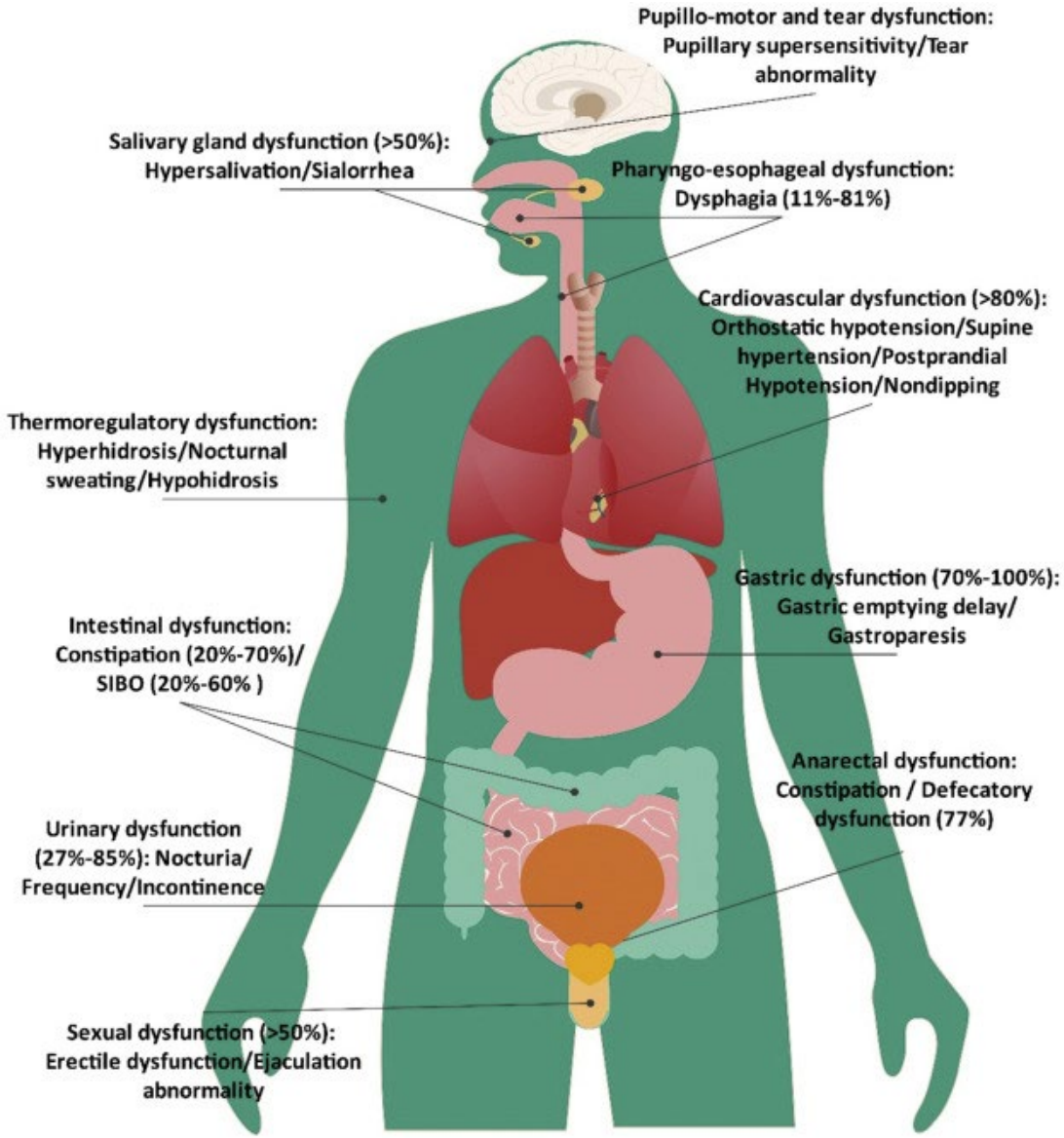
Movement Disorder Division

What is the Autonomic System?

- Controls and regulates the following processes:
  - Blood pressure
  - Heart and breathing rates
  - Body temperature
  - Metabolism
  - Balance of water and electrolytes
  - Sweating, tears, saliva production
  - Digestion and defecation
  - Urination
  - Sexual response

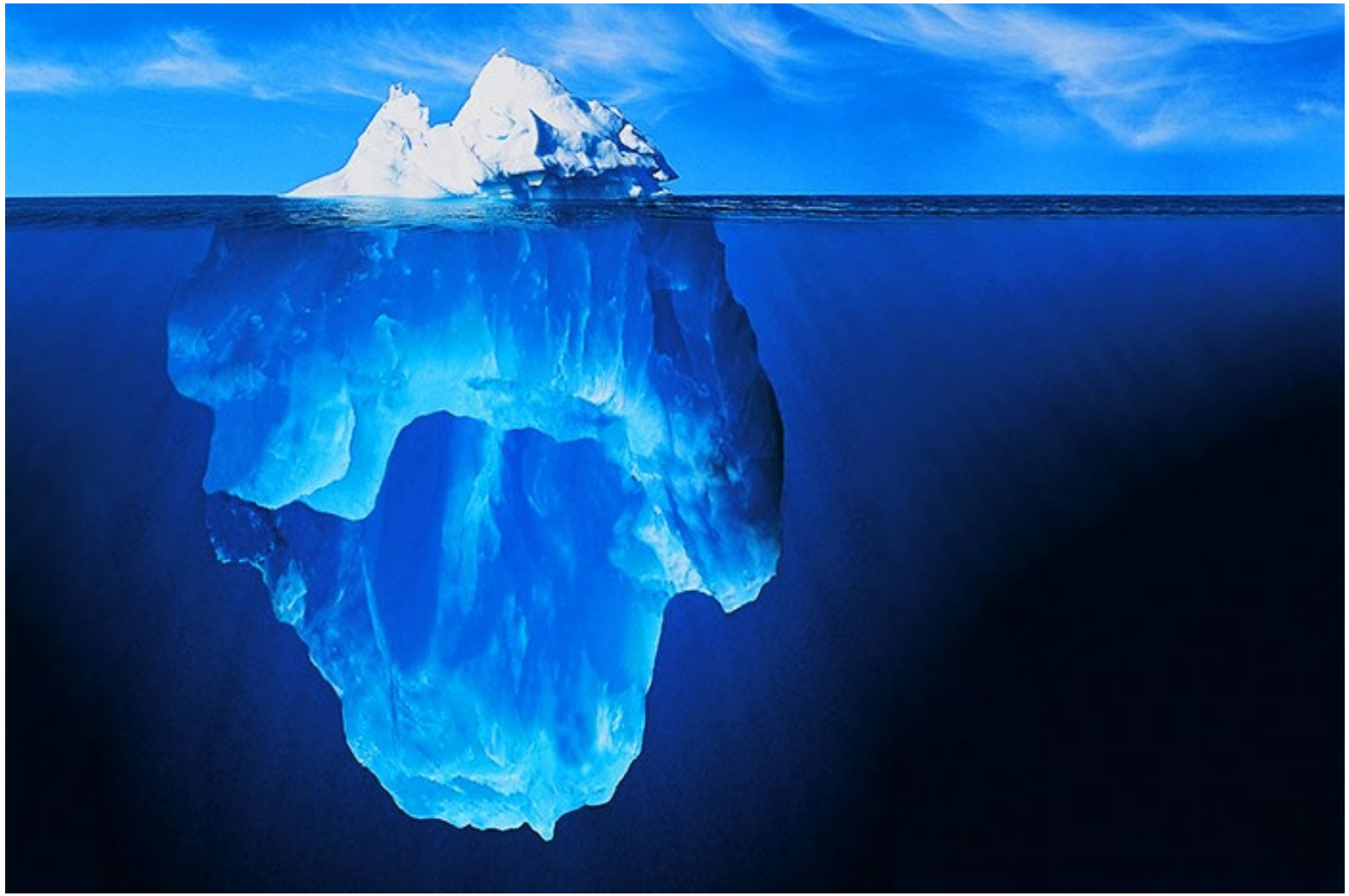


Autonomic Dysfunction in PD



- Motor symptoms
  - Bradykinesia/akinesia
  - Tremor
  - Rigidity/stiffness
  - Gait/balance changes

- Non-motor symptoms
  - Depression/anxiety
  - Psychosis
  - Sleep disturbance
  - Daytime sleepiness
  - Cognitive changes/bradyphrenia
  - **Urinary dysfunction**
  - **Constipation**
  - **Dizziness and hypotension**
  - **Drooling**
  - Sexual dysfunction
  - Fatigue
  - Pain



Orthostatic Hypotension

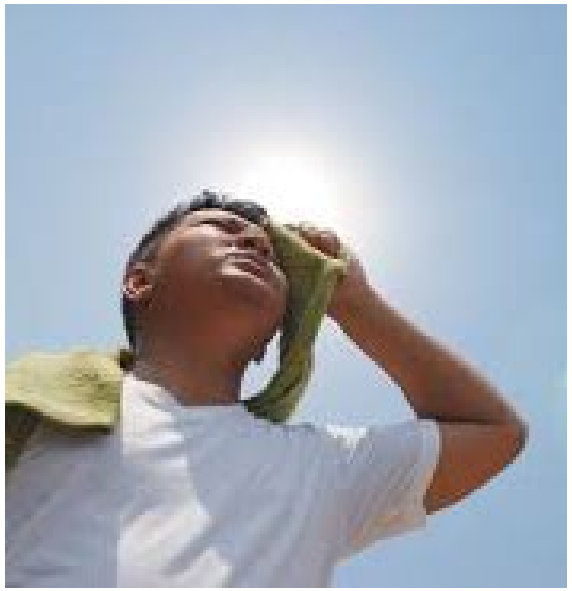
Orthostatic Hypotension

- A drop in blood pressure when changing positions or when standing for long periods
  - Sometimes called postural hypotension
- A very common cause of dizziness or lightheadedness in PD

Orthostatic Hypotension

- Very common in Parkinson's (40-60% experience it), caused by:
  - Parkinsons Disease, itself
  - Medications to treat PD

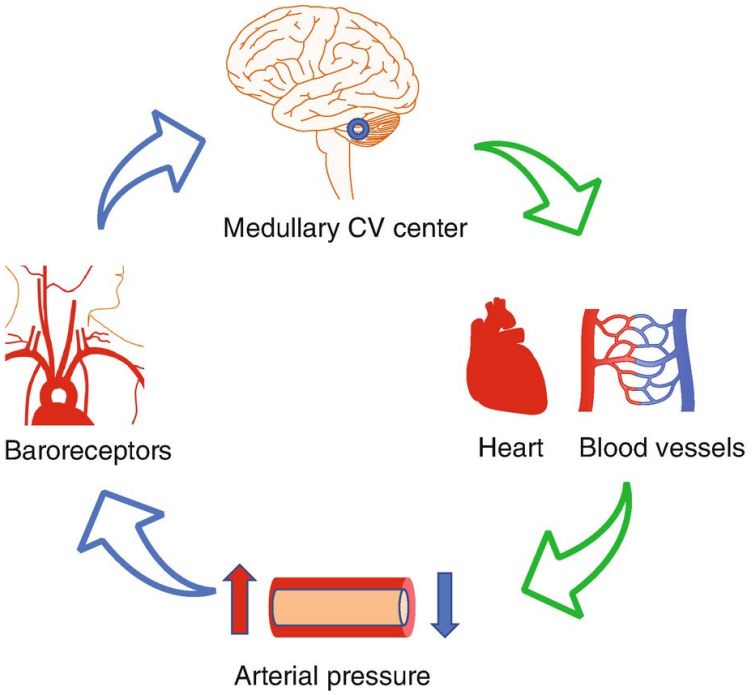
- Common triggers
  - Quick change of position (laying to standing, seated to standing)
  - Exercise
  - **Dehydration**
  - Eating large, carbohydrate-rich meals
  - Hot weather, taking hot shower/bath
  - Alcohol



Orthostatic Hypotension

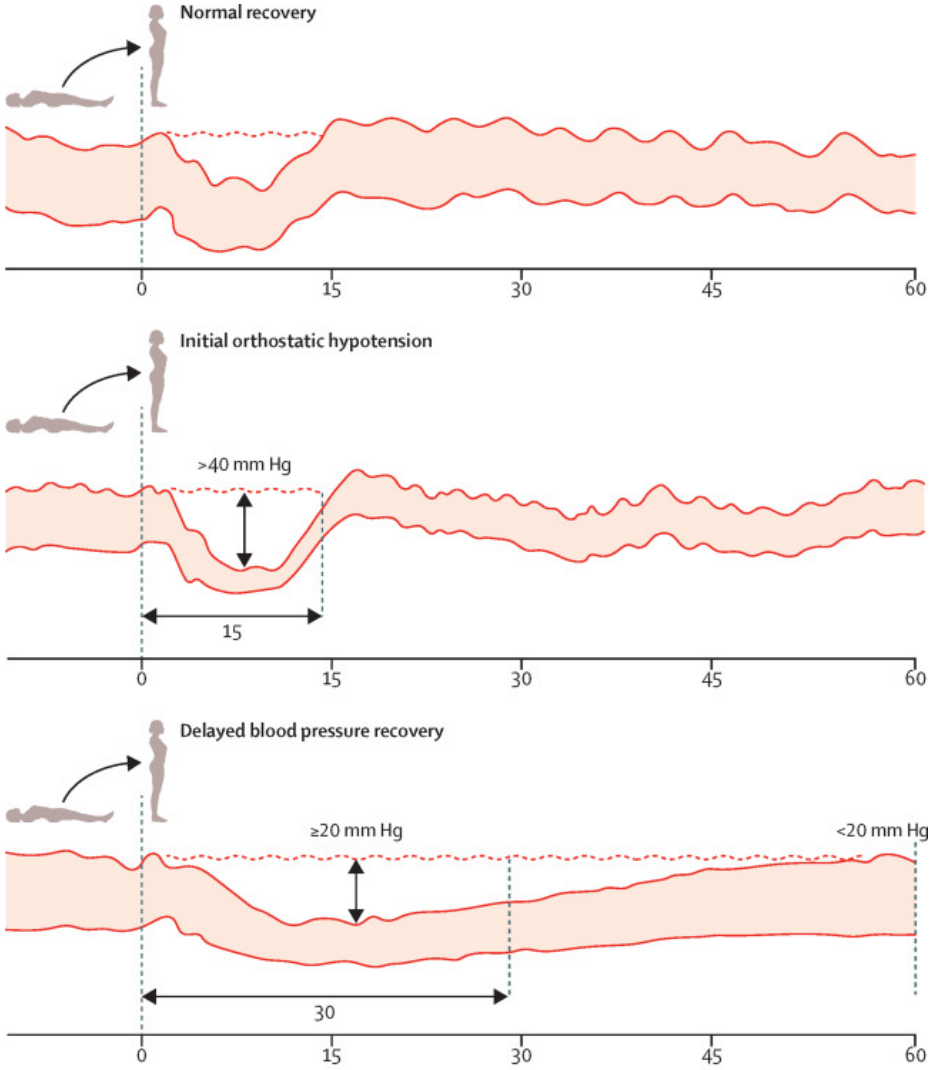
- Can also cause other symptoms:
  - Fainting (“passing out”)
  - Unexplained falls
  - Generalized weakness
  - Sleepiness or fatigue
  - Dull pain covering neck and shoulders (“coat hanger” pain)
  - Blurring of vision, tunnel vision
  - Cognitive changes (feeling slow, sluggish)
    - Due to reduced blood flow to the brain

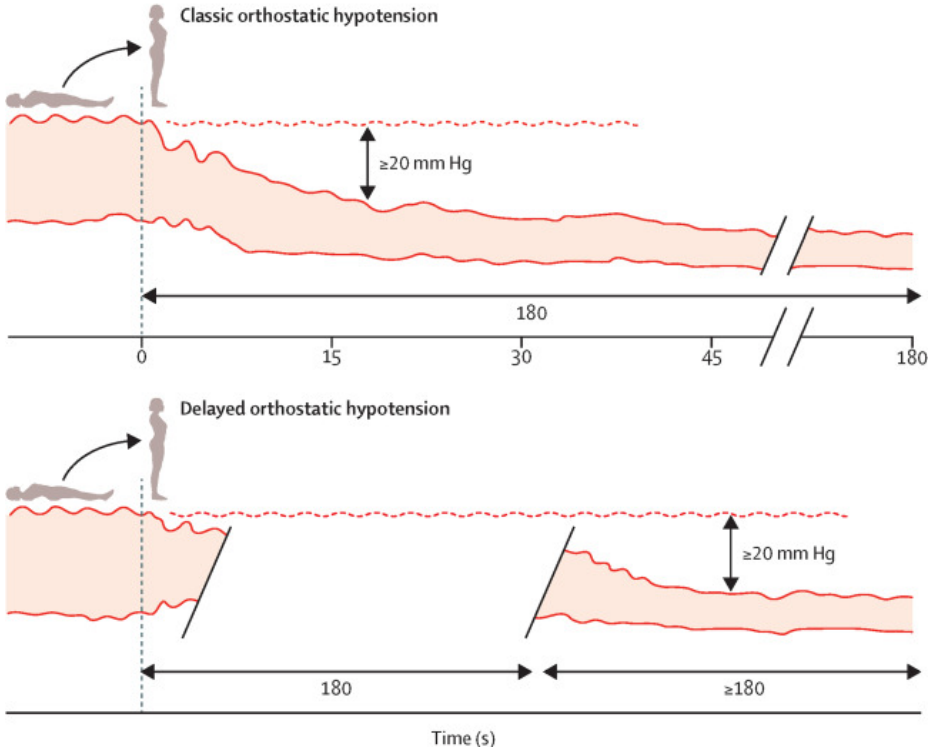
Orthostatic hypotension: Why does this occur?



- When we stand up, gravity pulls our blood down to the expandable venous system in the lower body
- This fluid shift causes less blood flow return to the heart so it pumps less blood and then causes a drop in the blood pressure
- This drop in blood pressure is detected by baroreceptors (blood pressure sensors) in the arteries and triggers increased heart rate and vasoconstriction via release of **norepinephrine** (adrenaline) which normally acts to restore the blood pressure.
- Orthostatic hypotension can occur when this system fails
  - **In PD there are reduced levels of norepinephrine and reduced innervation to the heart**

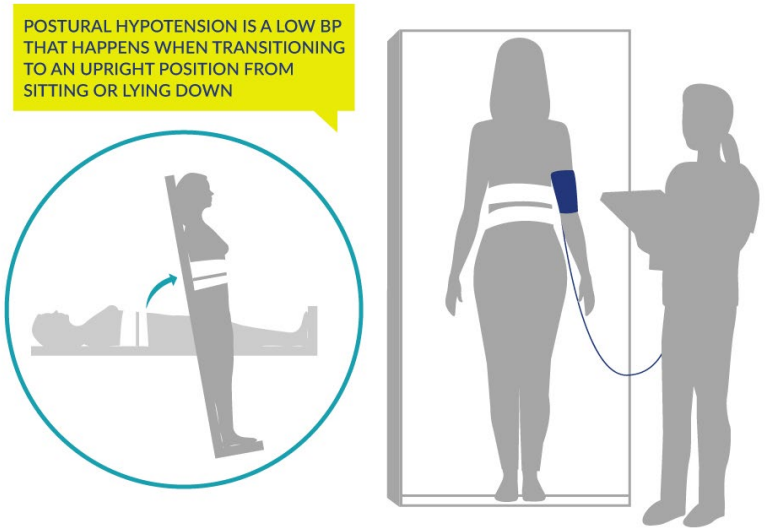
Different forms of Orthostatic Hypotension





How to test for orthostatic hypotension:

1) Take blood pressure and pulse 3-5 minutes after sitting
2) Re-take blood pressure and pulse 3 minutes after standing up
3) If the systolic BP (top number) drops by 20 or more points or if the diastolic BP (bottom number) drops by 10 points = orthostatic hypotension
   - For example: 145/80 sitting but drops to 125/70 when standing



Testing at Home

1. Obtain heart rate and blood pressure after lying down for 5 minutes without pillows and record. *If lying flat compromises patient's breathing status or comfort level, assist them to a position as flat as possible.
2. Obtain heart rate and blood pressure after then sitting up for 3 minutes and record, feet flat on the floor and do not cross legs.
3. Obtain heart rate and blood pressure after then standing for 3 minutes and record.
4. Document the date, time and patient response such as dizziness or lightheadedness.

Measurement Techniques:

For consistency, use the same arm with the same cuff and the same location of pulse measurement should be used. This is easily accomplished by using electronic measuring devices. Please record date and time measurements are taken.

Date	Time	BP and Pulse Lying	BP and Pulse Sitting	BP and Pulse Standing	Comments

Ways to treat orthostatic hypotension

- Change positions slowly
    - Rise slowly from reclined to sitting; sitting to standing
- Increase water intake (up to 2.5 Liters per day)
- Increase salt intake (helps retain water)

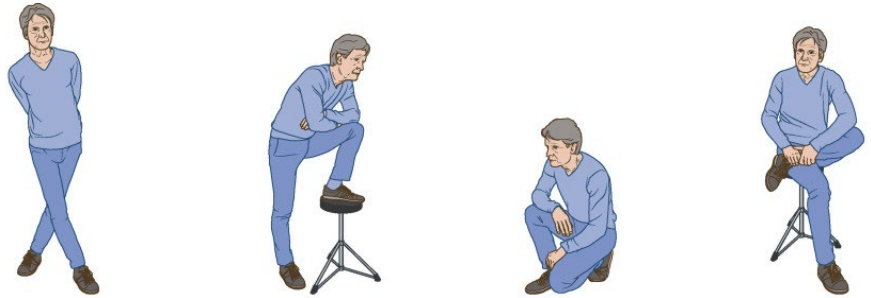
Ways to treat orthostatic hypotension

- Sleep with the head of the bed raised 4-6 inches (~30 degrees elevated)
    - Helps reduce excessively high BP when laying down
    - Helps reduce urination at night

- Physical activity with recumbent exercises (eg, stationary bicycle, rowing machine) or in a swimming pool

Ways to treat orthostatic hypotension

- Being careful about prolonged standing or exercise after a meal or when body temperature is elevated (fever, hot climate, hot shower/bath)
- Physical counter maneuvers (clenching leg muscles, leg crossing/uncrossing, buttock clenching)



Ways to treat orthostatic hypotension

- Compression waist-high stockings that produce 15-20 mm Hg pressure
  - Knee or thigh-high stockings usually do not cut it!
  - Can be difficult to don/doff
    - Measure legs for proper sizing
    - Use of assist tools to help get on
    - Zipper stockings
    - https://www.wikihow.com/Put-on-Compression-Stockings

Ways to treat orthostatic hypotension

- Abdominal binder
- Drink 1-2 large glasses of COLD water before provoking activity
- Assessing blood pressure medication or other medications that can lower blood pressure
  - Levodopa and other dopaminergic medications can make it worse!
  - Diuretics ("water pills"), high blood pressure medications, nitrates, sildenafil

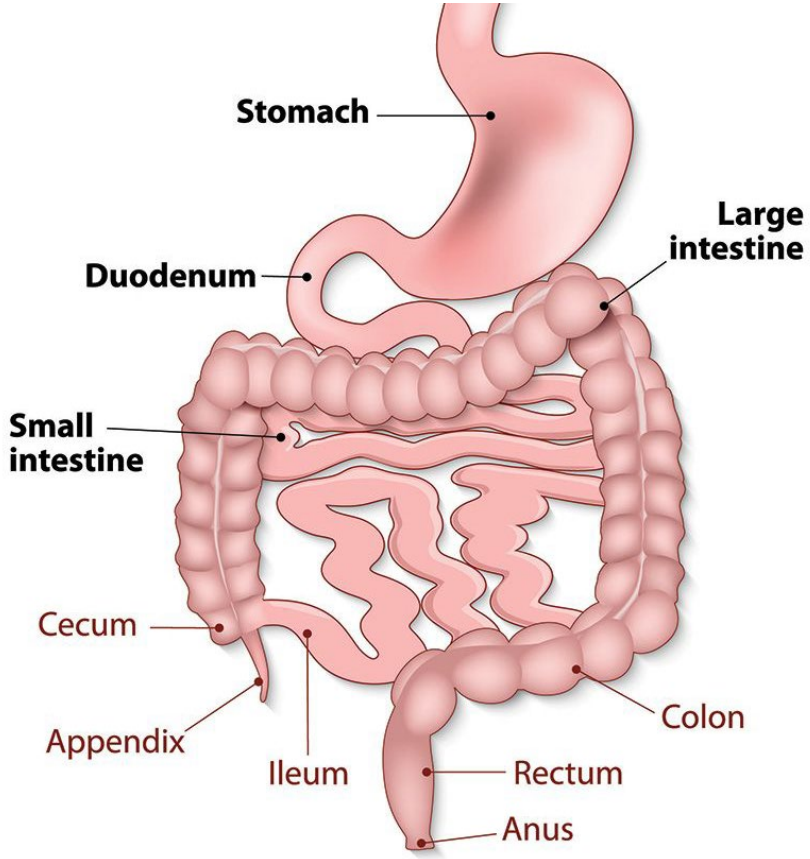
Medications to treat orthostatic hypotension

- **Midodrine**
  - Works by increasing the tone in blood vessels, causing them to tighten and increase blood pressure
- **Fludrocortisone**
  - Works by reducing salt lost by the kidneys – retaining salt increases volume in blood and increases blood pressure
- **Pyridostigmine**
  - Works by increasing blood pressure when standing, helps maintain the autonomic response
- **Droxidopa** (Northera)
  - The only FDA approved drug for neurogenic orthostatic hypotension
  - It is converted into **norepinephrine** which acts to increase blood pressure via the autonomic response
- Must monitor for high blood pressure – especially when laying down (Supine Hypertension)

Constipation

Constipation

- Common symptom in PD; can predate motor symptoms by years!
- Due to an overall slowing of the digestive tract
- Can range from inconvenience to severe and affects quality of life
  - Causing bloating, discomfort, nausea, loss of appetite
  - Inadvertently leading to weight loss
- Can alter medication absorption, such as levodopa

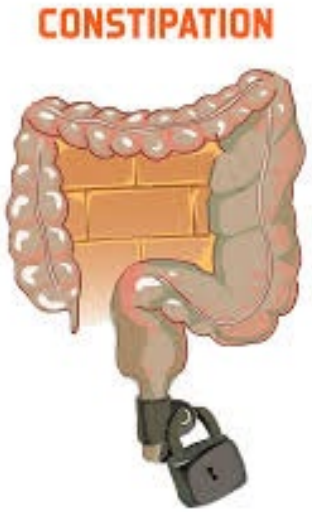


Exacerbating factors of constipation

- Narcotic pain killers
- Calcium antacids (Tums); Aluminum antacids (Mylanta)
- Iron supplements
- Artane or Trihexyphenidyl
- Lack of physical activity
- Lack of adequate water intake
- Lack of fiber in diet

How to Treat Constipation?

- Usually, it can be corrected with **time, patience and dietary changes**.
  - Constipation is not failure to have a daily bowel movement.
  - Constipation is bowel movements that become more infrequent and are dry and difficult to pass.
- The key to relief is patience and consistency. Bowel training usually takes 2 to 3 months.
  - It is tempting to try to control bowel function with enemas or simulating laxatives. However, these can damage the lining and function of the bowel. You should avoid regular use of these agents.



Steps to good Bowel management

- **STEP 1 - Diet and fluid intake**
  - Eat meals at consistent times
  - Include fruits, vegetables, whole grain breads and cereals in daily meals.
  - Drink 6 to 8 glasses (8oz each) of fluid daily.
  - Drink warm liquids on rising and with breakfast.
  - Establish a relaxed, regular time of the day for bowel movements.
  - Increasing evidence for probiotics!

Steps to good Bowel management

- **STEP 2 - Bulk formers (Fiber supplements)**
  - Examples are Bran, Metamucil and Fibercon. They are not habit-forming.
  - Use bulk formers daily
  - Drink 6-8 cups of liquid daily with bulk formers. If you do not, your constipation may worsen.
- DO NOT increase the amount of bulk former too quickly. Gas formation or stomach fullness may result.
- BE PATIENT. Bulk formers may take 2 to 3 months to correct constipation.

Steps to good Bowel management

- **STEP 3 - Stool softeners**
  - Stool softeners, like bulk formers, are not habit-forming and may be purchased without a prescription.
    - An example: Docusate
    - Begin with one a day. Increase to one each morning and evening if needed.

Steps to good Bowel management

- **STEP 4 - Laxatives**
  - Stimulating laxatives **should be used with caution** and long-term use may actually harm the bowel. Avoid: Ex-lax, Ducolax, Feenamint, Correctal and Castor Oil.
    - DO NOT use these while trying to establish a bowel program.
  - **MiraLax**: which is an osmotic laxative, is thought to be safe to use on a regular, continuous basis

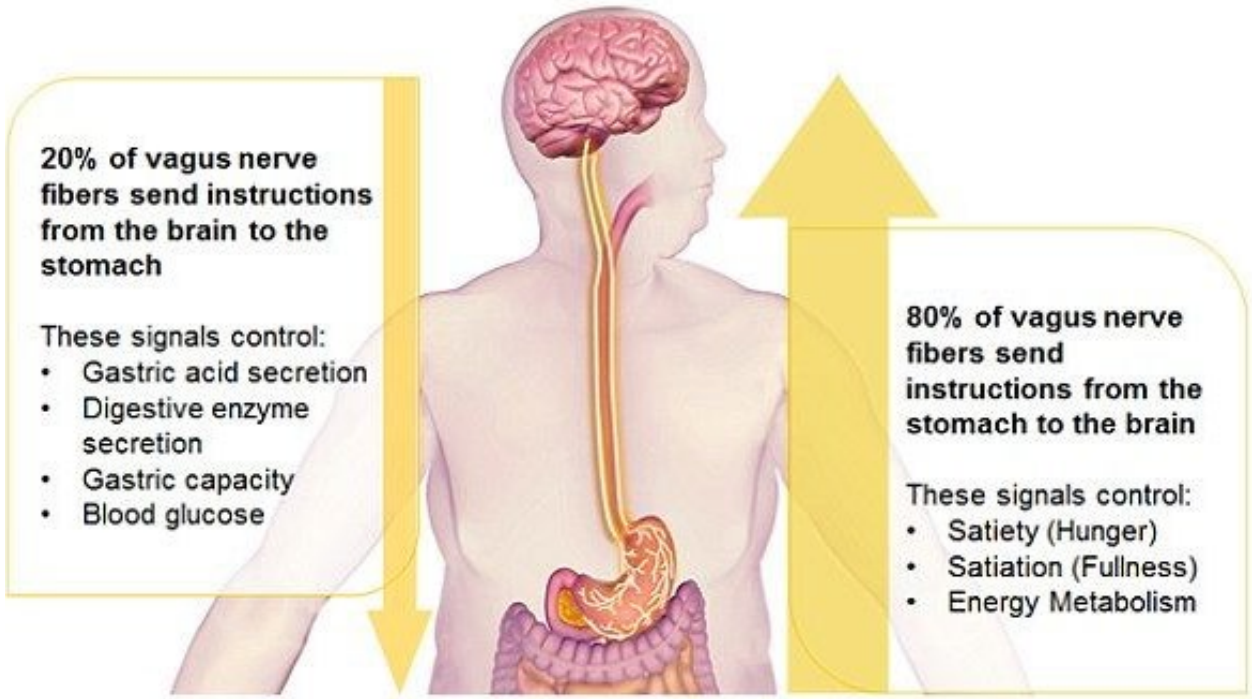
Steps to good Bowel management

- **STEP 5 – Suppositories and Enemas**
  - Suppositories provide rectal stimulation to empty the bowel. You may need to use suppositories while establishing a bowel program.
  - The bowel can easily become dependent on **enemas**. Only use when nothing else works.

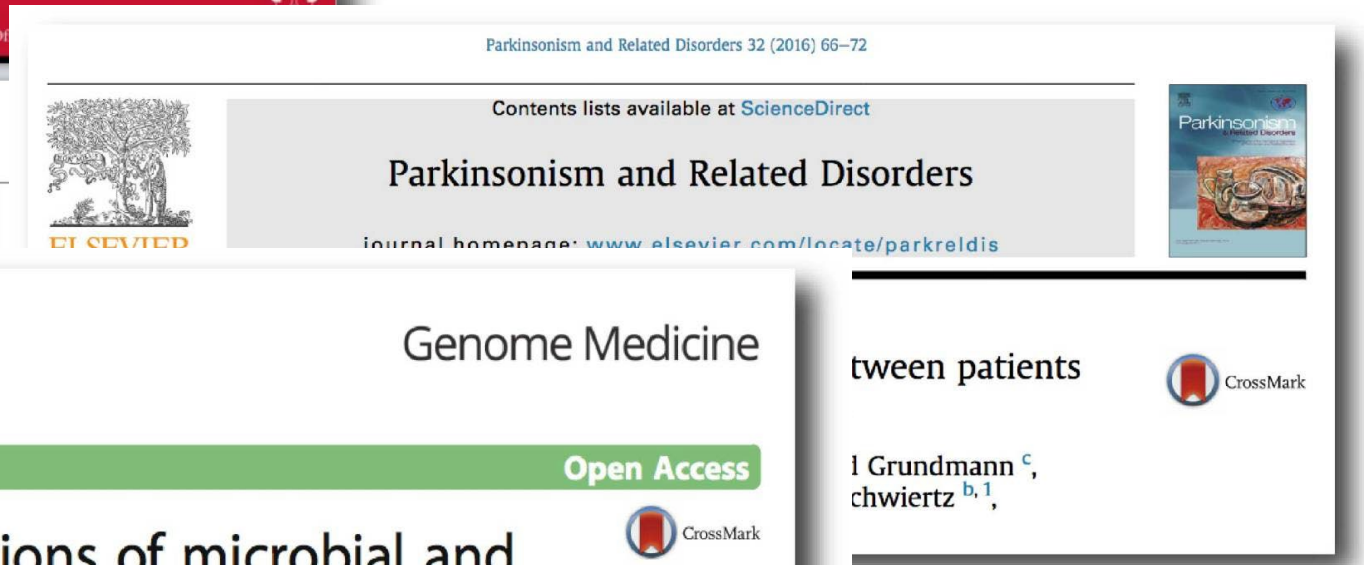
CONSISTENCY AND PATIENCE ARE THE KEYS TO MANAGEMENT OF CONSTIPATION.

Gut – Brain connection

- **Alpha-synuclein** – the same protein that clumps in brains in people with PD – is also found in the gut
  - Pathological evidence of misfolded alpha synuclein has been found in the nerves of the enteric system (gut) in people with PD
  - Some researchers believe that PD may start in the gut and spread to the brain




Movement Disorders
RESEARCH ARTICLE
Gut Microbiota Are F
Filip Scheperjans, MD, PhD,[1*] Velma Aho,
Eero Pekkonen, MD, PhD,[1] Elena Haapani
Marjatta Pohja, MD, PhD,[1] Esko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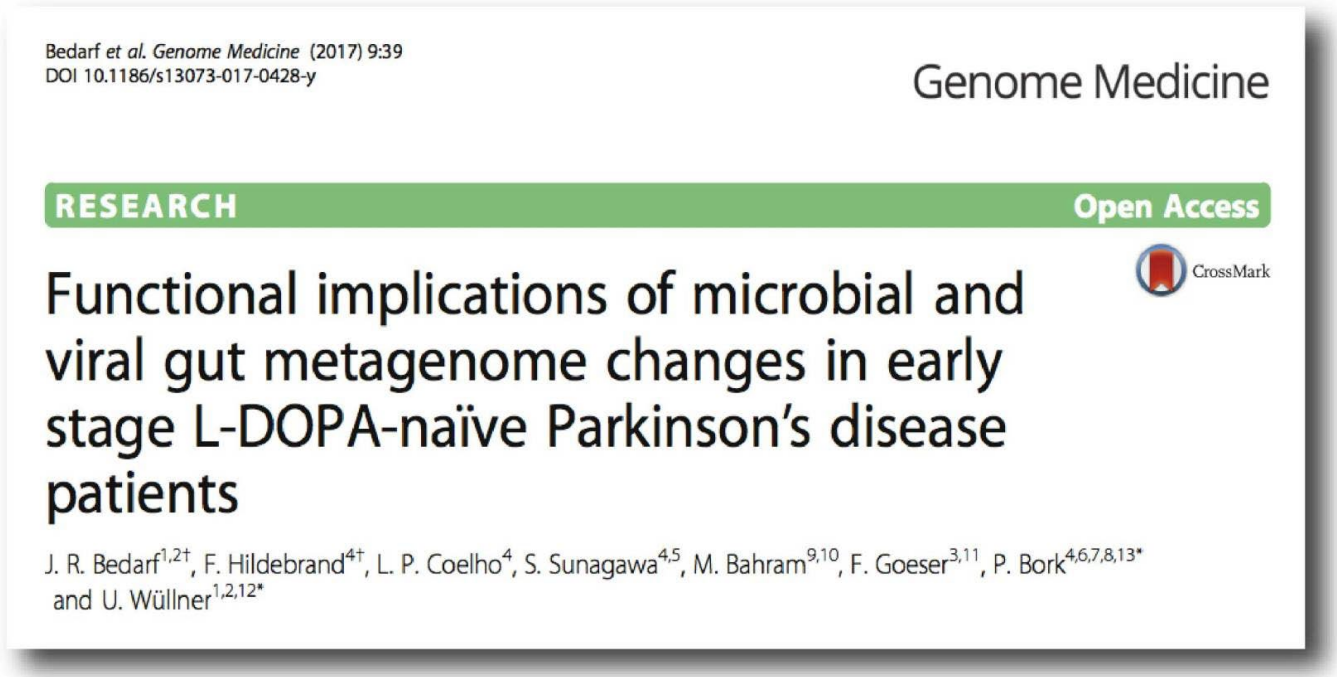
Bedarf et al. Genome Medicine (2017) 9:39
DOI 10.1186/s13073-017-0428-y
Genome Medicine
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Functional implications of microbial and viral gut metagenome changes in early stage L-DOPA-naïve Parkinson's disease patients
J. R. Bedarf[1,2†], F. Hildebrand[4†], L. P. Coelho[4], S. Sunagawa[4,5], M. Bahram[9,10], F. Goeser[3,11], P. Bork[4,6,7,8,13*] and U. Wüllner[1,2,12*]


Movement Disorders
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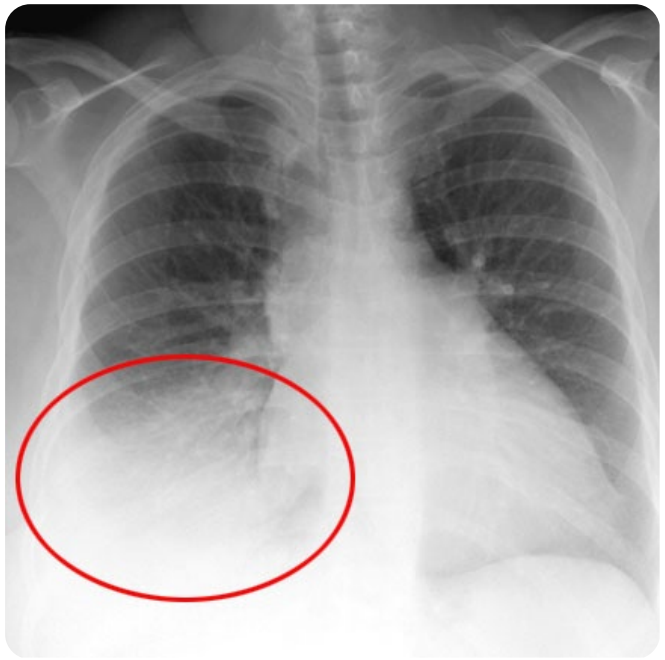
Parkinson's Disease and Parkinson's Di
Distinct Signatures of the Gu
Erin M. Hill-Burns, PhD,[1] Justine W. Debelius, PhD,[2] James T. Mor
Matthew R. Lewis, MS,[1] Zachary D. Wallen, MS,[1] Shyamal D. Peddada, Ph
Cyrus P. Zabetian, MD, MS,[7] Rob Knight, PhD,[2,3,8] an

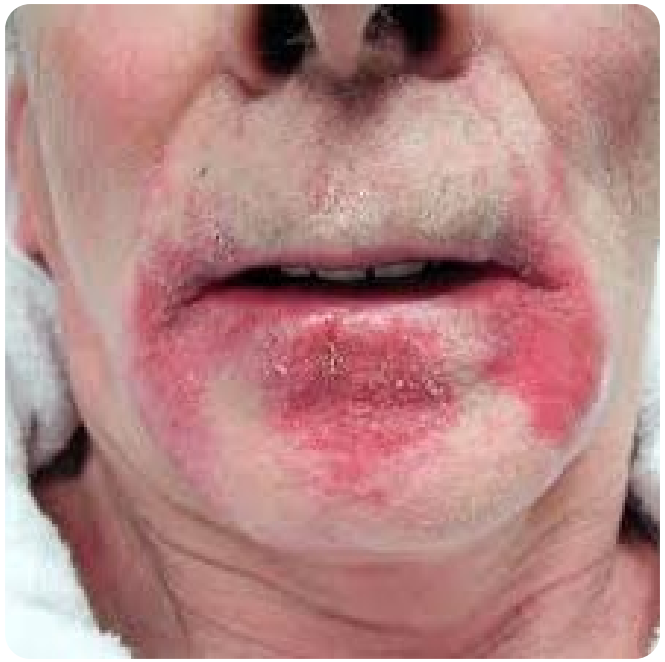

Colonic Bacterial Composition in Parkinson's Disease
Ali Keshavarzian, MD,[1,6,7,8*] Stefan J. Green, PhD,[3,4] Phillip A. Engen, BS,[1] Robin M. Voigt, PhD,[1] Ankur Naqib, BS,[3]
Christopher B. Forsyth, PhD,[1,5] Ece Mutlu, MD,[1] and Kathleen M. Shannon, MD[2]

Sialorrhea

Sialorrhea

- Otherwise known as: “drooling”
- Excessive pooling and poor control of saliva in the the mouth
  - In PD, it is unclear if this is due to either “poor clearance” (swallowing dysfunction) or increased production of saliva
  - Head and mouth position may also play a part
  - Tends to be more prominent during “off” period
- Occurs in up to 50-80% of people with PD





Sialorrhea

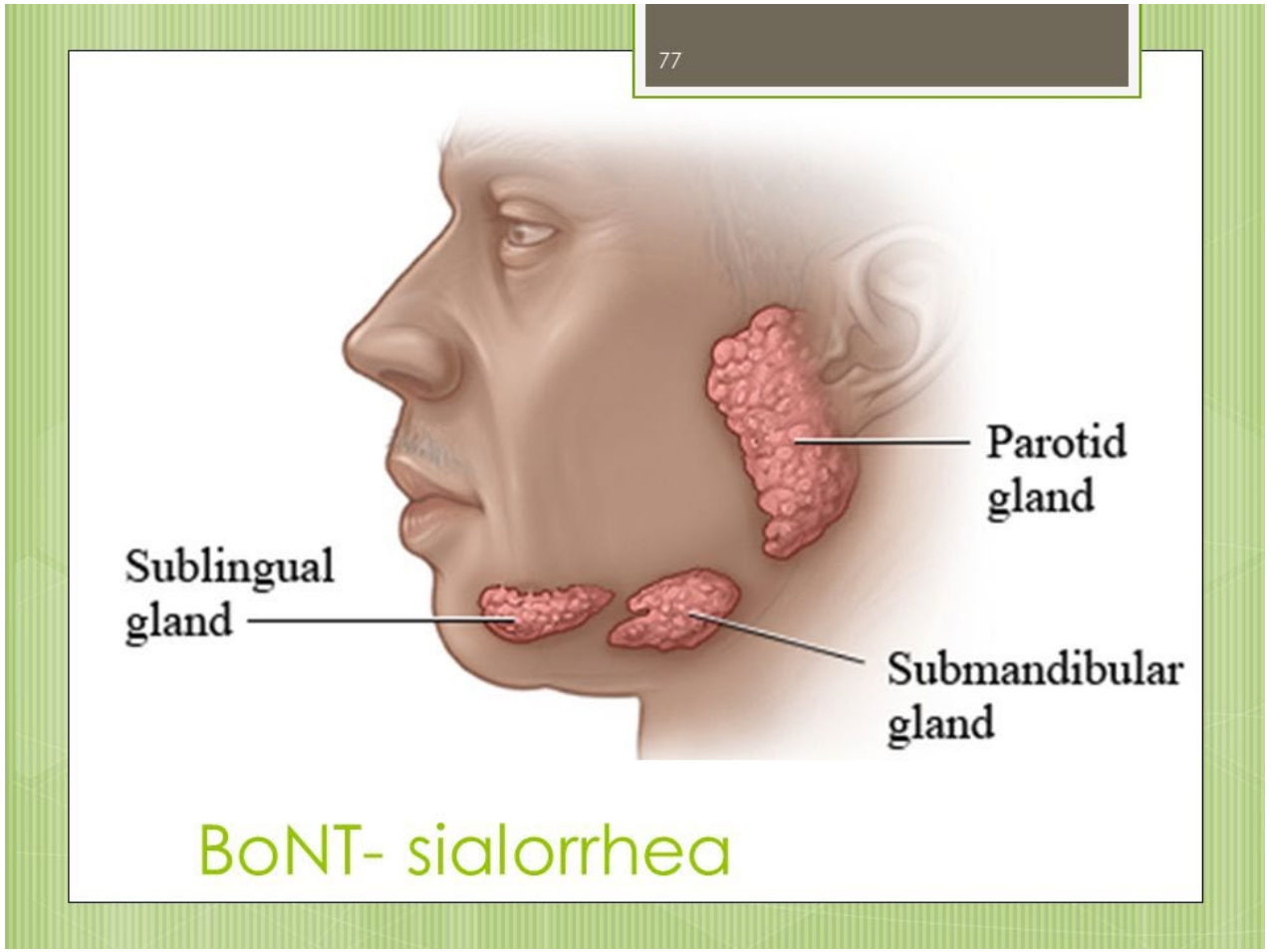
- Symptoms can range from wetting of pillow at night to embarrassing excessive saliva in social situations
  - Severe issues can be related to concerning swallowing issues that can lead to choking; needs assessment from speech language pathologist
- Factors possibly associated with drooling:
  - Severity of PD symptoms
  - Male gender
  - Older age
  - Presence of hallucinations
  - Duration of disease

Drooling Management

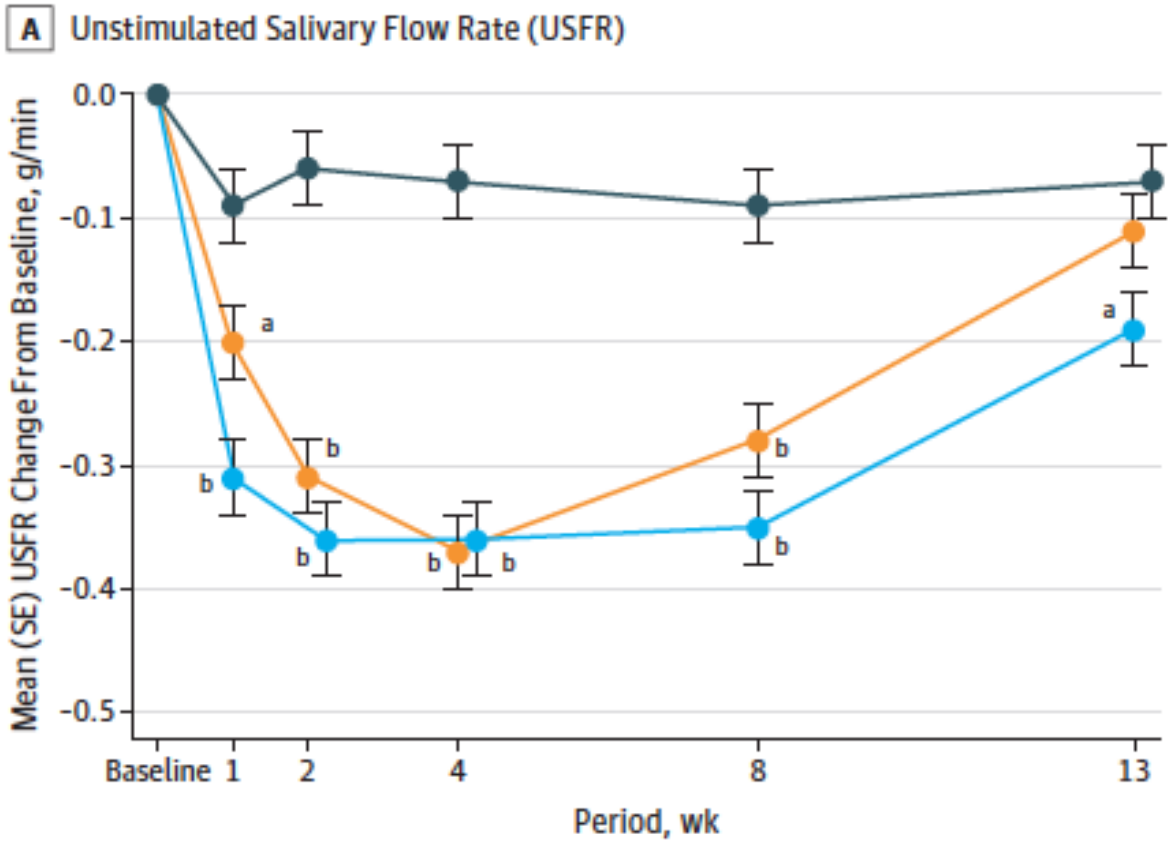
- Stopping or reducing medications that can aggravate/cause drooling:
    - Donepezil/galantamine and quetiapine are common
- Non-medication options
    - Chewing gum; sucking hard candies
    - Behavioral modification
- Medications
    - Glycopyrrolate and atropine drops (possible side effects: confusion)
    - Clonidine (can lower blood pressure; less evidence)
    - **Botulinum toxin injections** (over 21 studies showing effectiveness)

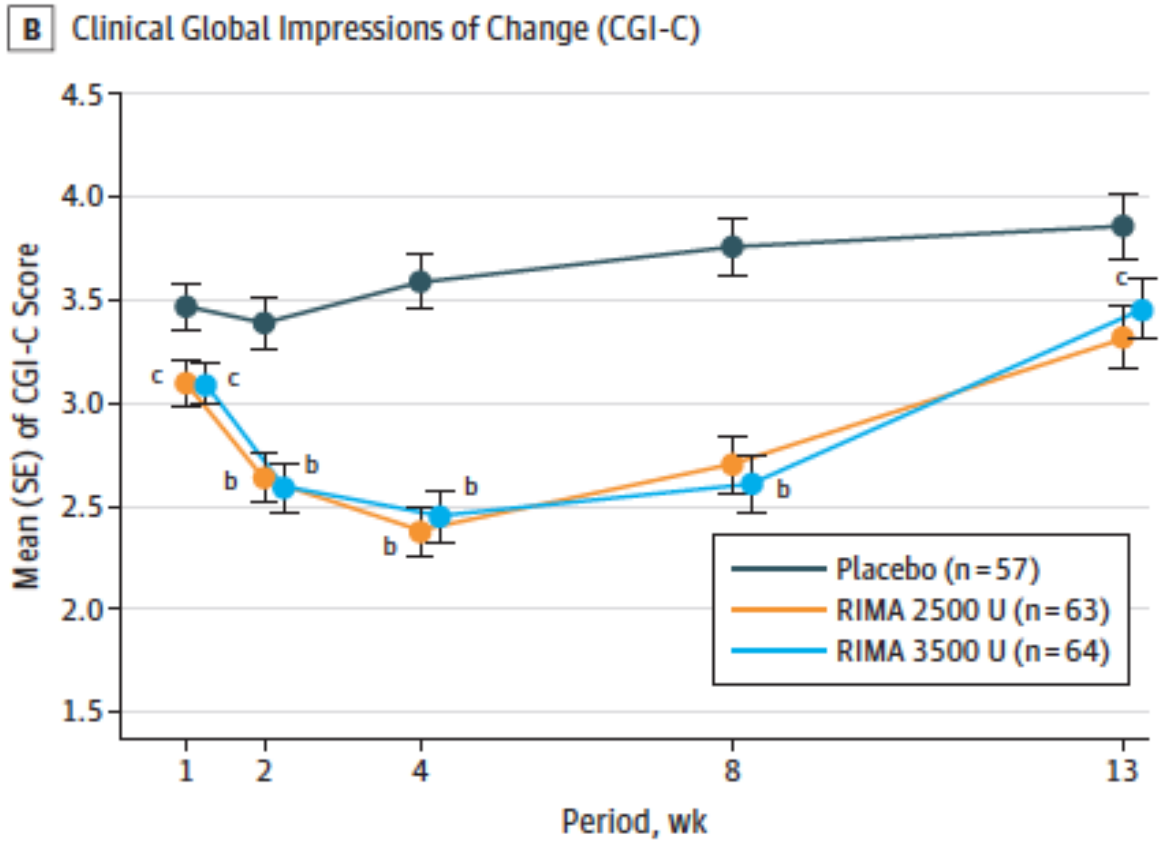
Botox for Drooling

- Injected directly into the salivary glands
  - 4-6 injections with a very small needle
  - Procedure takes just a few minutes
- Very effective at reducing saliva production
- Benefit typically lasts for 3-6 months at a time before needing to repeat
- Minimal side effects: temporary bruising/discomfort, dry mouth, difficulty swallowing



Efficacy of Botox for Sialorrhea





*Normal rate of saliva production is about 0.4 g/min

RimabotulinumtoxinB for Treatment of Sialorrhea in Adults

Urinary dysfunction

Urinary Dysfunction

- **Urinary symptoms** are the most prevalent autonomic symptom in PD across several studies (up to 85% of people with PD)
  - Can occur in “early-stage” PD
- Urinary irritative symptoms (“overactive bladder”)
  - Urinary frequency (needing to urinate very frequently)
  - Increase frequency at night (Nocturia)
  - Urinary urgency (“When you need to go – you need to go!”)
  - Urinary incontinence (Less common)
- Urinary obstructive symptoms
  - Incomplete emptying of the bladder
  - Difficulty starting flow
  - Increased risk of urinary tract infections (UTI’s)

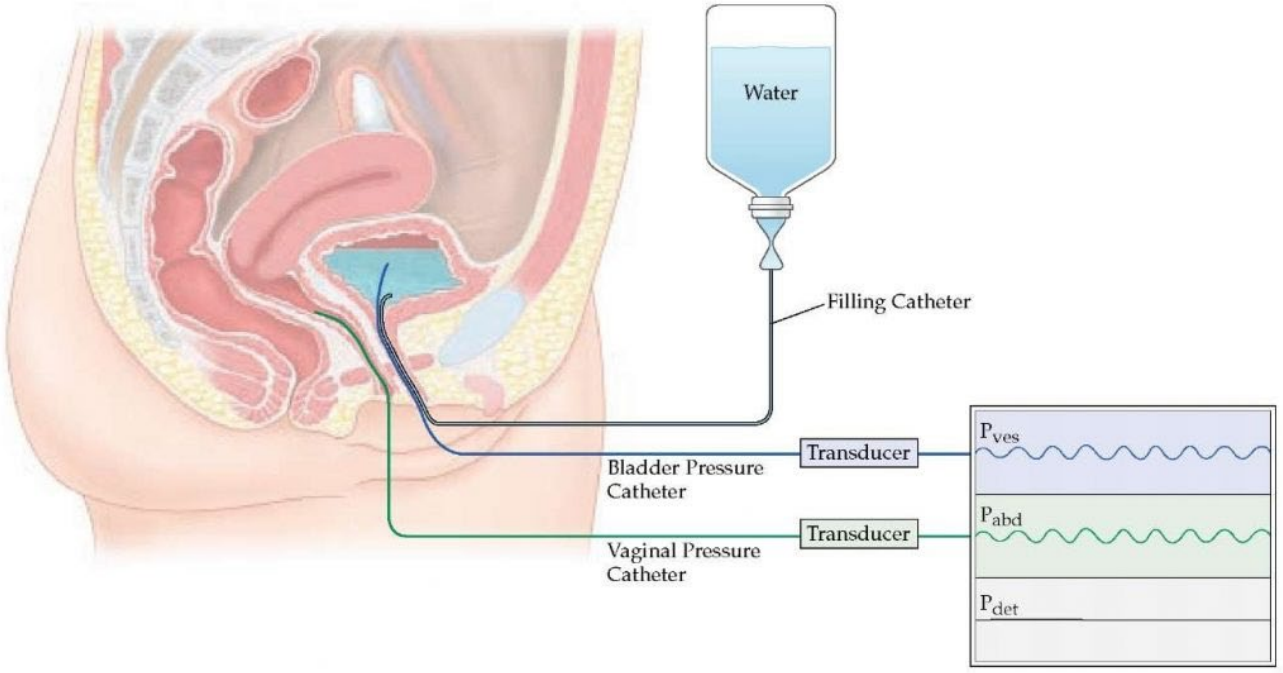
Urinary dysfunction

- Associated with:
  - Increase incidence of falls
  - Cognitive impairment
  - Worse motor and non-motor impairment

- Can cause issues in relationships, intimacy and disrupt social activities and lead to embarrassment
  - Impacting quality of life

Urinary Dysfunction

- May require referral with a Urologist and further testing:
  - Ultrasound of the bladder after urinating to check for residual urine in the bladder
  - Urodynamics studies: assess how well the bladder empties, assess the function of sphincters and the urethra to hold and release urine



Treatment of urinary symptoms

- Conservative measures:
  - Timed voiding
  - Bladder retraining/urge suppression to train bladder to hold for longer periods of time
  - Pelvic floor physical therapy
  - Avoiding spicy foods, caffeine, alcohol, artificial sweeteners and diuretics
- Medications:
  - Ditropan (oxybutynin); Vesicare (solifenacin); Detrol (tolterodine) - examples of anticholinergic medications that treat overactive bladder: side effects dry eyes and mouth, constipation, memory/cognitive issues
  - Mirabegron: different mechanism that does NOT have same SE's as the older bladder medications
- Procedures:
  - Botox injections in the bladder wall
  - Bladder stimulator; electrical pulses to the sacral nerves
  - Percutaneous tibial nerve stimulation


UNMC
Nebraska
Medicine
BUFFETT
CANCER CENTER
DURHAM RESEARCH CENTER
G.C. WERNER CANCER HOSPITAL

Thank you!

Research Updates in Parkinson's Disease

Miguel Situ-Kcomt, MD
Assistant Professor
Division of Movement Disorders

10/01/2025

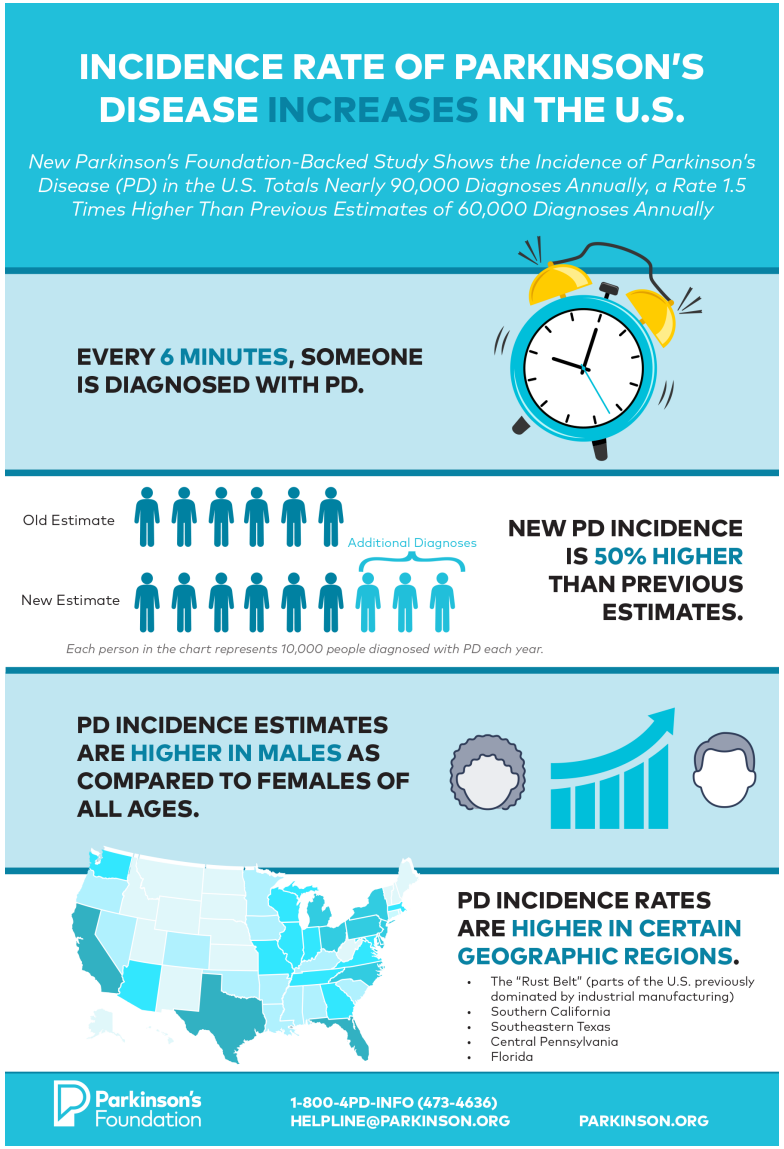
UNMC COLLEGE OF ALLIED HEALTH PROFESSIONS

Disclosures

None

Why we need to invest in PD?

- US$ 51.9 – 61.0 billion/year
  - US$ 20k to 23k annually per patient – direct and indirect costs.
- ~1.1 million Americans affected.
  - ~90k new diagnoses per year.

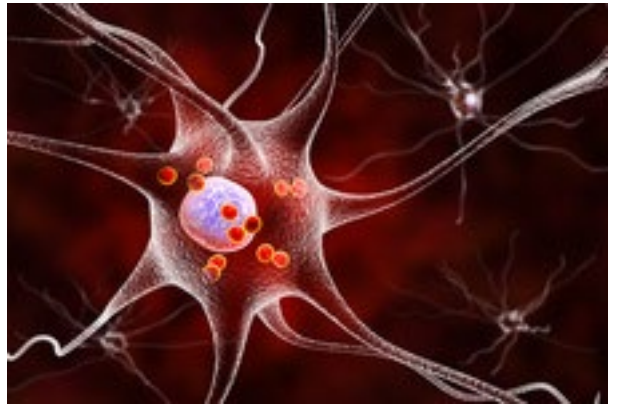


https://www.parkinson.org/

Do we even know how to diagnose it?

- 208 years since Dr. Parkinson described it and we still **mainly rely** on his examination findings (plus Dr. Charcot's rigidity description)

- The **absolute gold standard** remains the pathology in autopsy.



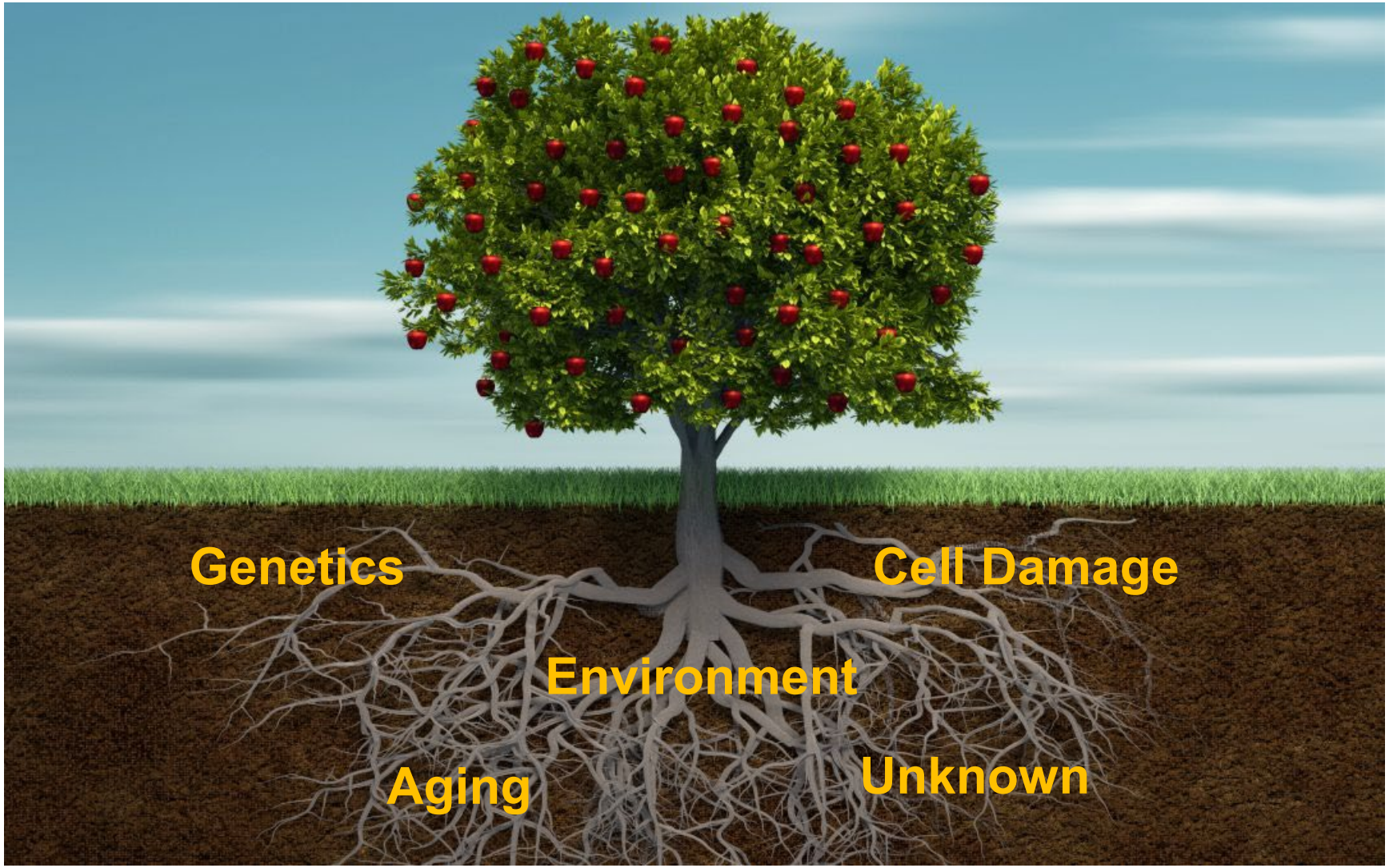
Paradigm Shifts in PD

1. Is it a disease or a syndrome?
   - **Disease:** a pathological condition with a known cause, course and specific underlying biology.

   - **Syndrome:** collection of signs and symptoms with a particular abnormality but with multiple causes.

2. Is alpha-synuclein protein a cause or a consequence?

The “cure” isn’t so straightforward



Courtesy: Dr. Erin Cameron-Smith

Topics to Address

1. Do we have **Cures/Disease-Modifying** Therapies

2. How to **Diagnose it Better**

1. Quality of Life **Improvements**

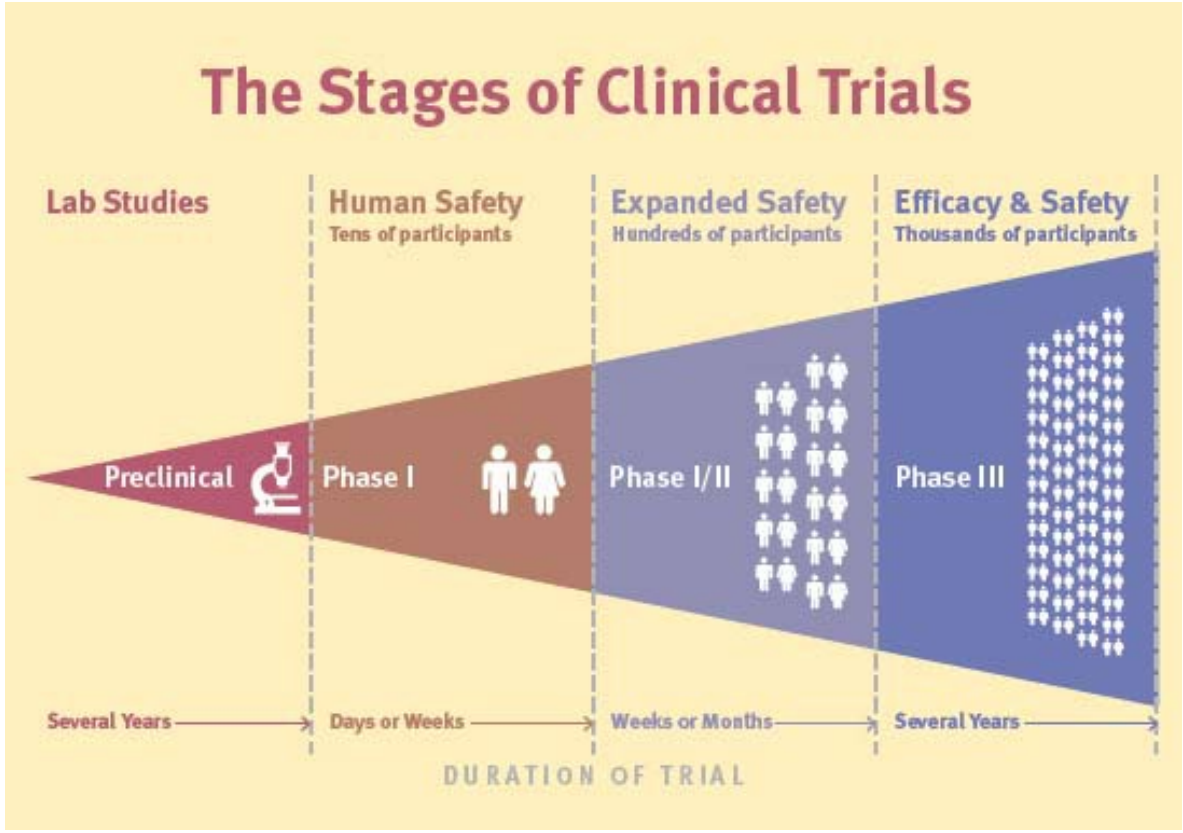
A bit of research lingo…

Phase 1: “Is it safe?” – tested on healthy volunteers.

Phase 2: “Is it safe and shows any promise in patients” – tested in PD patients.

Phase 3: “Is it useful in a large population of patients with a standard dose”

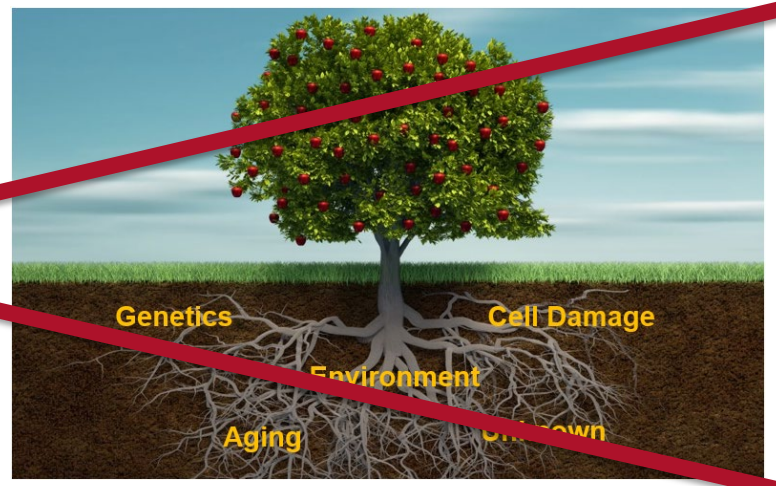
Phase 4: “How does it perform long-term in a real-world setting?” – it is analyzed after approved.



Cures/Disease-Modifying

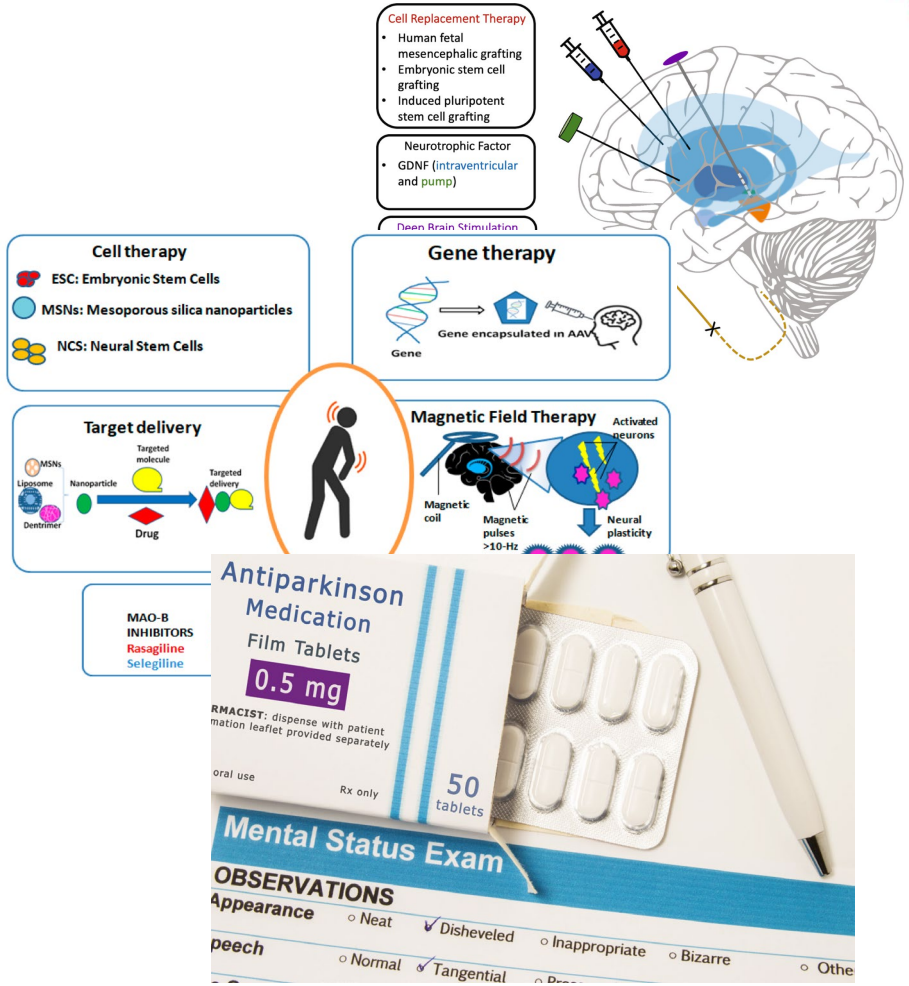
- By **intercepting the mechanism**

- By attacking the **root cause**

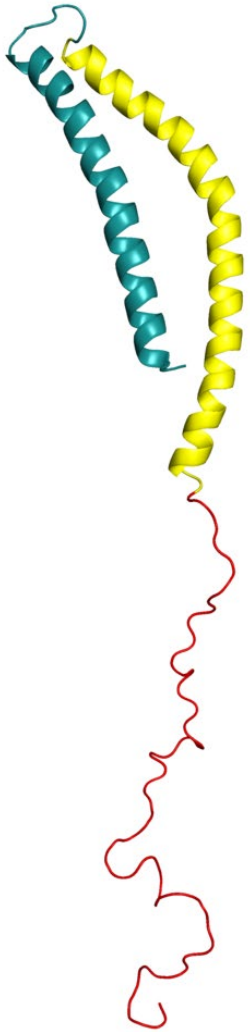


Intercepting the Mechanism

- Alpha-synuclein aggregation/spread
- GLP-1 receptor agonists
- Stem Cell Therapy

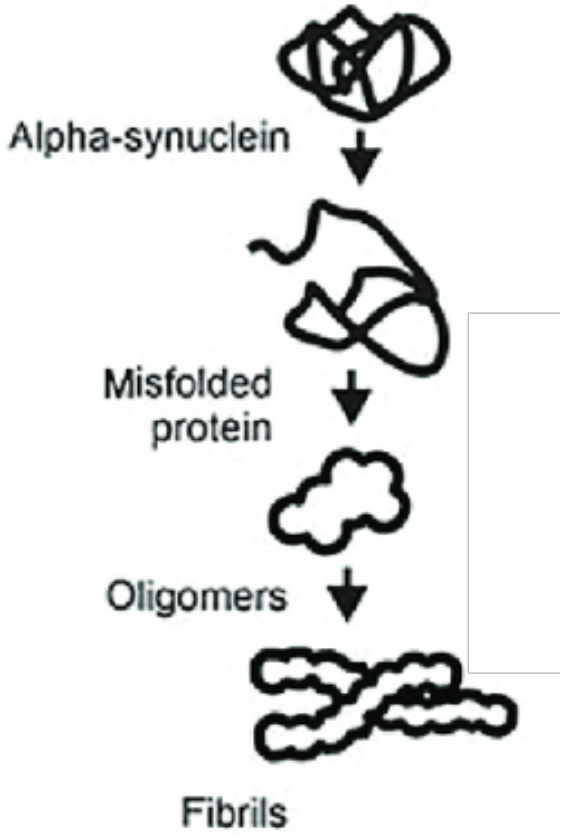


Alpha-synuclein aggregation



- α-synuclein is normal in our body.
- When it **misfolds**, then it accumulates/aggregates.

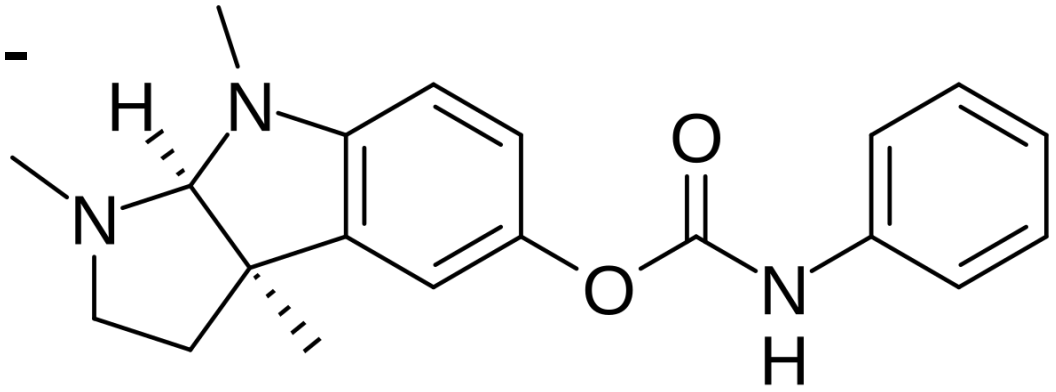
HYPOTHESIS: If we find it in PD, then taking the misfolded protein out will help in modifying the disease course.



Pauwels EKJ, Boer GJ. Parkinson's Disease: A Tale of Many Players. Med Princ Pract. 2023;32(3):155-165.

How many trials targeting it

- Being trialed on humans:
  - **Ambroxol** –
    Has shown to help in patients with GBA mutation
    Phase 2 ongoing
  - **Buntanetap** –
    Targets transport of mutated α-synuclein, amyloid-beta, tau proteins.
    Phase 3 is ongoing.



How many trials targeting it

- Not tried on humans:
  - **ABL301** – **In vitro and animal models** have been successful.
  - **ABBV-0805** – Phase I stopped in July 2020. Unknown reasons.
  - **ANLE138b** – Mild improvement **in rats.**
  - **MEDI1341** – Planned Phase I. No updates since 2022 though.

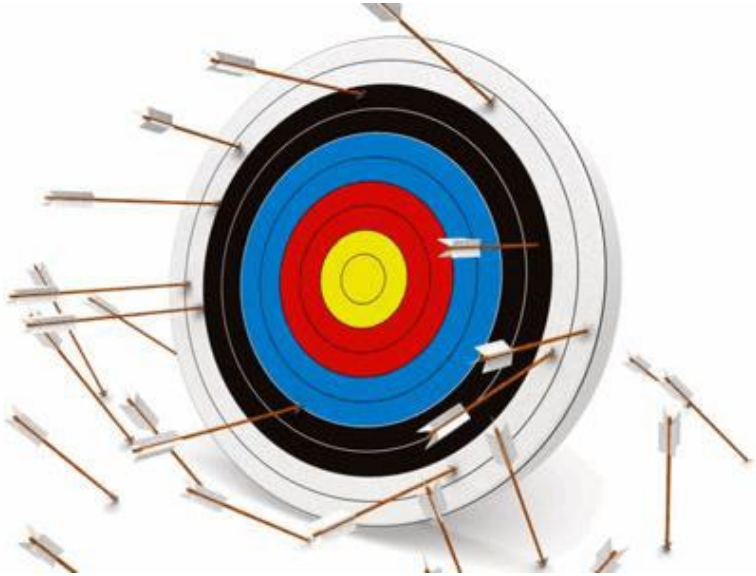
How many trials targeting it

- Vaccines (create alpha-synuclein antibodies):
  - **ACI-7104.56** – Phase 2 (VacSYn) enrolling.
  - **UB312** – Planned for human studies.
  - **ANLE138b** – Tried in **mouse models** and had shown mild improvement.
  - **AAV vector of antibody** – Development has been put on hold.

How many trials targeting it

- 3 Failed Agents:
  - **Cinpanemab** – Phase 2 SPARK trial failed to demonstrate benefit. Stopped trials.
  - **Mizasolmin** (UCB5099) – ORCHESTA trial failed to demonstrate benefit. Stopped trials.
  - **Prasinezumab** – PASADENA (Phase 2) and PADOVA (Phase 2b) trials failed.

    Extension analysis being performed as it seemed to help in a **subset** of early-stage PD.



doi: 10.1016/j.parkreldis.2024.107257. Epub 2024 Dec 29. PMID: 39798255.

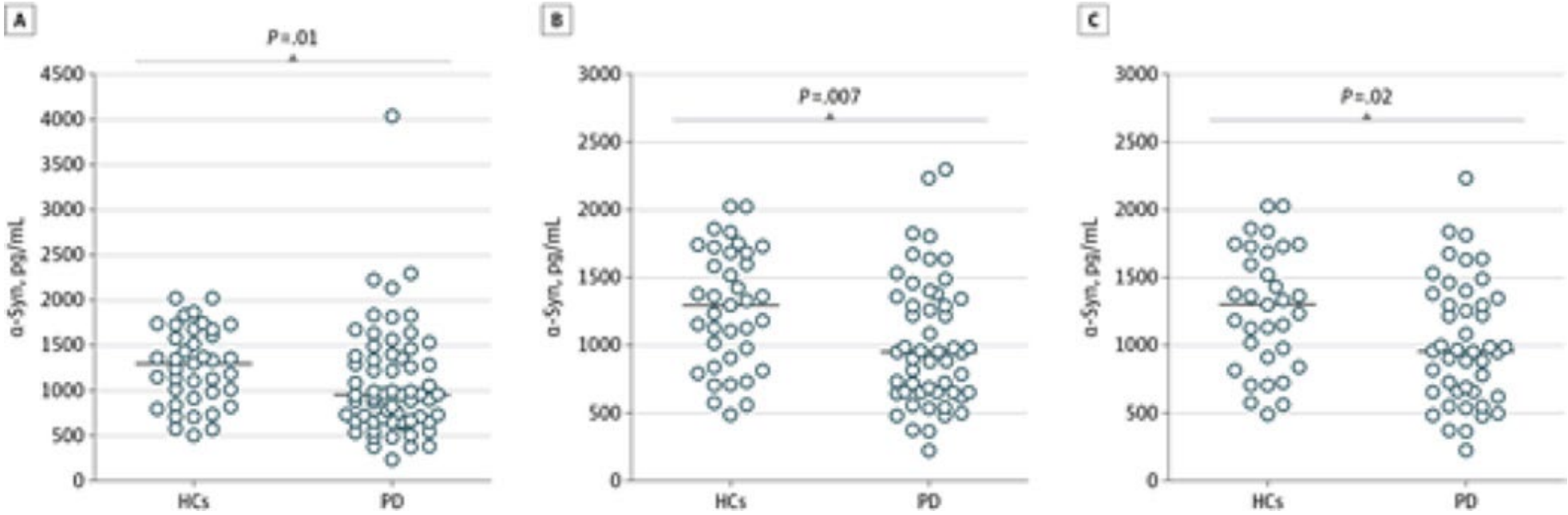
The underlying debate

Is **α-synuclein** **neurotoxic** or a **cellular defense mechanism**

Toxic?	Defense?
Some gene mutations cause misfolded protein and produce PD symptoms.	Presence and spread of it does not equate to disease severity.
Injecting misfolded α-synuclein **in animal** models produce PD symptoms	**In cell models**, clustering has shown decreased toxicity.

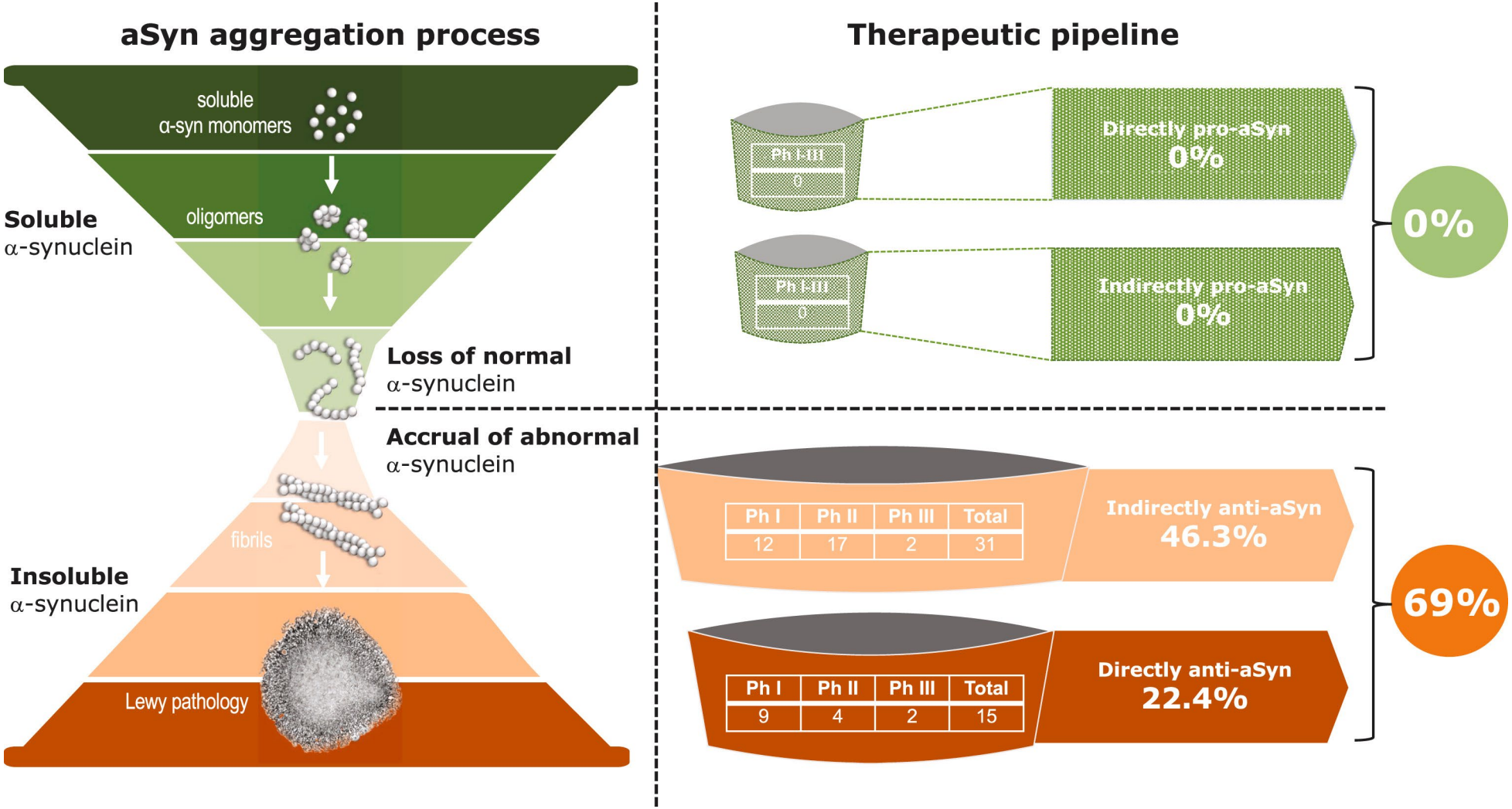
The underlying debate

- Some evidence that slightly lower **α-synuclein** is present in PD patients.



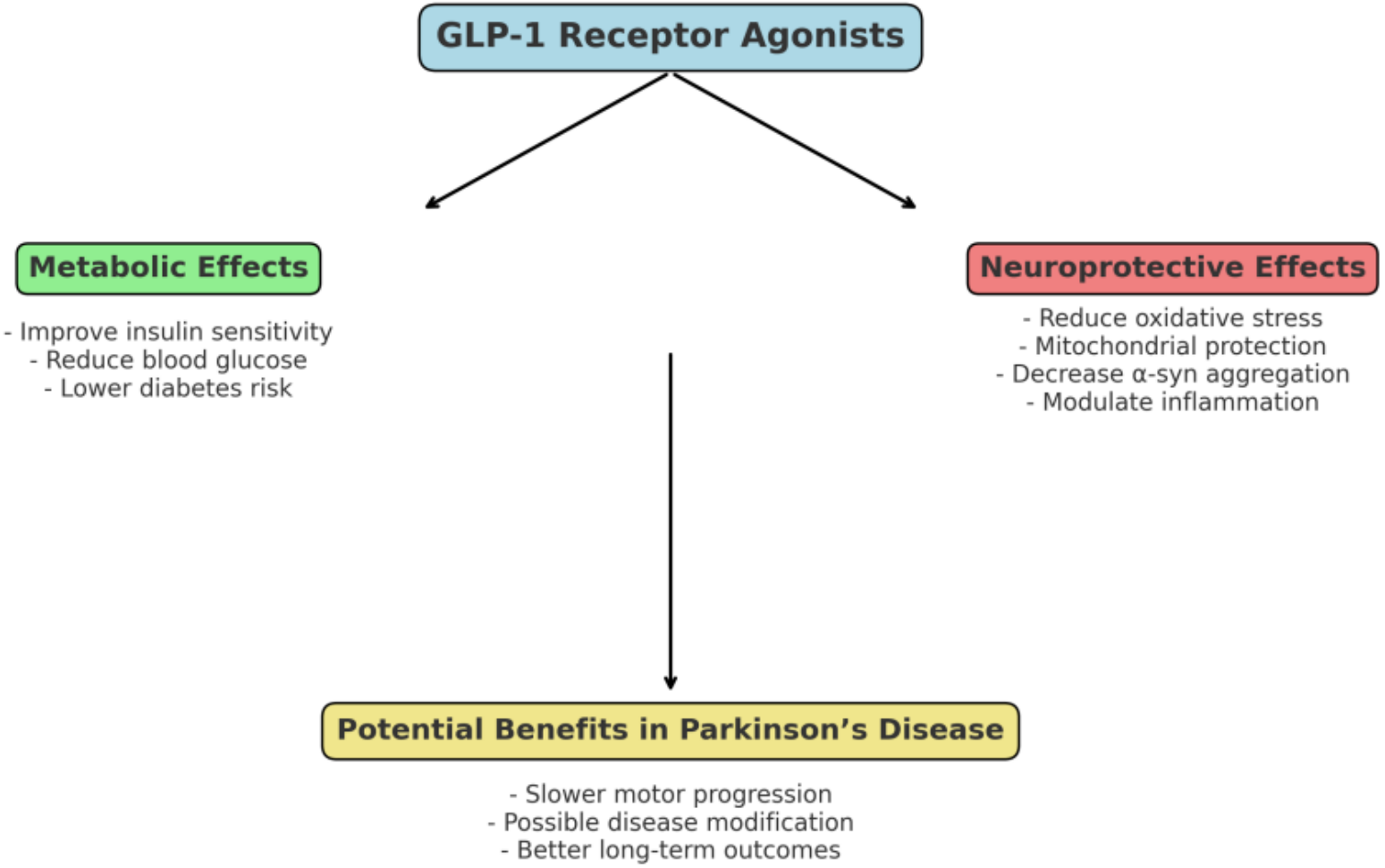
PMID: 23979011 (2013)

The underlying debate



PMID: 37244791 (2023)

GLP-Receptor Agonists



How many trials with them?

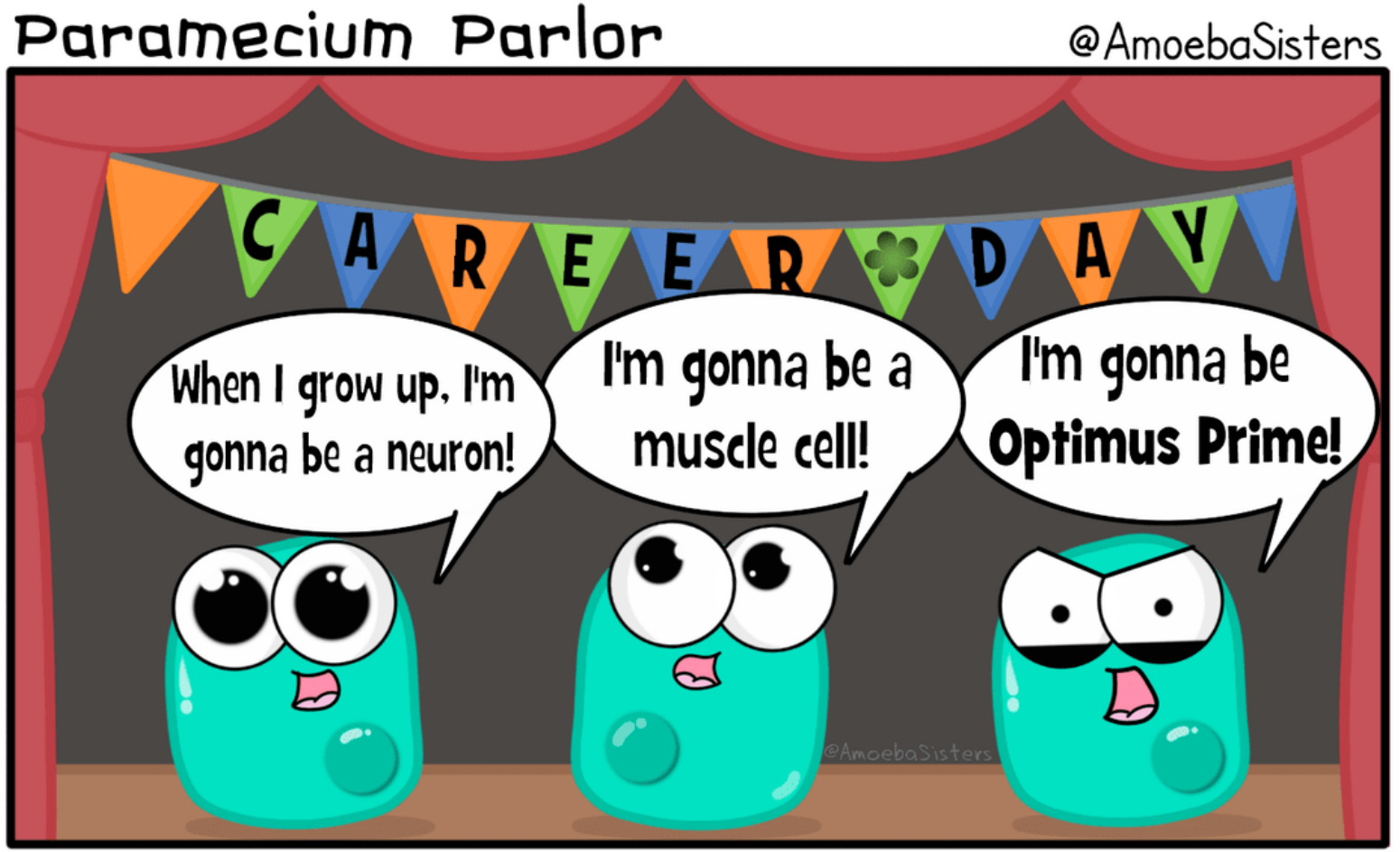
- **Exenatide**
  - Has shown stable symptoms for 1 year.
  - Ongoing Phase 3 trial in UK (EXENATIDE-PD3)
- **Lisexenatide**
  - LIXIPARK Phase 2 trial in France showed promised in 156 patients.
  - Planned Phase 3 trial but no confirmed.
- **Semaglutide**
  - Phase 2 trial in Europe for early-stage PD. No results yet.
  - Question about whether it crosses blood brain barrier or not.

April 19, 2024

Are GLP-1 Diabetes Drugs Like Ozempic Coming For Parkinson's Disease?

By Michael S. Okun

Stem Cells!



Stem cells on career day

How did it came to be?

Fetal Ventral Mesencephalic Tissue (FVM)

1980s all the way to 2000s.

Bioethical implications

Overall trials failed **BUT**:

- Some patients had long-term benefit.
- Some had graft-induced dyskinesias.

What are we doing now?

Embryonic Stem Cell (ESC)

STEP-PD – Progression to Phase 3 trial (NYSTEM)

Parallel trials in China, Sweden and Japan

Members of the New York State Stem Cell Science team at Memorial Sloan Kettering -- (Back from left) Isabelle Riviere, Stefan Irion, Mark Tomishima, Laurel DeGeorge, Abderrahman El-Maarouf and Michel Sadelain; (Front from left) Viviane Tabar, Urs Rutishauser, Claire Henchcliffe, Lorenz Studer

https://www.mskcc.org/research-programs/new-york-state-stem-cell-science-consortia

What are we doing now?

Human-induced Pluripotent Cells

› Cell Stem Cell. 2025 Mar 6;32(3):343-360.e7. doi: 10.1016/j.stem.2025.01.006. Epub 2025 Feb 13.

Pre-clinical safety and efficacy of human induced pluripotent stem cell-derived products for autologous cell therapy in Parkinson's disease

Jeha Jeon [1], Young Cha [1], Yean Ju Hong [1], In-Hee Lee [2], Heejin Jang [1], Sanghyeok Ko [1], Serhiy Naumenko [3], Minseon Kim [1], Hannah L Ryu [1], Zenith Shrestha [1], Nayeon Lee [1], Tae-Yoon Park [1], HoeWon Park [4], Seo-Hyun Kim [4], Ki-Jun Yoon [5], Bin Song [6], Jeffrey Schweitzer [6], Todd M Herrington [7], Sek Won Kong [2], Bob Carter [8], Pierre Leblanc [9], Kwang-Soo Kim [10]

Affiliations + expand

PMID: 39952239 PMCID: PMC11980241 (available on 2026-03-06)
DOI: 10.1016/j.stem.2025.01.006

› Regen Ther. 2020 Sep 15:13:18-22. doi: 10.1016/j.reth.2020.06.002. eCollection 2020 Mar.

iPS cell-based therapy for Parkinson's disease: A Kyoto trial

Jun Takahashi [1]

Affiliations + expand

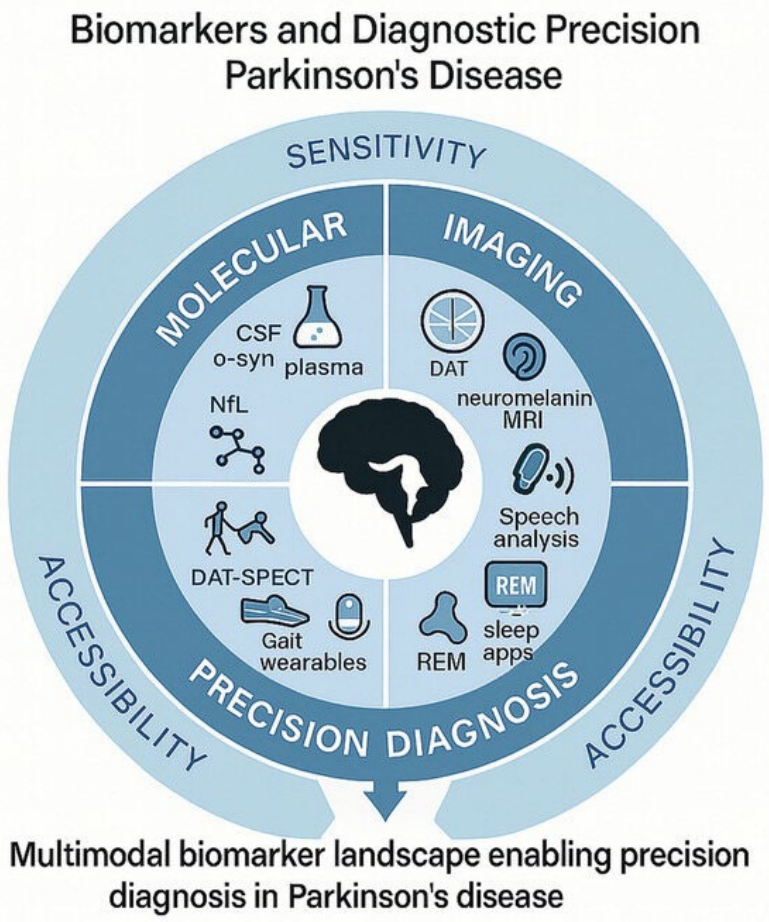
PMID: 33490319 PMCID: PMC7794047 DOI: 10.1016/j.reth.2020.06.002

Autologous cells = Your own cells

Diagnose it Better - Biomarkers

All about biological evidence of disease:

- Genetic/Molecular/Pathological
- Imaging
- Symptom/Digital Analysis



Tanaka M. Parkinson's Disease: Bridging Gaps, Building Biomarkers, and Reimagining Clinical Translation. *Cells*. 2025; 14(15):1161. https://doi.org/10.3390/cells14151161

Parkinson's Progression Markers Initiative

https://www.ppmi-info.org/

Other longitudinal databases

- **BioFIND** – Recruited from 2012 to 2015.

- **Parkinson's Disease Biomarker Program (PDBP)** – Active in the NIH/NINDS.

- **Harvard Biomarker Study** – Currently in its 2.0 iteration.

- **Cincinnati Cohort Biomarker Study (CCBP)** - Active

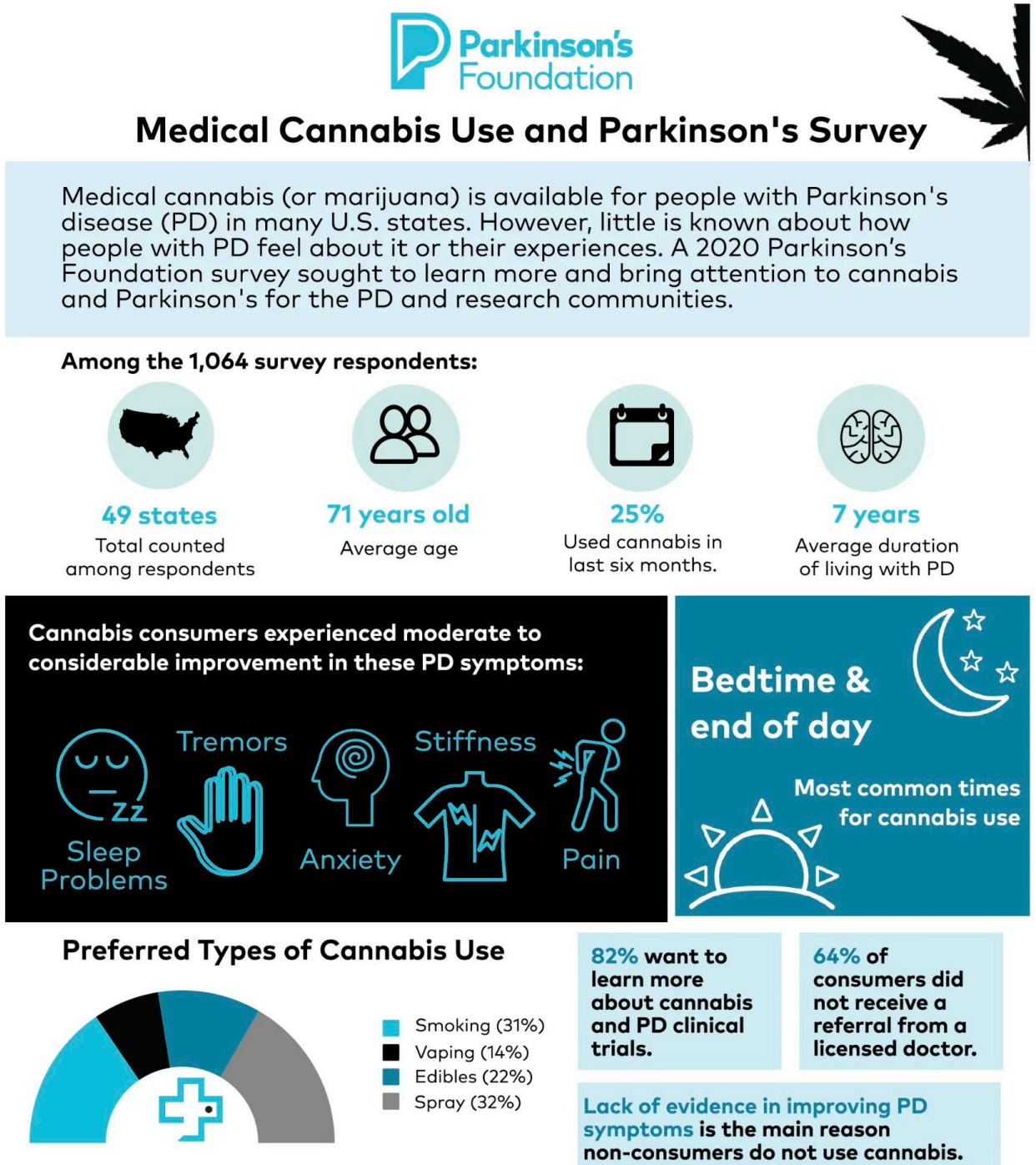
Biomarker	Notes
Saliva SAA for α-synuclein	Ongoing/not approved
Blood SAA for α-synuclein	Ongoing/not approved
Neurofilament Light Chain	Used in the PPMI for possible progression
Digital Devices	AI, video-analysis, biomechanical information.
Imaging	Functional MRI imaging, Magnetoencephalography

Quality of Life Improvements

- Cannabis
- Vibration Therapy
- Other agents regularly asked

What is up with Mary Jane?

Cannabis - Marijuana



Feeney, M.P., Bega, D., Kluger, B.M. et al. ***Weeding through the haze: a survey on cannabis use among people living with Parkinson's disease in the US.*** *npj Parkinsons Dis.* ***7****, 21 (2021). https://doi.org/10.1038/s41531-021-00165-y*

Cannabis – Marijuana in the USA

Mixed Results using Epidiolex for PD (2020)

High doses provided some benefit but with significant liver enzyme elevation and side effects.

No benefit using CBD/low THC mix (2024)

Worse sleep and cognition; ADLs were more impaired.

Very short-term study (2-3 weeks)

University of Colorado Study Group – Bainbridge J et al.

Cannabis around the world

Study	Location	Design	Status
CBD-EP-2/Kanbis	Mendoza, Argentina	CBD - Phase 2 trial – for motor symptoms	**Ongoing – ~88 patients**
CAN-PDP	King's College London, UK	CBD - Phase 2 trial – assessing for hallucinations/delusions	Just finished recruiting 144 patients – Results Pending
MDC-CAN-PD	Toronto, Canada (2023)	Cannabis Oil - Phase 2 trial – Pain in PD (15 patients)	Completed – Was helpful. Small sample size.
NMS-Nab	Innsbruck, Austria (2021)	Synthetic cannabinoid (Nabilone) – assessing sleep, anxiety, pain	Completed – Improved all symptoms assessed. Short-term study.

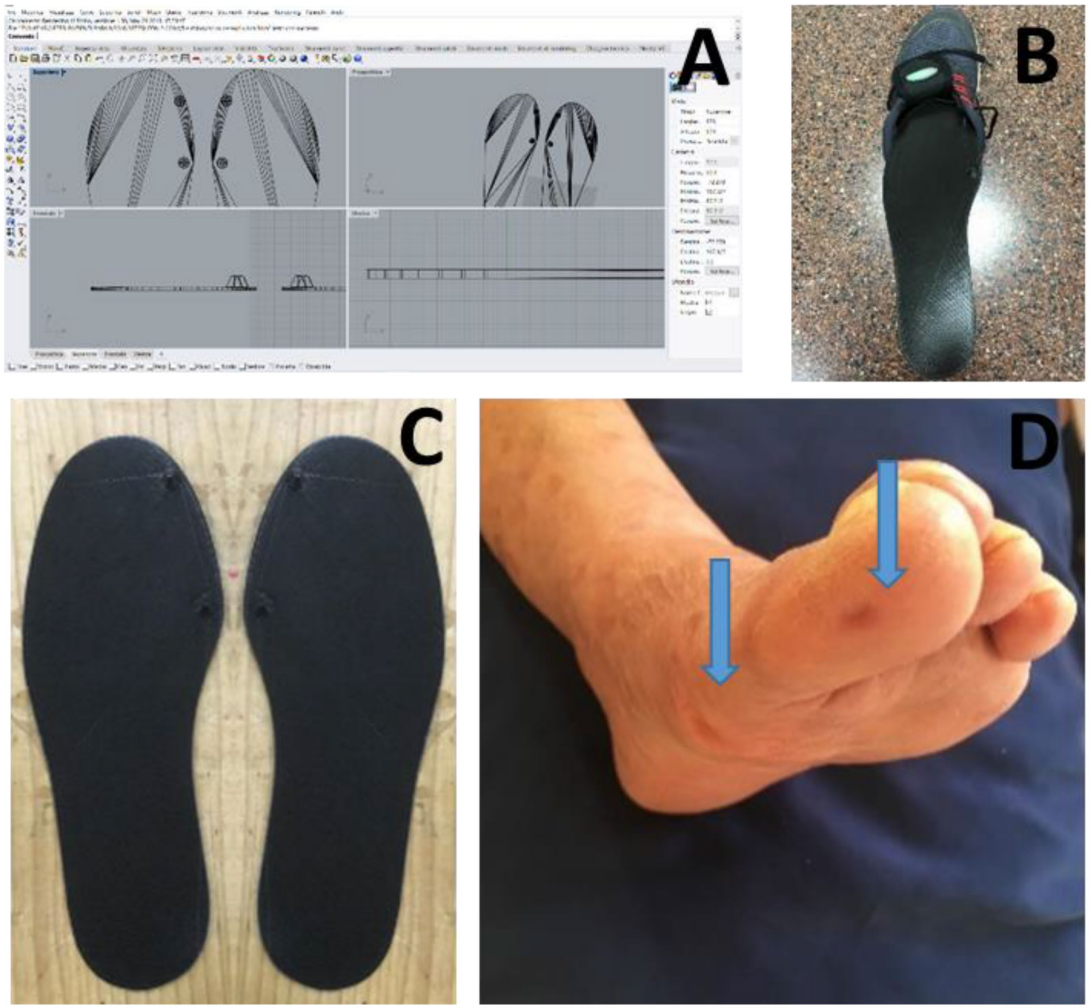
Gloves for symptoms…

Alexandra Becker - Apr. 9, 2025

POSTED IN: **RICE NEWS** > **Current News** > **2025**

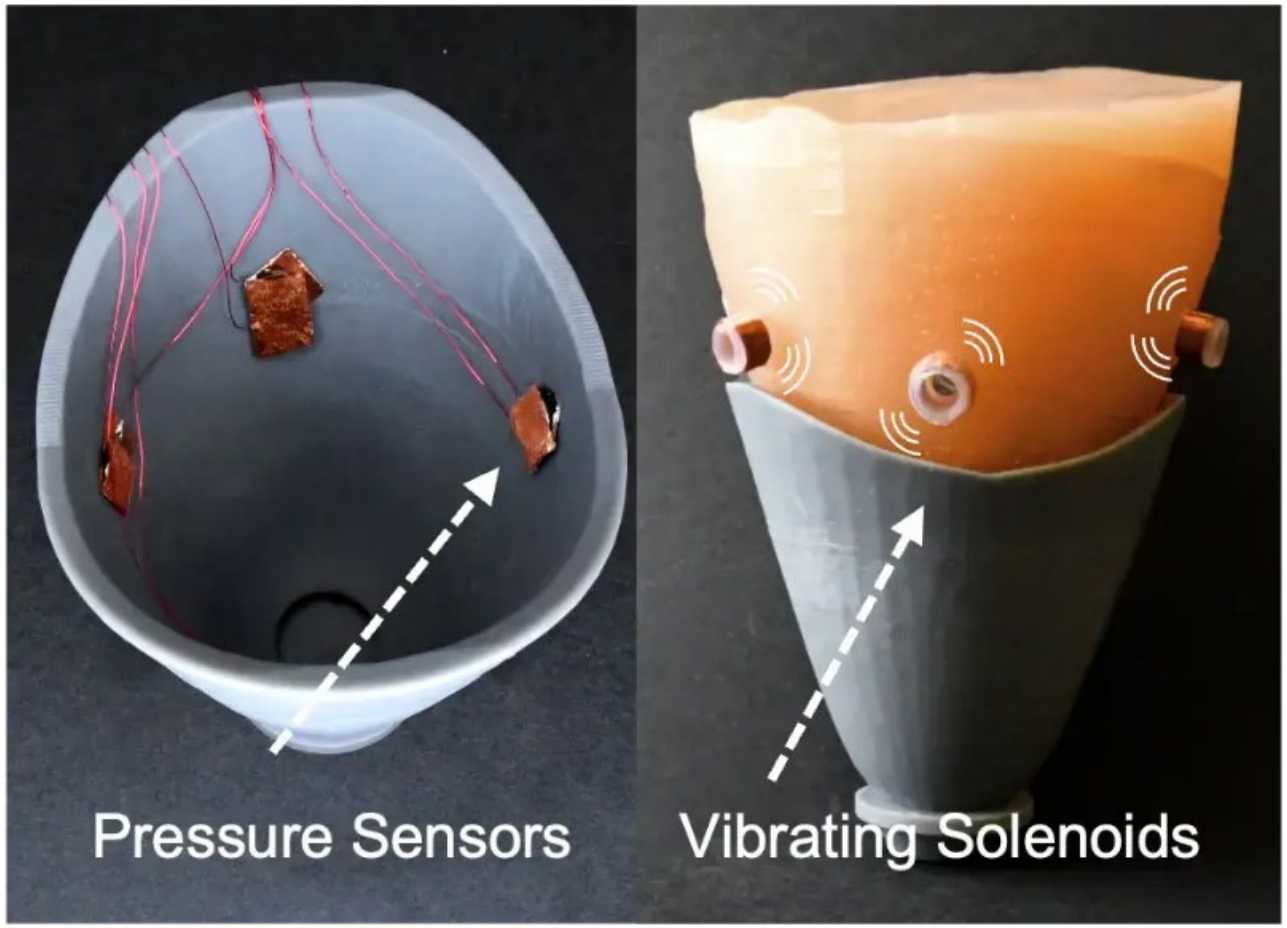
Rice students develop low-cost vibrotactile glove to help treat Parkinson's disease

…soles too…



https://www.mdpi.com/2076-3425/10/2/69

… and vibrating prosthetics for amputees.



Pressure sensors inside this prosthetic leg prototype can detect excess pressure, sending vibration further up the leg.
(Courtesy of Daeha Joung)

https://news.vcu.edu/article/2025/02/wearable-and-vibrating-technology-from-vcu-inventors-could-help-parkinsons-patients

But what about a button?

CUE1+
FOR PARKINSON'S

https://doi.org/10.14802/jmd.21076 / J Mov Disord 2021;14(3):236-238
pISSN 2005-940X / eISSN 2093-4939

CASE REPORT

Focused Vibrotactile Stimulation with Cueing Effect on Freezing of Gait in Parkinson's Disease: Two Case Reports

Xiu Sheng Tan,[1,2] Floyd Pierres,[2,3] Alex Dallman-Porter,[2] William Hardie-Brown,[2] Kyum-Yil Kwon[4]

[1]School of Clinical Medicine, University of Cambridge, Cambridge, United Kingdom
[2]Charco Neurotech Ltd., London, United Kingdom
[3]Department of Critical Care, North West Anglia NHS Foundation Trust, Peterborough, United Kingdom
[4]Department of Neurology, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, Seoul, Korea

Improves movement

Utilising non-invasive, focused vibrotactile stimulation and cueing to improve movement.

Medication reminders

A wearable, discreet and adjustable medication reminder and recording system.

Symptom tracking

Track symptoms, progression and quality-of-life measures with the CUE app.

https://charconeurotech.com/

Naloxone – opioid-receptor antagonist

Observational Study > J Neurol. 2015 Sep;262(9):2164-70. doi: 10.1007/s00415-015-7823-3.

Epub 2015 Jul 2.

Efficacy and safety profile of prolonged release oxycodone in combination with naloxone (OXN PR) in Parkinson's disease patients with chronic pain

Graziella Madeo [1], Tommaso Schirinzi [1], Silvia Natoli [2], Mariangela Pierantozzi [1], Alessandro Stefani [1 3], Mario Dauri [2], Antonio Pisani [4 5]

Affiliations + expand

PMID: 26134157 DOI: 10.1007/s00415-015-7823-3

Low-Dose Naltrexone

- Longer-acting than naloxone
- Anecdotal reports
- Research in pain and depression

NO research-supported data

NOT FDA approved

Methylene Blue – yes or NO

Has proven to reduce degeneration in dopaminergic neurons **in animal models and in vitro studies.**

Animal models DOES NOT EQUATE to human subjects

PD is a human phenomenon and does not occur naturally in other species. Artificial generation is not the same as what humans experience.

Ibogaine

Only studied in rodents and its involvement in the brain (not specifically in PD models)

May help in animal cases with dopamine transporter mutations

NO HUMAN STUDIES DONE

Non-standardized consumption has shown potential psychedelic effects and cardiac toxicity manifesting in arrhythmias.

Ivermectin – the famed horse dewormer

Antiparasitic (used in humans too!)

Data in animal studies to understand neuronal and glial function.

In some rat models, it has potentiated levodopa effects

NO HUMAN STUDIES REGARDING PD

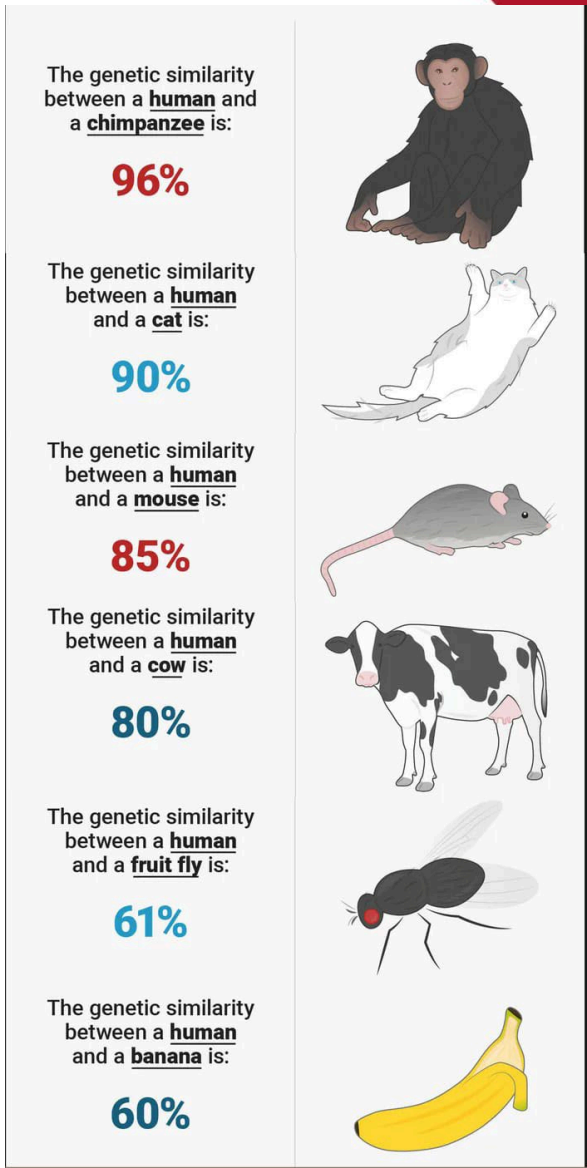
BOTTOM LINE

Just because there is a mechanism related to the agent **does not mean it's a cure/therapy**

Rats **are not** Humans

Random cells in plastic dishes (in vitro) **are not** Humans

Anecdotal cases attest to a unique biology in Humans



Visit **clinicaltrials.gov**

Call or email the **UNMC Research Advocate Office**

unmcrsa@unmc.edu

402-559-6941

Reference the **UNMC Clinical Trial Database:**
https://net.unmc.edu/ctsearch/index_unmc.php

Useful Websites

- http://www.pdtrialtracker.info
- www.apdaparkinson.org
- www.michaeljfox.org
- World Health Organization (WHO) Registry

University of Nebraska Medical Center

Who Cares About the Care Partner? (hint, we do)

Colleen Hoarty, LCSW
Medical Social Worker
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October 1, 2025
Parkinson's Disease Symposium

University of Nebraska Medical Center

Nebraska Medicine

Today's Objectives

- Clarify the difference between the words ***caregiver*** and ***care partner***
- Identify **common considerations** for care partners who assist with care for someone with Parkinson's Disease (PD)
- Share information on **resources** that may be helpful for care partners
- Discuss ways to **build resilience** as a care partner

What is a *Care Partner*?

- A ***care partner*** is someone assisting an individual with a health condition with a recognition that people with the condition are also contributing to their own care
- Caring **WITH** the person who has PD and partnering with them
- Today focusing today on informal care partners – spouse, adult children, friends, other family members.

Why Do We Care?

- We know that Parkinson's Disease can be a challenging disease with progression over time and requires both people with PD and their care partners to navigate multiple challenges:
  - Physical
  - Neuropsychiatric
  - Cognitive

PD Care Partners

- The National Alliance on Caregiving put out a report earlier this year called ***Parkinson's Disease Caregiving in the U.S.*** Some of the key findings were:
  - There is a **more substantial time commitment** on the part of PD care partners (weekly and number of years)
  - There are **extensive care needs** PD care partners are addressing
  - PD care partners may be **balancing care and employment**
  - It can take a **more pronounced physical and emotional toll** on the care partner

What Can Care Partners Do?

- Just as PD progresses over time, the care partner's care and role will likely change over time
- Caring with someone else can take a lot of time and energy – being prepared for different stages and for progression can make a big difference!
- Increasing resilience can improve quality of life for both the care partner and the person with PD

Care Partners and a New Diagnosis/Early Stages

- Learning new language
- Gathering information
- Figuring out role as a care partner
- Planning for the future
  - Meeting with financial advisor or attorney
  - Completing Family Medical Leave (FMLA) paperwork
  - Getting Advance Directives in place
  - Communicating on what things are important

Early-Stage Care Partner Resources

- **Parkinson's-specific organizations**
  - Parkinson's Nebraska (parkinsonsnebraska.org)
  - Parkinson's Foundation (parkinson.org)
  - Davis Phinney Foundation (davisphinneyfoundation.org)
  - Michael J. Fox Foundation (michaeljfox.org)
  - Young Onset Parkinson's Network (yopnetwork.org)
- **Care Partner websites**
  - Family Caregiving Alliance (caregiver.org)
  - Caregiver Action Network (caregiveraction.org)
- **Employment**
  - Job Accommodation Network (askjan.org)
  - Department of Labor (dol.gov/general/topic/benefits-leave/fmla)
  - PD-specific organizations have information on their sites as well
- **Disability benefits**
  - Accessing employer-sponsored or private disability benefits and Social Security Disability benefits
  - ssa.gov and ssa.gov/disability
- **Advance Directives and long-term care planning**
  - Speaking with an elder law attorney and/or financial advisor
  - The Conversation Project – theconversationproject.org

Caring in the Middle Stages

- Role changes and an increase in tasks at home
- Making adjustments
- Handling more appointments
- Increase in hands-on care may be needed
- Increase in assistive devices or home modifications
- Possible addition of more care at home
- A need to develop a backup plan/build up your care team

Caring With Advanced PD

- More hands-on care
- May be responsible for all tasks at home or unable to leave your loved one home alone
- May be exploring alternate care arrangements
- Changing feelings of grief and loss (identity, plans, goals)
- Potentially feeling more overwhelmed and/or burned out

Middle Stage and Advanced Stage Care Partner Resources

- **Parkinson-specific organizations and websites**
- **Area Agencies on Aging (AAA)** – information, programs and services for people 60 and over all over the country. Many of them offer a *Caregiver Support Program* that provides support and respite resources in addition to grants or programs for in-home services
- **In-home care or respite resources** – private home care agencies, AAA, adult day services
- **Increased emotional support**
  - Support groups
  - Behavioral health therapy (psychologytoday.com)
  - Presence Care Project (presencecareproject.com)
- **Veteran Resources**
  - Depending on the level of service connection and disability rating, a veteran may be eligible for more comprehensive services and care partners may be eligible for additional services
  - Must be connected to VA Healthcare. Eligibility and enrollment line, 402-995-4050

Middle and Advanced Stage Care Partner Resources

- **Senior living advisors/Housing navigators**
  - Can assist with finding long-term care communities
- **Safety/home modifications**
  - Local companies for home assessment/modification
  - HELP Equipment for donated supplies and gently used equipment (helpequipment.org)
- **Palliative Care**
- **Hospice Care**
- **NE Caregiver Tax Credit – LB 937 (2024)**
  - Eligibility depends on income
  - Applies to care receiver living in a private residence
  - Credit applies to 50% of expenditures paid out
  - Maximum credit of $2000 (or $3000 if care receiver is a veteran or has dementia)
  - Can apply now for credit in 2026 when filing taxes
  - revenue.nebraska.gov/caregiver-tax-credit-act

Building Resilience as a Care Partner

What is *Resilience?*

- From the American Psychological Association: "Resilience is the process and outcome of successfully adapting to difficult or challenging life experiences, especially through mental, emotional, and behavioral flexibility and adjustment to external and internal demands."
- Resilience is the **ability to adapt to changes in life that are often stressful and to maintain overall a sense of well-being despite those changes and stressors.**

Building Resilience Like an Athlete

- Mental toughness – sports psychologists help athletes with regaining focus, managing anxiety, staying motivated and coping with setbacks
- Can be applied to anyone

Preparation!

Fueling your body – eating well, getting enough rest, working out

Be Adaptable

Don't lock into one goal with rigid expectations. Create layers of goals and alternative plans.

Use visualization

- I'm going to attend a support group
- I'm going to reach out to a home care agency to get more information
- I'm going to take a 10-minute walk around the block

Ask for Help!

- Are you F.I.N.E?
- Who can you go to?

Control the Controllables

Focus on the things that you CAN control.

Practice, Practice, Practice

- These things take practice!
- It can feel overwhelming to start everything at once
- Choose 1-2 to implement to see if they work for you

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Thank you!

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University of Nebraska Medical Center

Nebraska Medicine

Movement Break

by

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Nutrition Tips and Tricks for Parkinson's Disease

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Nebraska Medicine

Topics to Cover

- Nutrition Issues in PD
- Drug-Nutrient Interactions
- Healthy Eating for PD

Importance of Nutrition in PD

- Increases energy levels
- Affects strength
- Protects muscle mass
- Improves ability to fight off other illnesses
- Optimizes how well medications work
- Improves bowel regularity

Importance of Nutrition in PD

- Higher risk of unintentional weight loss
  - Up to 50% may experience weight loss
  - Often occurs before PD diagnosis or mid to late stages

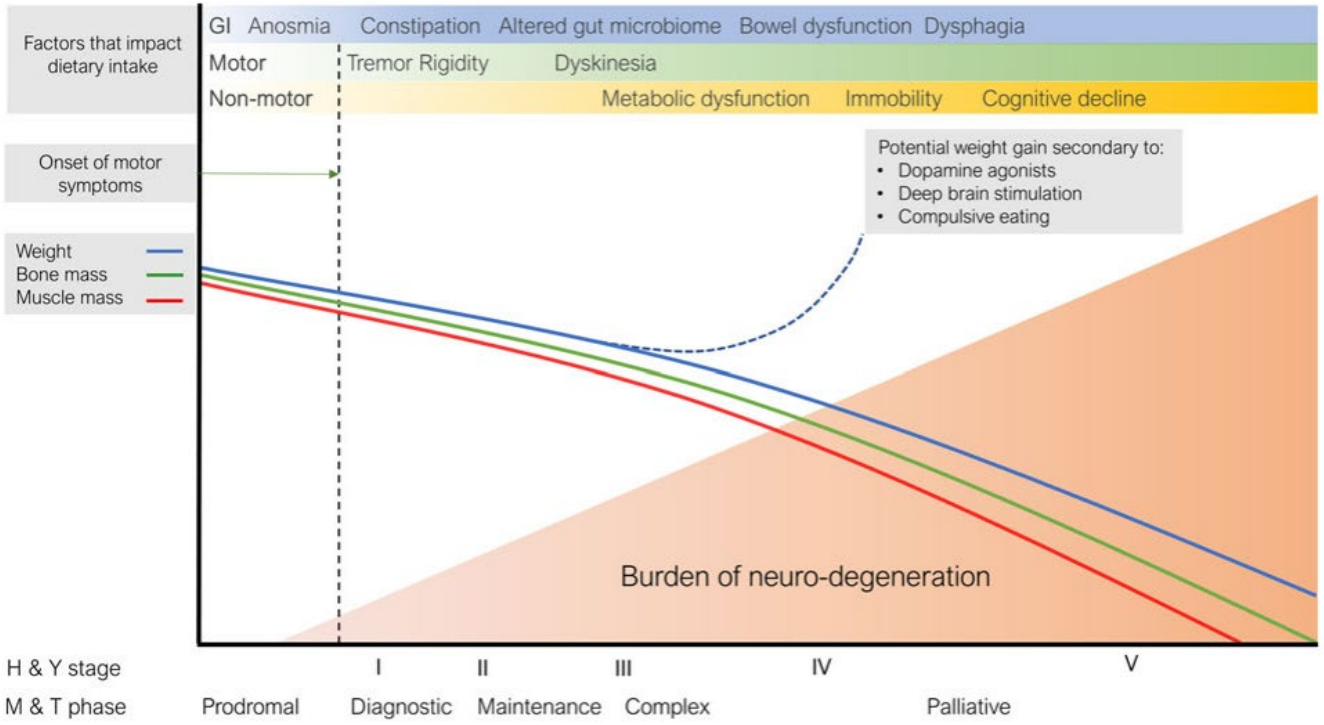


Fig. 2. Putative representation of the dynamic and interacting factors that impact nutritional status in Parkinson's disease. GI, gastrointestinal; M & T, MacMahon and Thomas[8]; H & Y, Hoehn and Yahr[6].

Nutrition Issues & Strategies to Help

Decreased Appetite

- Lose desire to eat
- Do not feel hungry

❖Leads to someone eating less, skipping meals, getting less variety of foods and nutrients and unintentional weight loss.

Strategies

- ➢ Have small, frequent meals and snacks
  - ➢ Breakfast, morning snack, lunch, afternoon snack, dinner, evening snack
- ➢ Plan meals and snacks based upon food preferences
- ➢ Try new foods, snacks, or flavors of products
- ➢ Try liquid sources of nutrition
- ➢ Have nutrient-dense foods and beverages first
- ➢ Avoid low-fat, low-calorie products

Decreased Taste and Smell

- Often develops years before motor symptoms

❖Leads to someone losing interest in eating, affects intake of certain food groups, less variety of foods and nutrients and possible weight changes.

Strategies

- ➢ Try different flavors of products
- ➢ Use seasonings when cooking
- ➢ Fresh herbs and spices
- ➢ Add some spice/kick
- ➢ Add color and texture to meals to make food more interesting

Nausea

- Upset stomach
- Side effect from medications

❖Leads to someone eating less and unintentional weight loss.

Strategies

- Have food with medications if safe to do so
  - Check with doctor or pharmacist
- Eat light, bland foods
  - Saltine crackers, toast, pretzels
- Avoid strong flavors, greasy or fried foods, and sweets
- Eat and drink slowly
- Do not mix hot and cold foods
- Try room temperature foods or chilled foods
- Have small, frequent meals and snacks
  - Breakfast, morning snack, lunch, afternoon snack, dinner, evening snack

Fatigue

- Feeling more tired than usual
- Needing to nap more often

❖Leads to someone eating less, skipping meals, difficulty preparing meals and unintentional weight loss.

Strategies

- Seek assistance with shopping and meal preparation
- Online grocery shopping to pick up or deliver
- Help from friends, family, community groups, church groups, etc.
- Keep easy to prepare foods on hand
- Freeze leftovers
- Utilize frozen meals, ready to drink shakes, pre-cut produce, etc.
- Have largest meal in the morning
- Have small, frequent meals and snacks
  - Breakfast, morning snack, lunch, afternoon snack, dinner, evening snack
- Food assistance programs (Meals on Wheels, Mom's Meals, community centers)

Difficulty Chewing and Swallowing

- Called “dysphagia”
- Due to lack of coordination of muscles in mouth, throat, and esophagus
- Cough or choke when eating or drinking
- Feels like food gets “stuck”

❖ Leads to someone eating less, getting less variety of foods and nutrients, unintentional weight loss and risk of aspiration pneumonia.

Strategies

- ➢ Have swallow study with Speech Language Pathologist
- ➢ Follow swallowing techniques and strategies
- ➢ Modify texture and liquid consistencies
  - ➢ Soft & bite-sized, minced & moist, pureed diet
  - ➢ Slightly, mildly, moderately thick liquids (nectar/honey)
- ➢ Significant dysphagia may require feeding tube

Constipation

- Fewer than 3 bowel movements a week
- Hard stools, difficult to pass

❖Often results from low fiber intake, low fluid intake, inactivity, travel or routine changes, stress and medications.

Strategies

- Slowly increase fiber intake
  - Whole grain bread, whole grain pasta, brown rice, bran cereal, oatmeal, fruits, vegetables, beans, nuts, seeds
  - Must also increase fluid intake at the same time
- Increase fluid intake
  - Minimum of 64 fl oz a day of non-caffeinated beverages (water, milk, juice, sports drinks)
  - Try warm liquids
- Probiotics
  - Yogurt, kefir, kombucha, sauerkraut
- Prunes and prune juice
- Regular physical activity
- Stool softeners/laxatives
  - Try lifestyle changes first
  - Consult with health care provider before starting

Constipation Recipes

Chia Seed Pudding

Servings: 4

Ingredients: 1/3 cup chia seeds

1 1/2 cups milk

2 Tablespoons maple syrup or honey

1/2 teaspoon vanilla

Optional ingredients/toppings: Fruit, chopped nuts, coconut flakes

Instructions: Combine all ingredients in container with lid. Put lid on and shake ingredients. Chill for about an hour, then return to the container and shake it up. Let chill for at least 4 hours and overnight is even better. Chia seeds will expand and turn into the consistency of pudding/applesauce. Add optional ingredients/toppings before serving.

Oats, Prune Juice and Applesauce Constipation Remedy

Ingredients: 2/3 cup old fashioned oats

1/2 cup prune juice

1/2 cup applesauce

Instructions: Mix together all ingredients and store in the refrigerator. Have 2-4 Tablespoons a day or more as needed.

Unintentional Weight Loss/ Malnutrition

- Increased energy expenditure from resting tremors, dyskinesias and metabolic changes
- Inadequate intake

❖Leads to nutrient deficiencies, muscle wasting/weakness/fatigue and impacts the immune system/mental function/muscle strength.

Strategies

- Add scheduled snacks between meals
- Include oils, butter, heavy whipping cream, mayonnaise, peanut butter, salad dressing, sour cream, cream cheese, cheese, avocados, sauces, and gravies with foods
- Use full fat dairy products
- Have shakes or smoothies
  - Homemade or ready to drink (Ensure, Boost, Carnation Breakfast Essentials, Naked Juice, Bolthouse Farms, Orgain, Muscle Milk)
  - Look for versions with >300 calories

Unintentional Weight Gain/Obesity

- Can have lower energy expenditure if less active
- Eating high calorie foods/beverages frequently

❖Can experience new cravings for less healthy foods and behavioral changes leading to impulsive eating.

Strategies

- Reduce calorie-containing beverages
  - Soda, juice, lemonade, sports drinks
- Evaluate snacks
- Reduce portion sizes
- Substitute processed foods with whole foods
  - Ex: have raw vegetables instead of chips with sandwich
- Practice mindful eating
- Plan meals ahead of time
- Cook more meals at home
- Increase physical activity

Drug-Nutrient Interactions

Carbidopa-levodopa

- Protein competes for absorption of levodopa
- High protein intake may **decrease** the effectiveness of medication

- Recommendations:
  - Take carbidopa-levodopa on an empty stomach 30 minutes before a meal with protein OR 60 minutes after a meal with protein
  - If it causes nausea, take carbidopa-levodopa with crackers, bread, or fruit
  - Do NOT eliminate protein completely from diet

Protein Sources

- Meat
- Eggs
- Yogurt
- Cow’s Milk
- Cheese
- Cottage Cheese
- Nuts/seeds
- Peanut butter
- Beans and lentils
- Soy products
- Tofu
- Protein shakes
- Protein bars

How much protein do you need?

- Varies depending on age, gender, body size, activity level, illnesses, healing from an injury, etc.
- Typically 1.0-1.2 grams per kilogram body weight for an average adult with PD
- Examples:
  - 130 lbs (59 kg) = 59-71 grams per day
  - 150 lbs (68 kg) = 68-82 grams per day
  - 170 lbs (77 kg) = 77-92 grams per day

Carbidopa-levodopa

- Oral iron supplements and multi-vitamins with iron may **decrease** effectiveness

- Recommendations:
  - Take iron and multi-vitamins with iron 2 or more hours apart from carbidopa-levodopa

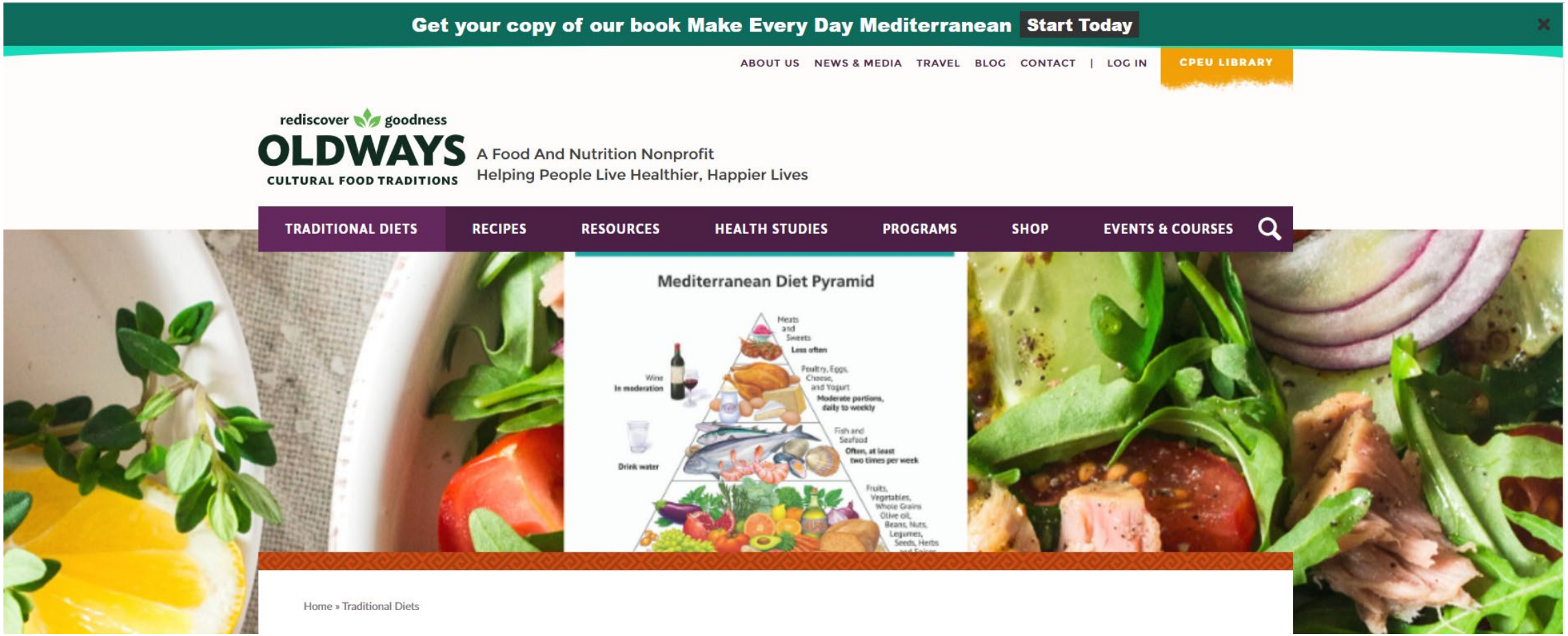
Healthy Eating Patterns & Tips

University of Nebraska Medical Center

Nebraska Medicine

Mediterranean Diet

- Eat plenty of **plant-based foods** (fruits, vegetables, whole grains, legumes, nuts, seeds)
- Replace butter with **olive oil**
- Use **herbs and spices** instead of salt to flavor foods
- Eat **fish** at least twice per week
- **Limit red meat** to a few servings or less per month
- Sweets are rarely eaten
- Drink **red wine** in moderation (optional)
    - Females: up to 1 glass/day (5 oz)
    - Males: up to 2 glasses/day (10 oz)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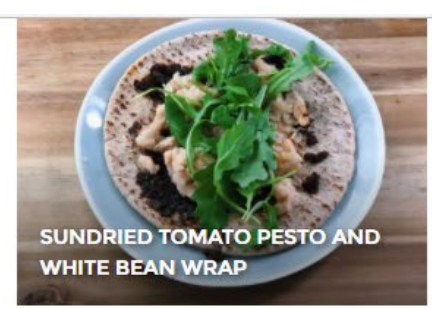
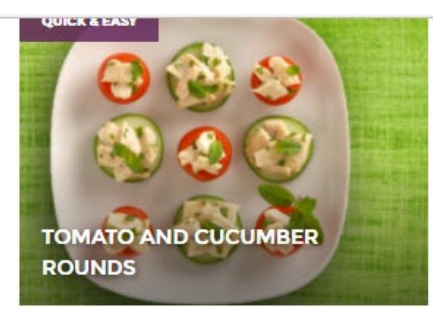
A Food And Nutrition Nonprofit
Helping People Live Healthier, Happier Lives
TRADITIONAL DIETS RECIPES RESOURCES HEALTH STUDIES PROGRAMS SHOP EVENTS & COURSES
Mediterranean Diet Pyramid
Meats and Sweets
Less often
Wine
In moderation
Poultry, Eggs, Cheese, and Yogurt
Moderate portions, daily to weekly
Drink water
Fish and Seafood
Often, at least two times per week
Fruits, Vegetables, Whole Grains, Olive oil, Beans, Nuts, Legumes, Seeds, Herbs
Home » Traditional Diets


QUICK & EASY
POTATO & CRABMEAT SALAD

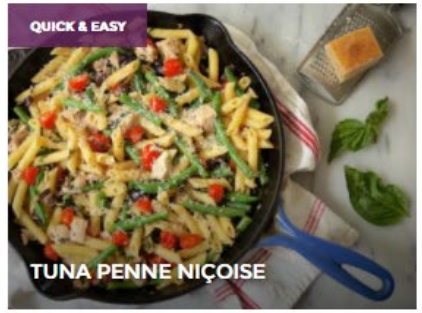

SUNDRIED TOMATO PESTO AND WHITE BEAN WRAP


QUICK & EASY
TOMATO AND CUCUMBER ROUNDS

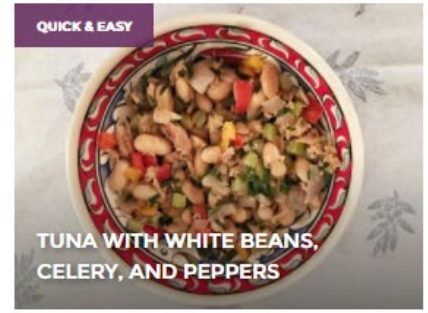

QUICK & EASY
TOMATO SALAD EL ALFAMA

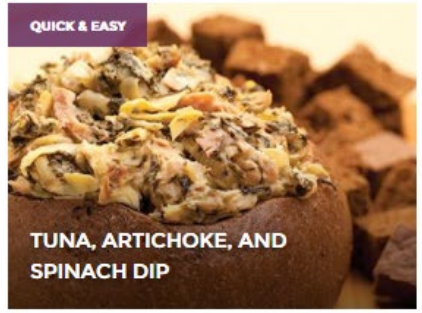

TORTILLA ESPAÑOLA - SPANISH POTATO OMELETTE

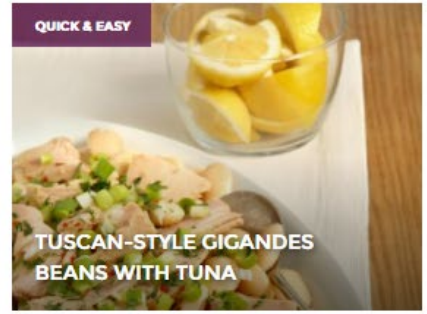

TUNA AND CALIFORNIA WILD RICE NICOISE ON BABY GREENS


QUICK & EASY
TUNA PENNE NIÇOISE


QUICK & EASY
TUNA PUTTANESCA


QUICK & EASY
TUNA WITH WHITE BEANS, CELERY, AND PEPPERS


QUICK & EASY
TUNA, ARTICHOKE, AND SPINACH DIP


QUICK & EASY
TUSCAN-STYLE GIGANDES BEANS WITH TUNA

MIND Diet

- **M**editerranean-DASH **I**ntervention for **N**eurodegenerative **D**elay
- Originally studied in dementia/Alzheimer's disease
- Encourages 10 foods to include and 5 foods to avoid

MIND Diet – Foods to Include

Food	Minimum Frequency
Green Leafy Vegetables	≥6 servings a week
Other Vegetables	≥1 servings a day
Whole Grains	≥3 servings a day
Extra Virgin Olive Oil	primary oil used
Nuts	≥5 servings a week
Berries	≥2 servings a week
Beans and Legumes	≥3 servings a week
Fish	≥1 serving a week
Poultry	≥2 servings a week
Red Wine	1 serving a day

MIND Diet – Foods to Limit

Food	Maximum Frequency
Butter and Stick Margarine	**<1 Tbsp a day**
Red Meat and Processed Meat	**<4 servings a week**
Regular Cheese	**<1 serving a week**
Pastries and Other Sweets	**<5 treats a week**
Fried Foods and Fast Foods	**<1 time a week**

Anti-oxidants and Anti-inflammatory Foods

Berries	Spinach	Kale	Mushrooms	Walnuts	Pistachios
Cashews	Almonds	Ground flax seeds	Chia seeds	Salmon	Tuna
	Herbs and spices	Extra virgin olive oil	Green tea	Coffee	

Tips to Change

- Choose ONE thing to change at a time

  Focus on a specific food group, snacking, beverages, etc.
- Write down your goal and monitor progress
- Find an accountability partner
- Be open to trying something new

Ideas to Start

- Have fruit as a snack
- Add berries to yogurt or oatmeal
- Make a fruit smoothie
- Add chopped onions, bell peppers, tomatoes, mushrooms, or spinach to omelet
- Have raw vegetables with lunch
- Include a side salad with dinner

Ideas to Start

- Switch to whole grain bread
- Use brown rice instead of white rice
- Add chia or flax seeds to oatmeal, yogurt, cereal, or smoothie
- Sprinkle chopped nuts on oatmeal, yogurt, cereal, or salads
- Snack on mixed nuts or trail mix
- Use olive oil when cooking
- Try a new recipe with a new ingredient: quinoa, chia seeds, flax seeds, squash, beans, lentils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Deep Brain Stimulation for Parkinson's Disease

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Stereotactic and Functional Neurosurgeon

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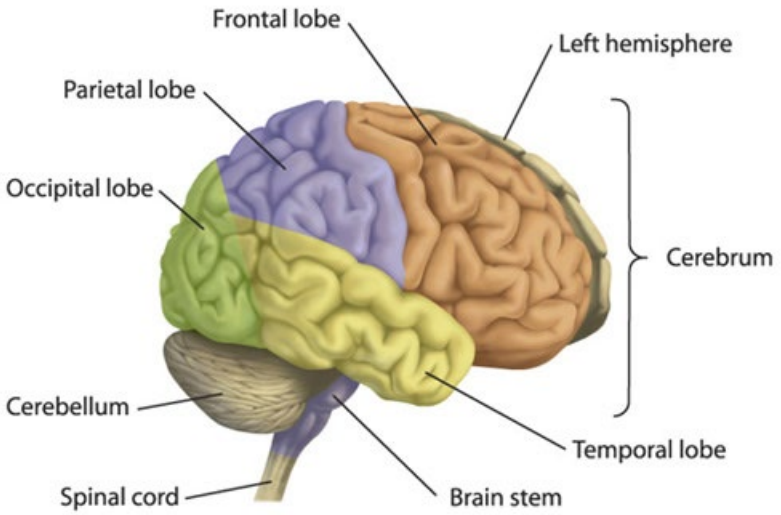
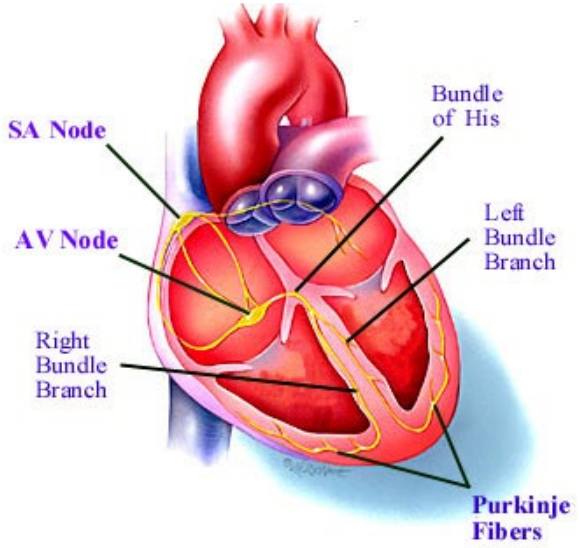
University of Nebraska Medical Center

What is DBS?



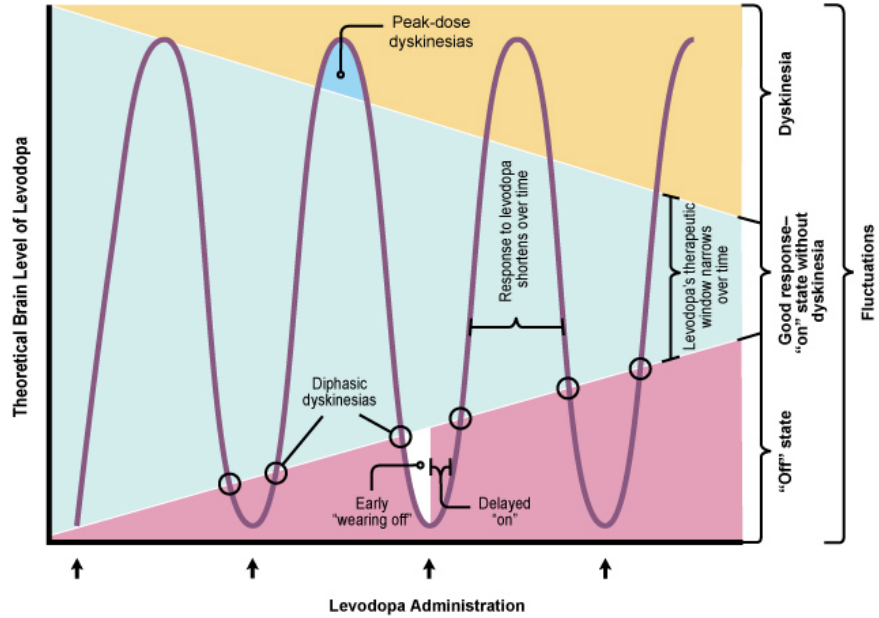


The Brain, much like the Heart is an electrical organ

Deep Brain Stimulation (DBS)>>*Brain Pacemaker*

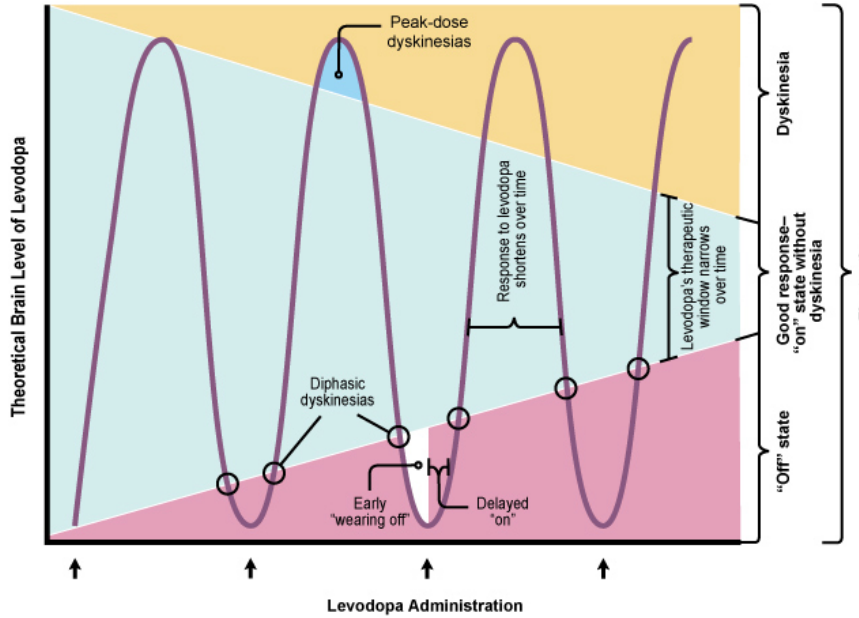
When to Consider DBS

- Too much “off” time…“up and downs”



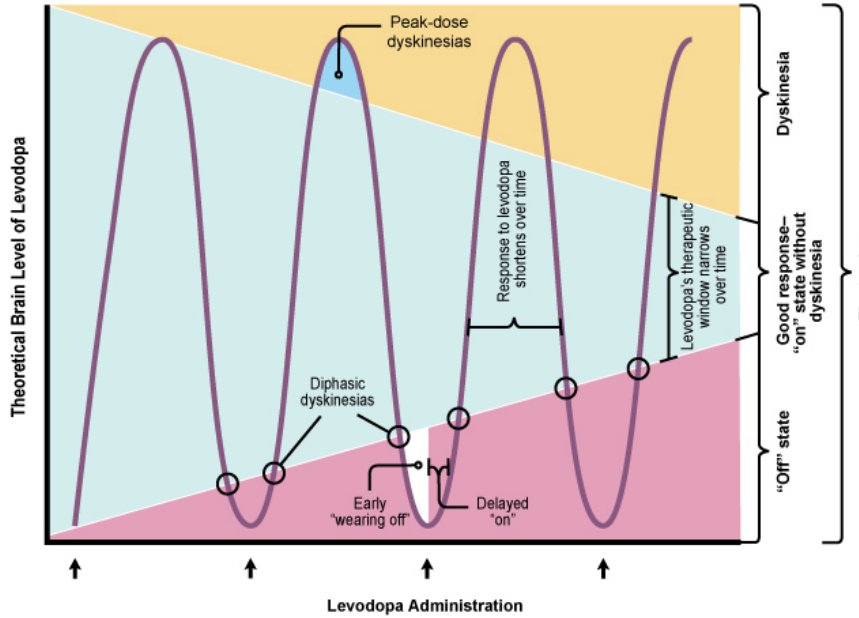
When to Consider DBS

- Too much “off” time…“up and downs”
- Intolerable side-effects of meds



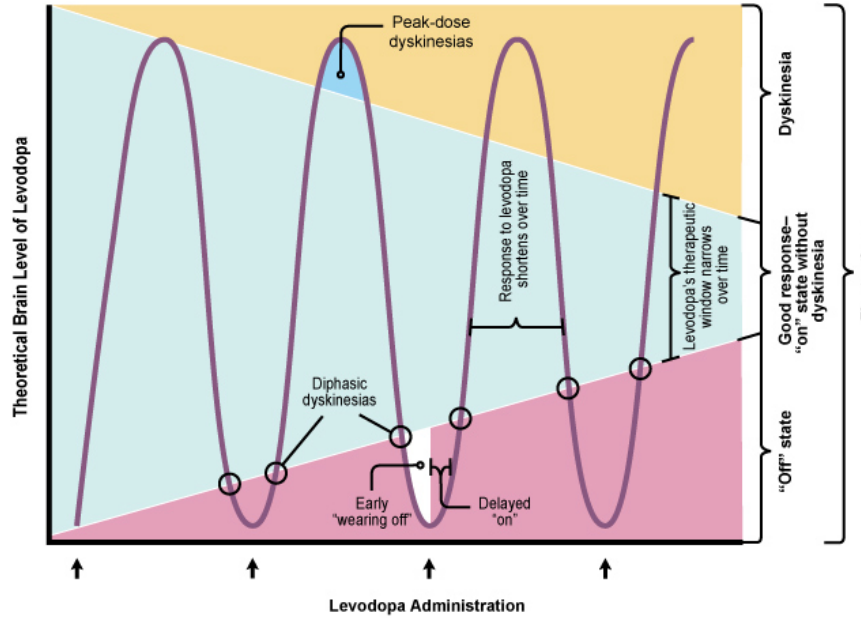
When to Consider DBS

- Too much “off” time…“up and downs”
- Intolerable side-effects of meds
- Insufficient tremor control
- Troublesome dyskinesias



When to Consider DBS

- Too much “off” time…“up and downs”
- Intolerable side-effects of meds
- Insufficient tremor control
- Troublesome dyskinesias
- Thinking about stopping hobbies/job



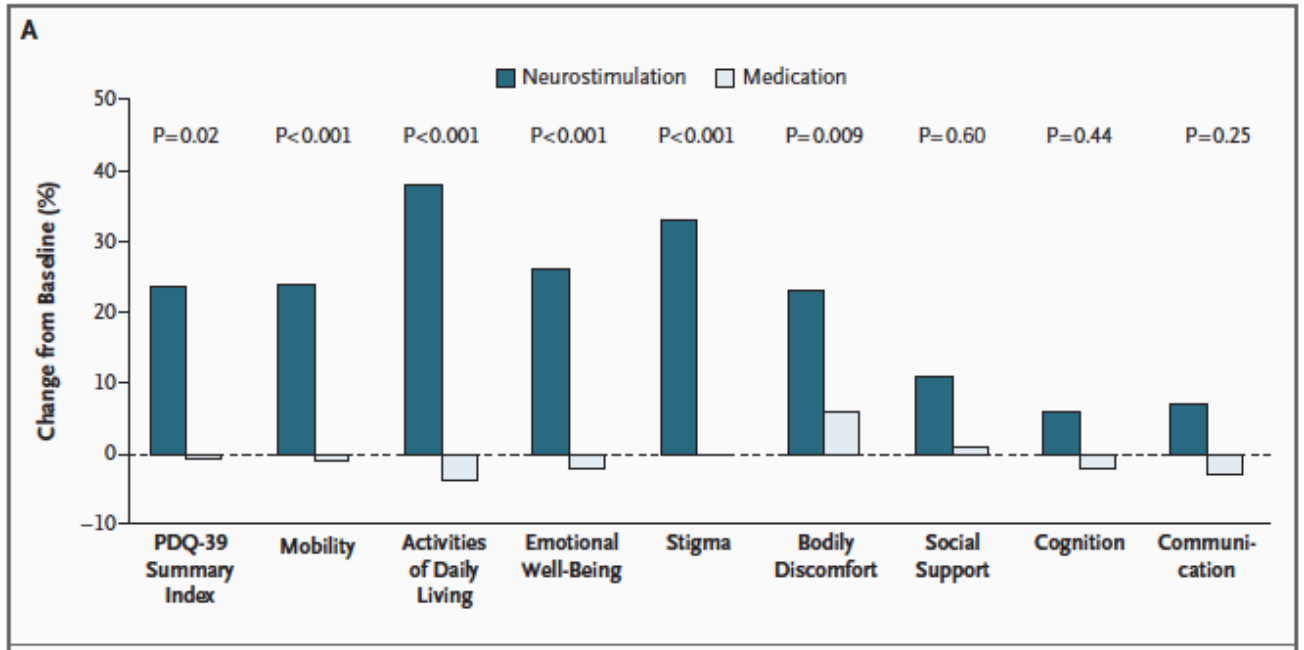
How we define candidacy?: Team

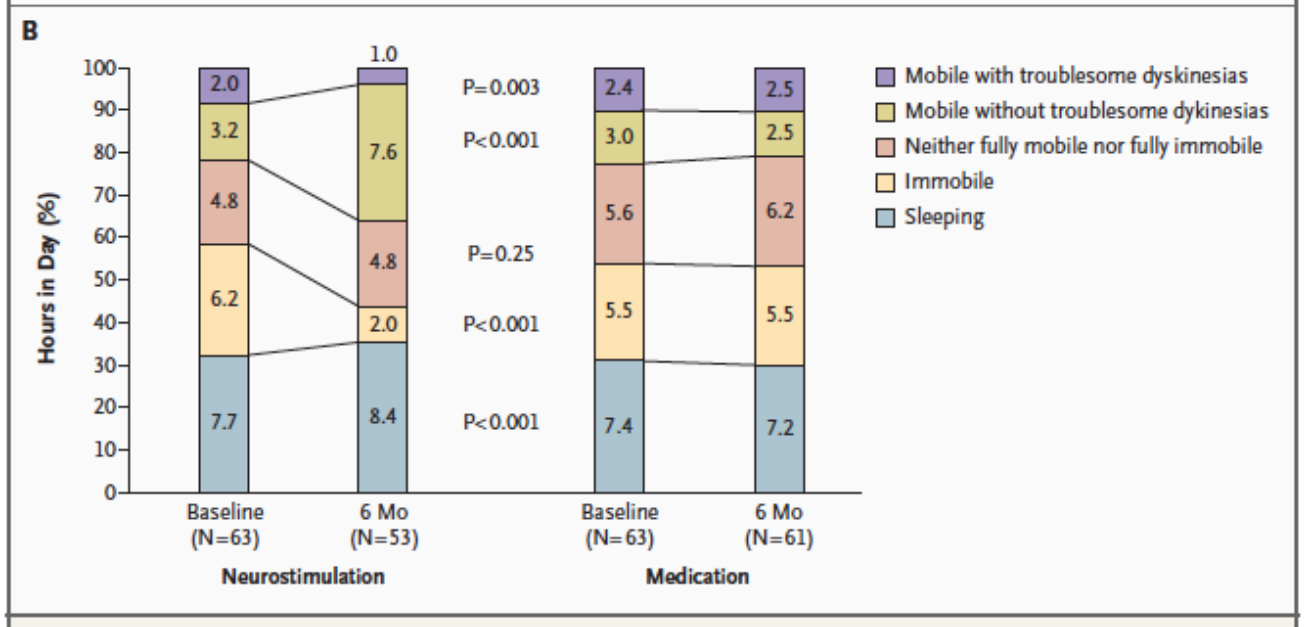
- Neurologists
- Neurosurgeons
- Neuroradiologists
- Neuropsychologists
- Advanced practice providers
- Anesthesiologists
- Neurophysiologists
- Psychiatrists

How we define candidacy?: Workup

- History & Neurological examination
- Levodopa responsiveness ON/OFF
- UPDRS Scales
- Imaging
- **Diagnosis**
- **Co-morbidities: Psychiatric**
- Quality of life: work and personal life
- Conservative treatments tried
- Neuropsychological evaluation

Clinical Results of DBS





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Deep-Brain Stimulation for Parkinson's Disease

Günther Deuschl, M.D., Ph.D., Carmen Schade-Brittinger,

DBS is surgery of Last Resort?


DBS is surgery of Last Resort?

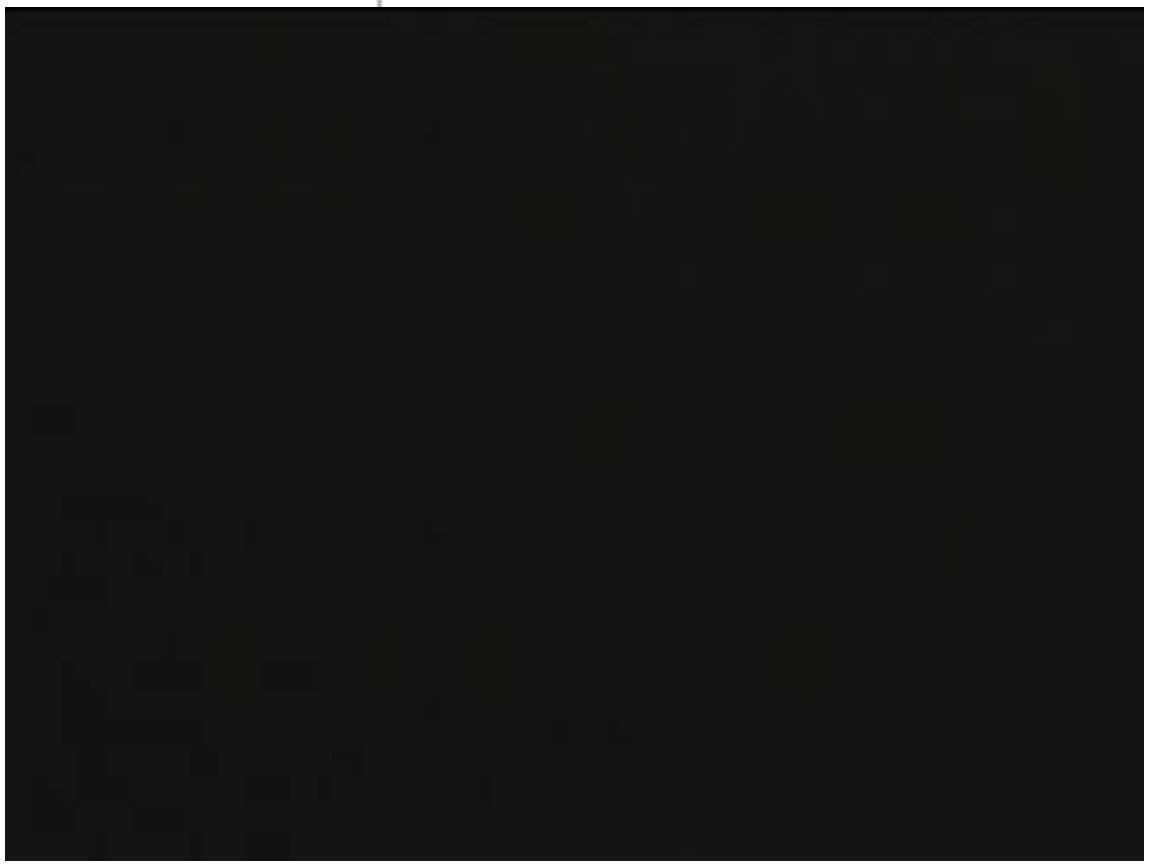
It's **not** about getting patients out of the nursing home, it's about getting patients back on the golf course. . .

…..I waited too long….

It's **not** about getting patients out of the nursing home, it's about getting patients back on the golf course. . .

Parkinson's disease

Parkinson's disease



Goals of DBS

- To Improve quality of life>> symptomatic treatment
- Not Cure
- Hope for medically intractable patients

Expectations

- 70% reduction in dyskinesias
  - 50% medication reduction
- 80% reduction in resting tremor (Essential tremor)
- 60% reduction in bradykinesia
- 70% reduction in rigidity
- 60-70% reduction in dystonia

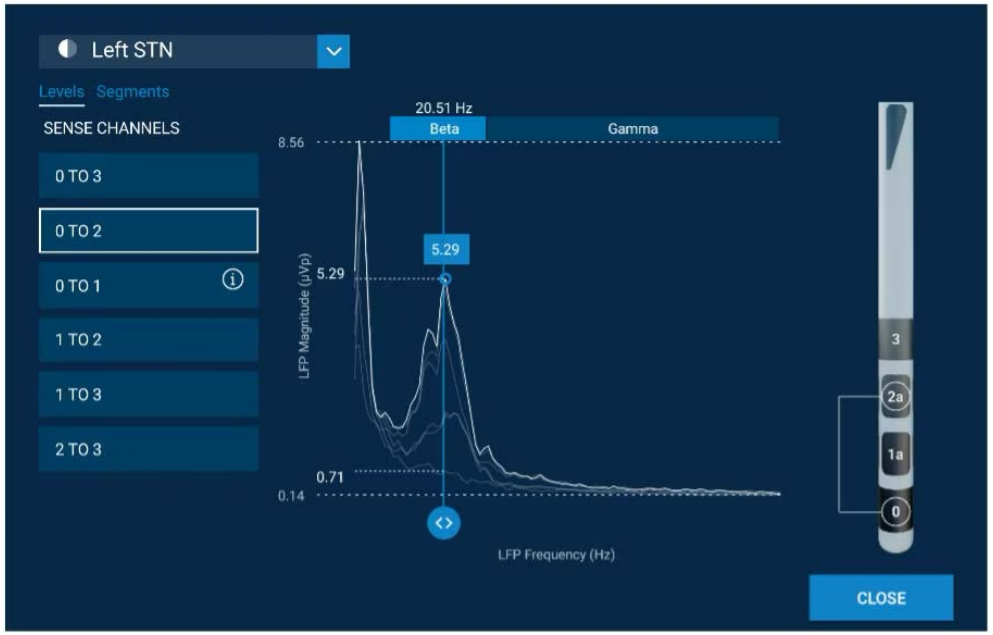
- 70% improvement in peak ON-time
- 70% reduction in worst OFF-time

Expectations

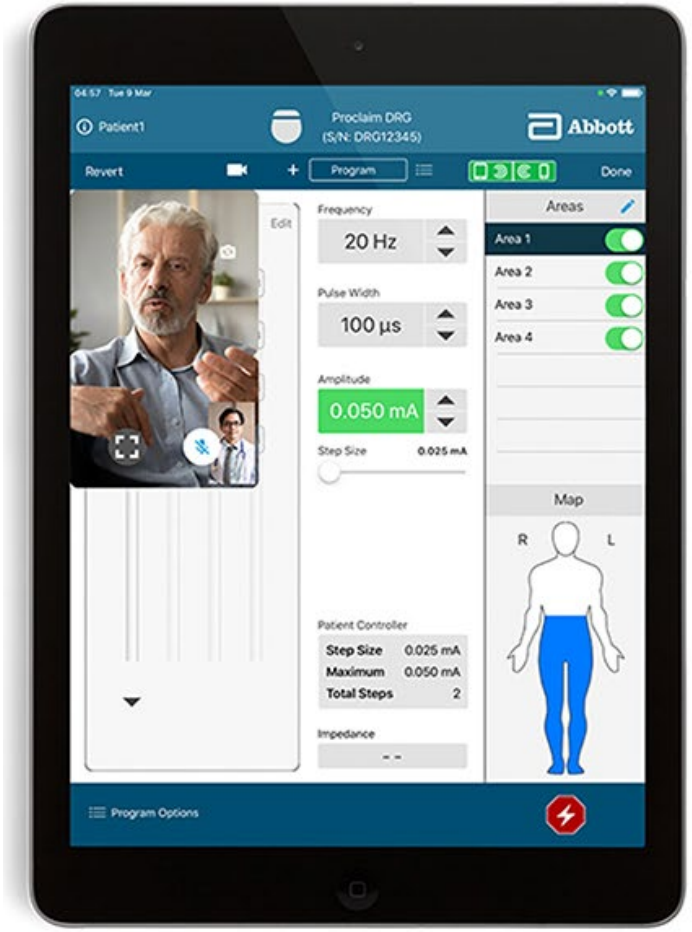
- Freezing of gait (especially ON-freezing)
- Axial Instability
- Balance issues (Tend to avoid STN)
- Cognitive issues (?)
- Apathy (?) (Better with STN)
- Depression and anxiety (?)

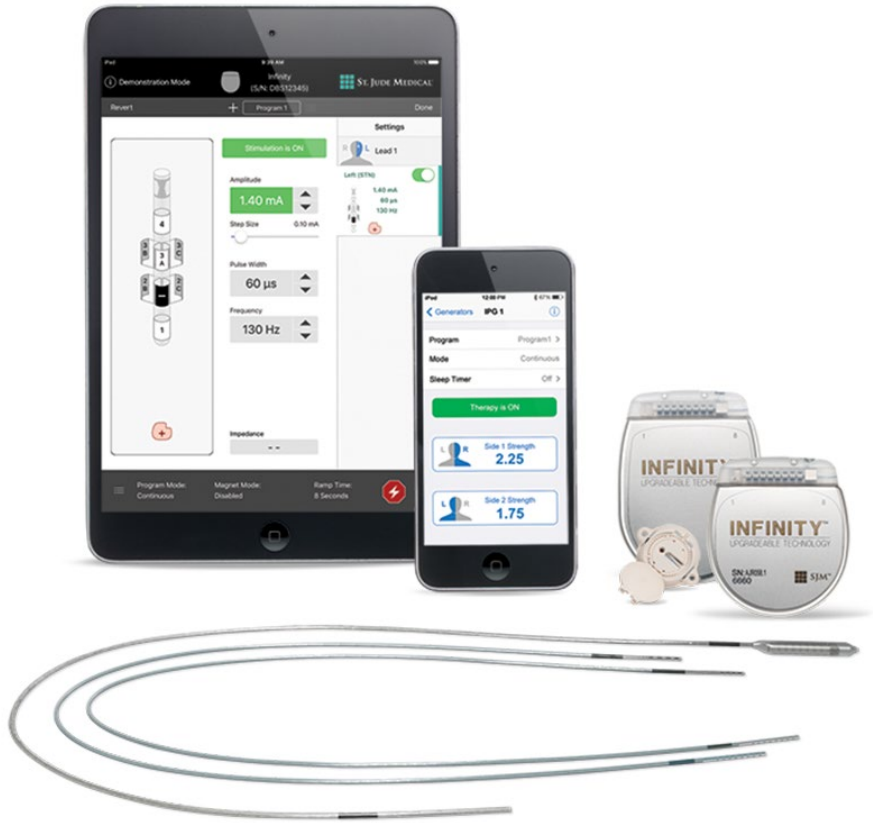
Before surgery

The Device: Medtronic

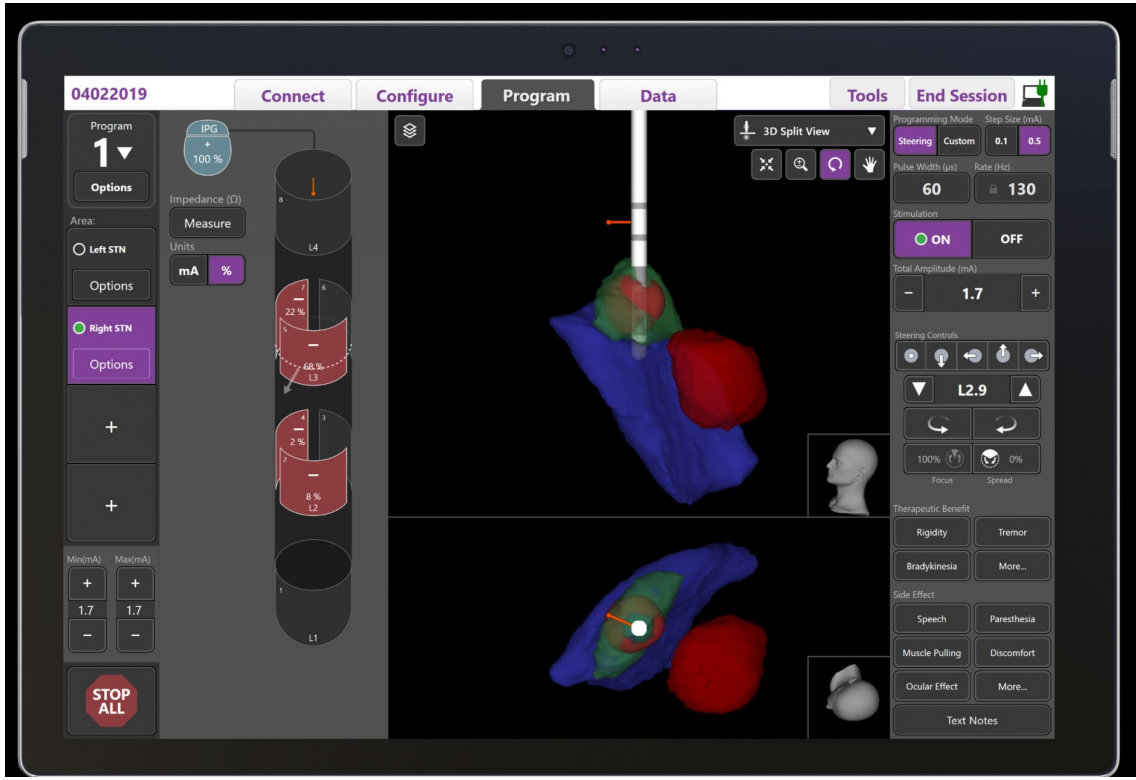


The Device: Abbott

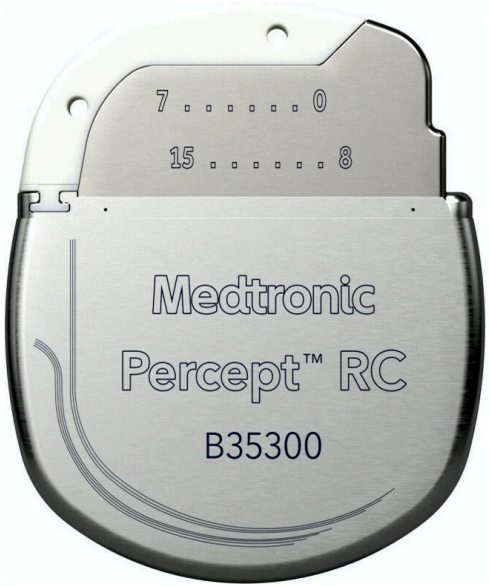


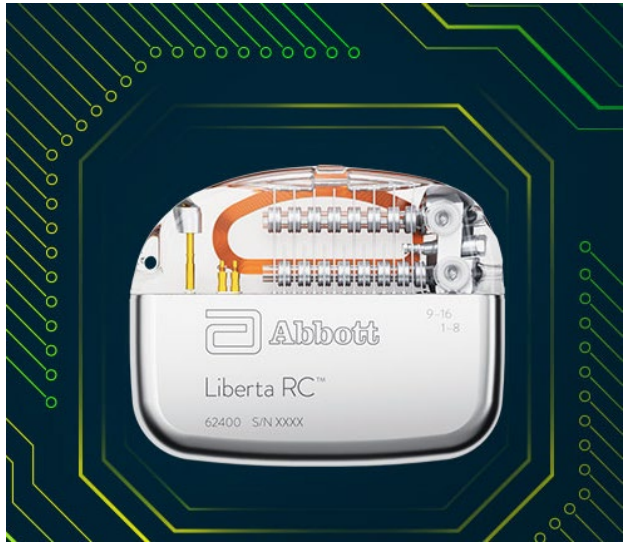


The Device: Boston Scientific



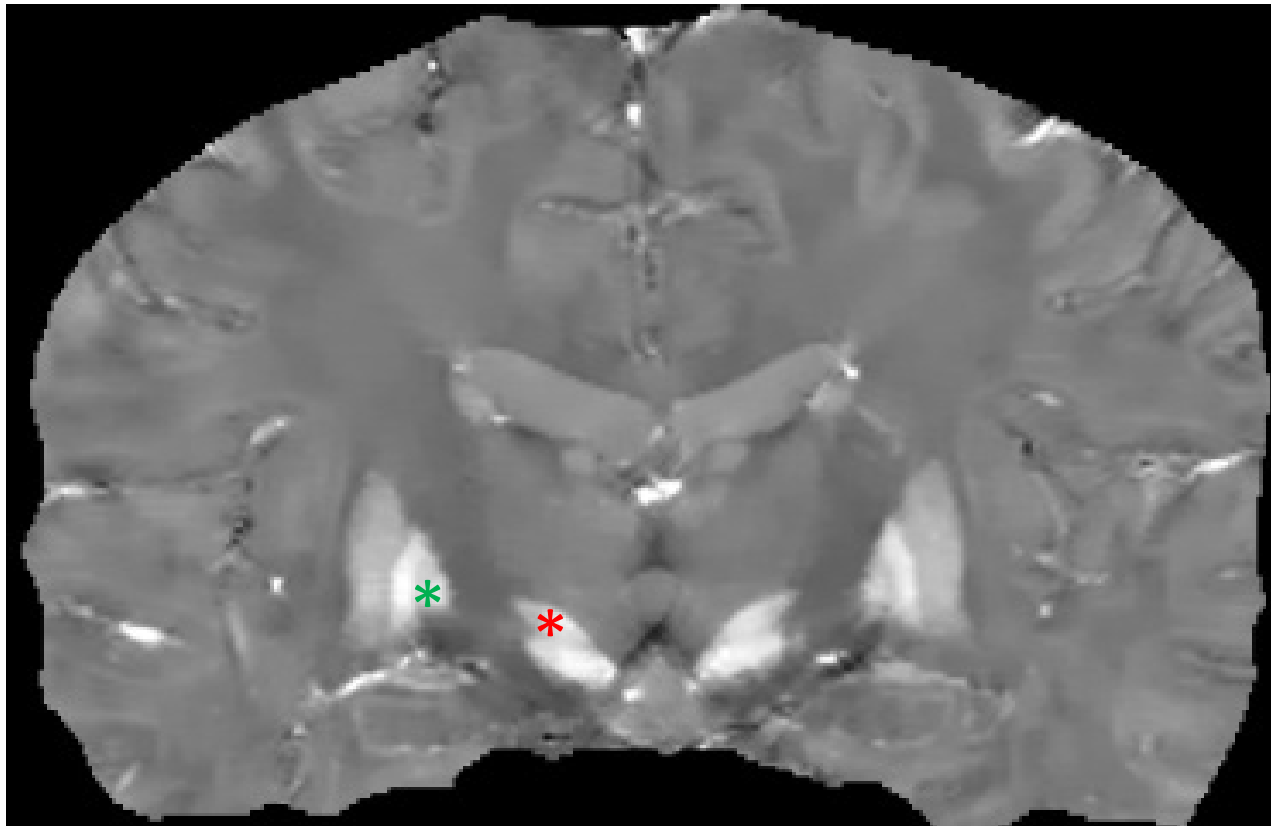
Rechargeable batteries





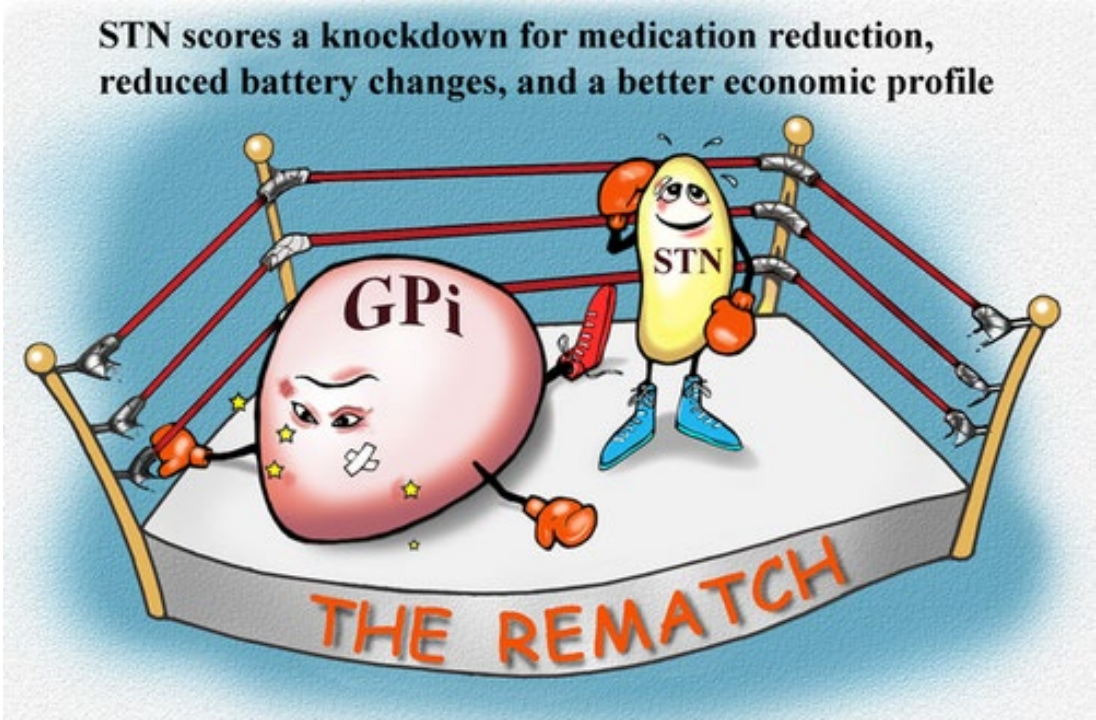
Targets

- Subthalamic nucleus
- Globus pallidus interna



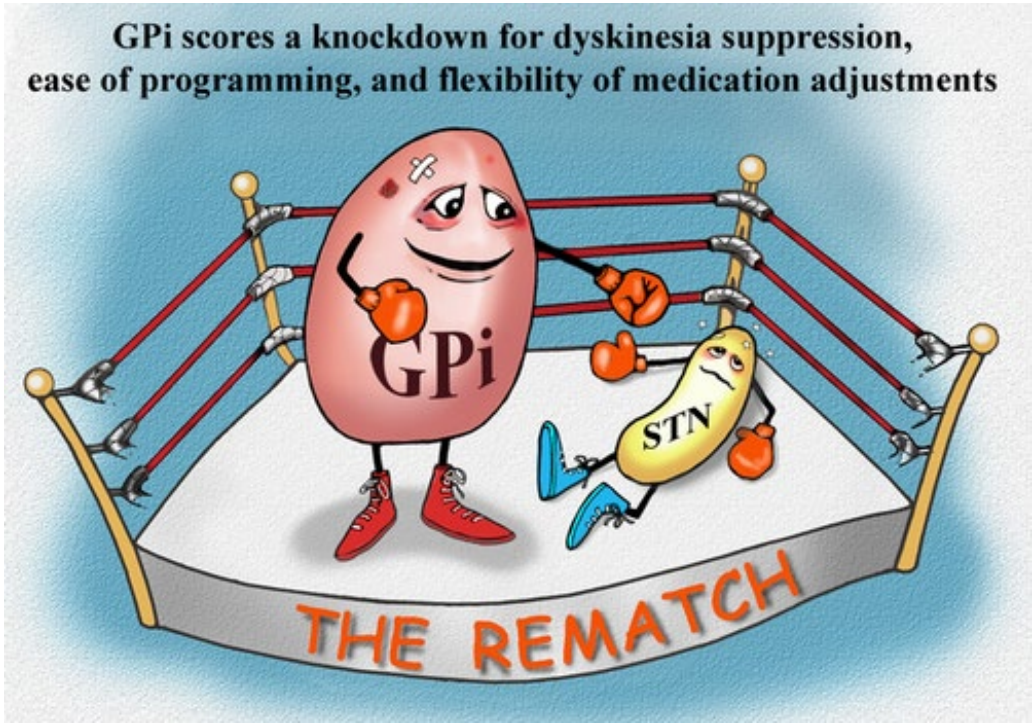
Targets: STN

- Medication reduction…
- Faster tremor control…



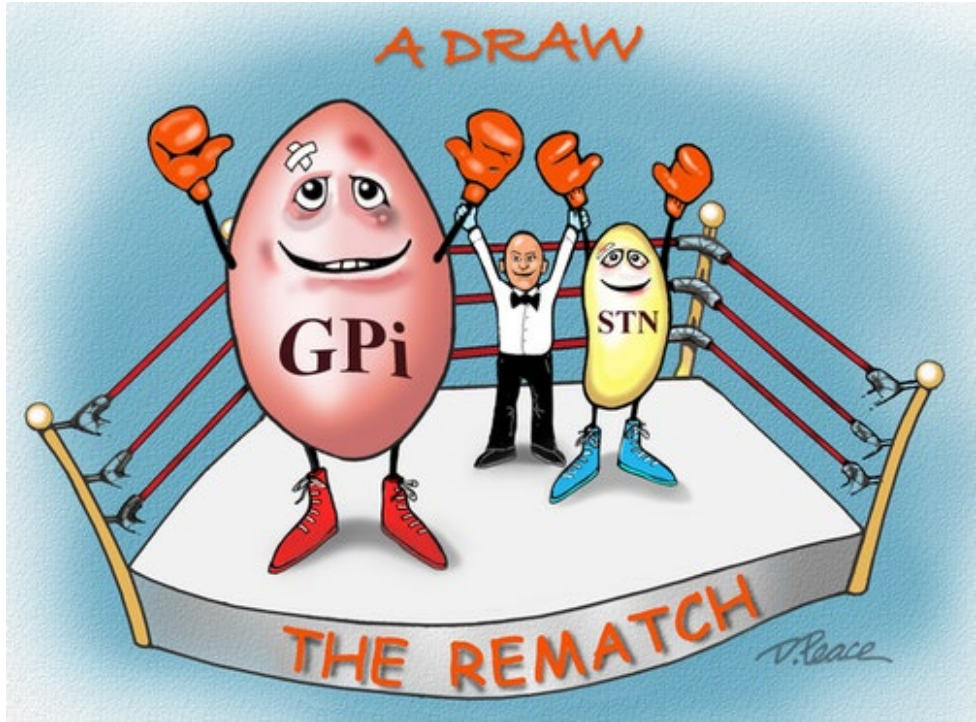
Targets: GPi

- Dyskinesias…
- Dystonia…
- Easy programming and flexible med adjustments



Targets: GPi and STN

- Both targets equivalent in overall motor benefit
- Team expert with both targets
- Personalize based on patient needs!

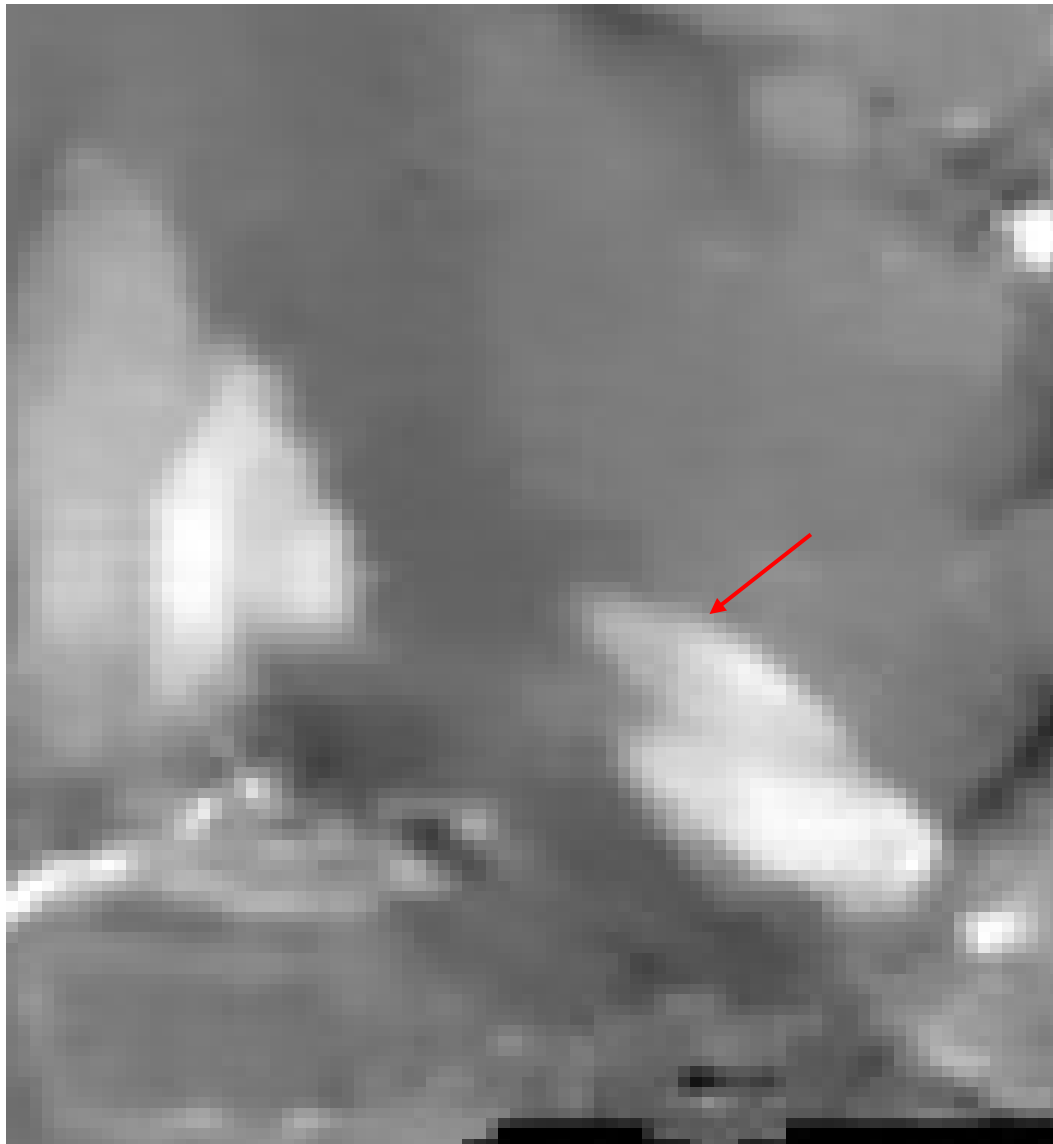


Imaging at UNMC

- MRI under general anesthesia
- At least 2 weeks before procedure

Imaging at UNMC

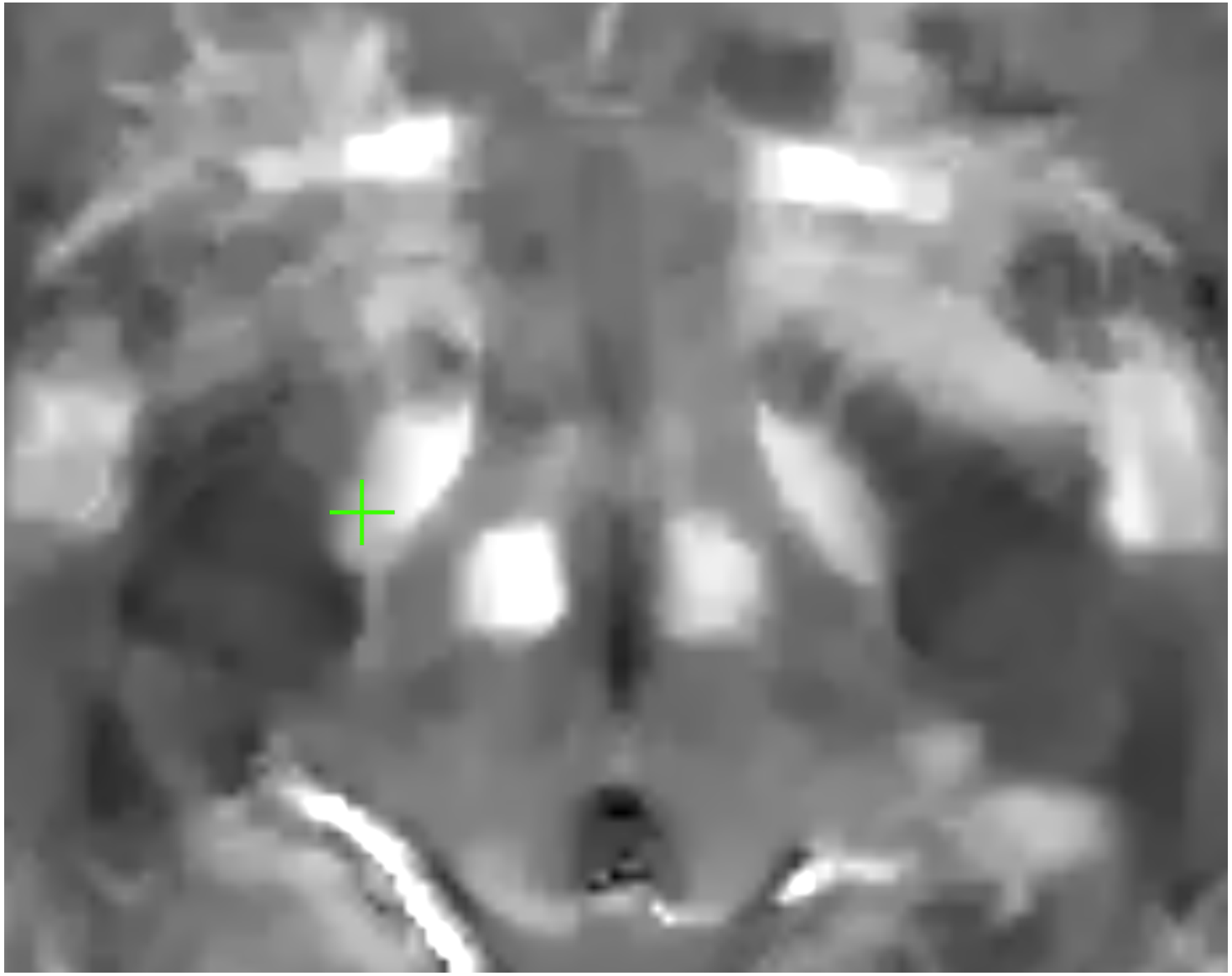
Imaging at UNMC

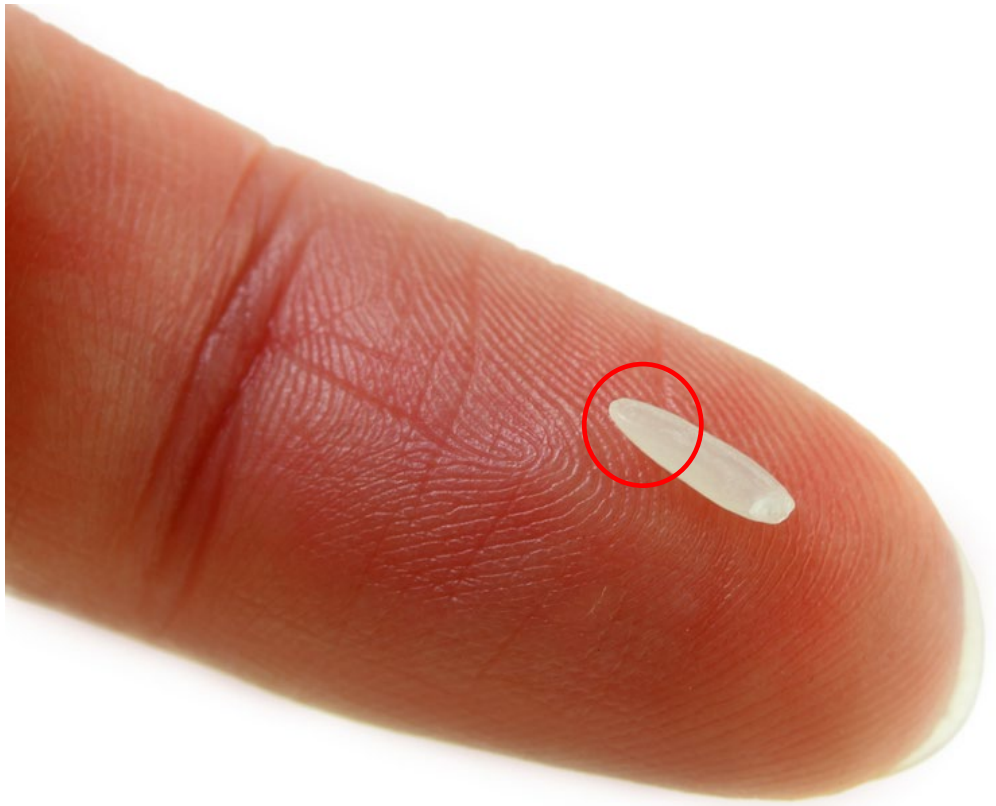


Surgery

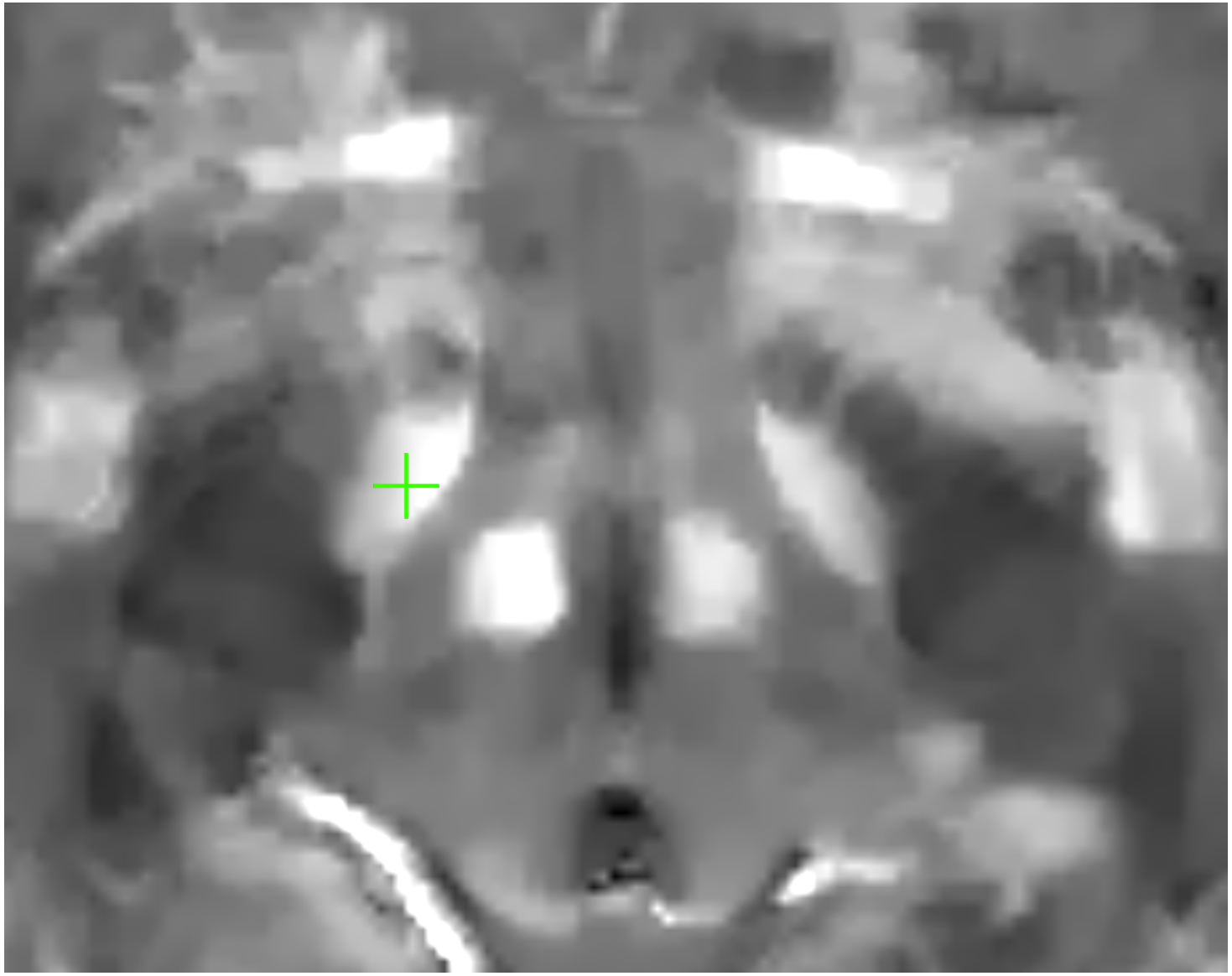
Sleep vs Awake Surgery

Planning: Targeting

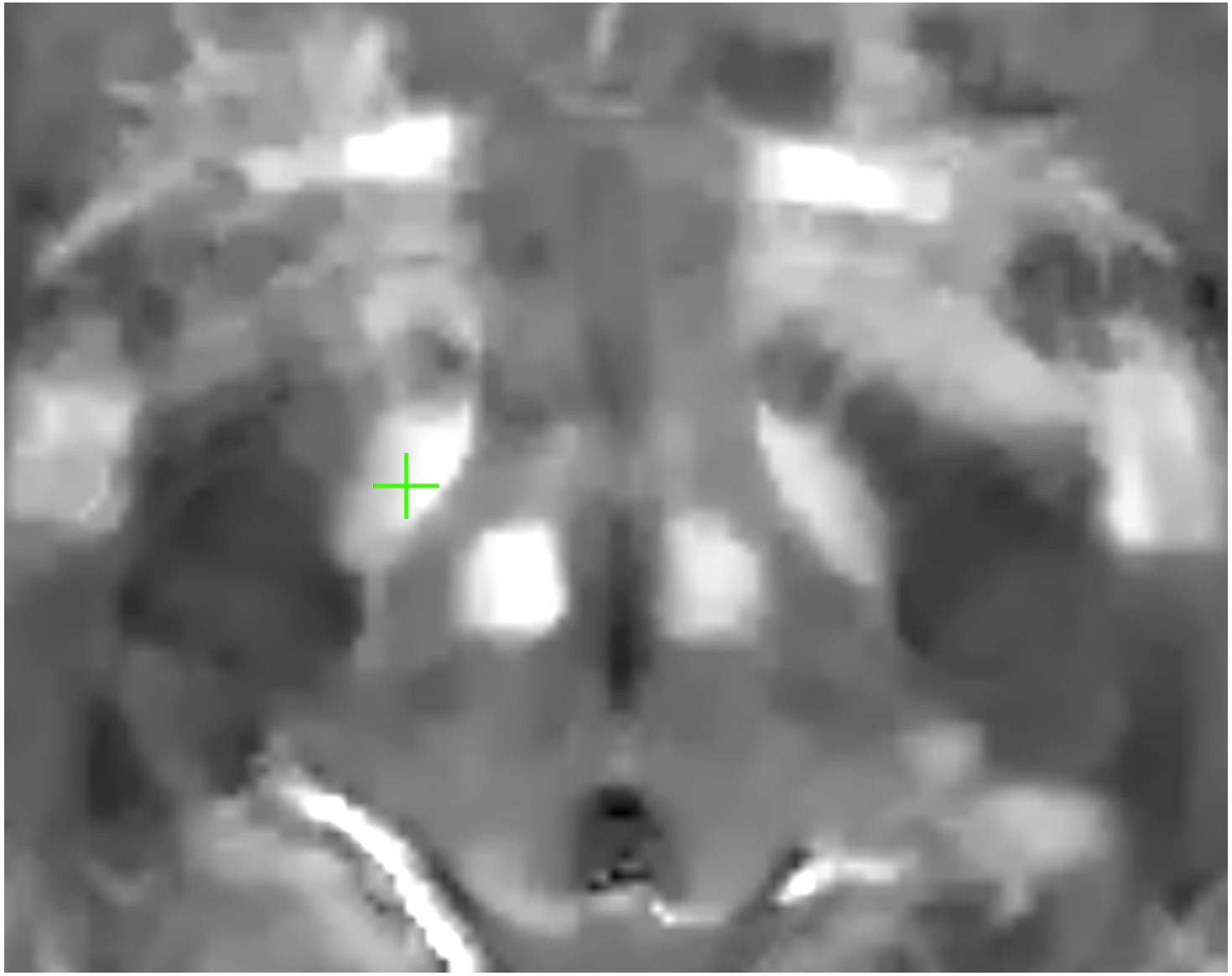


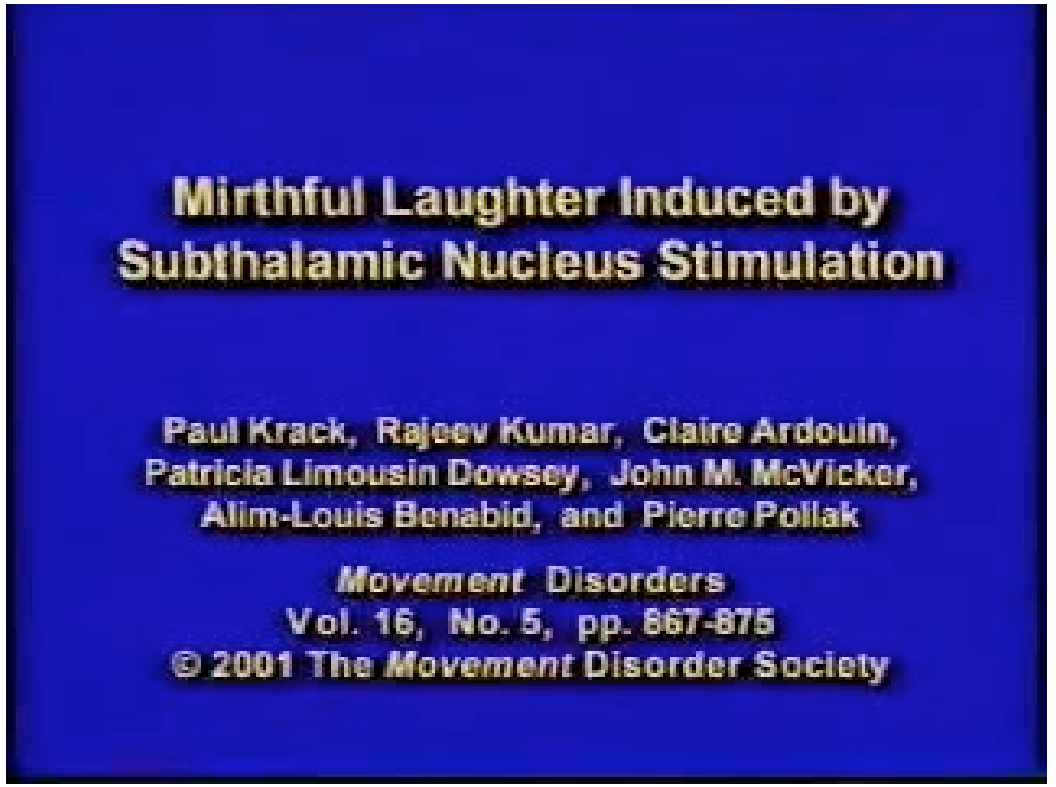


Millimeters matter!



Millimeters matter!

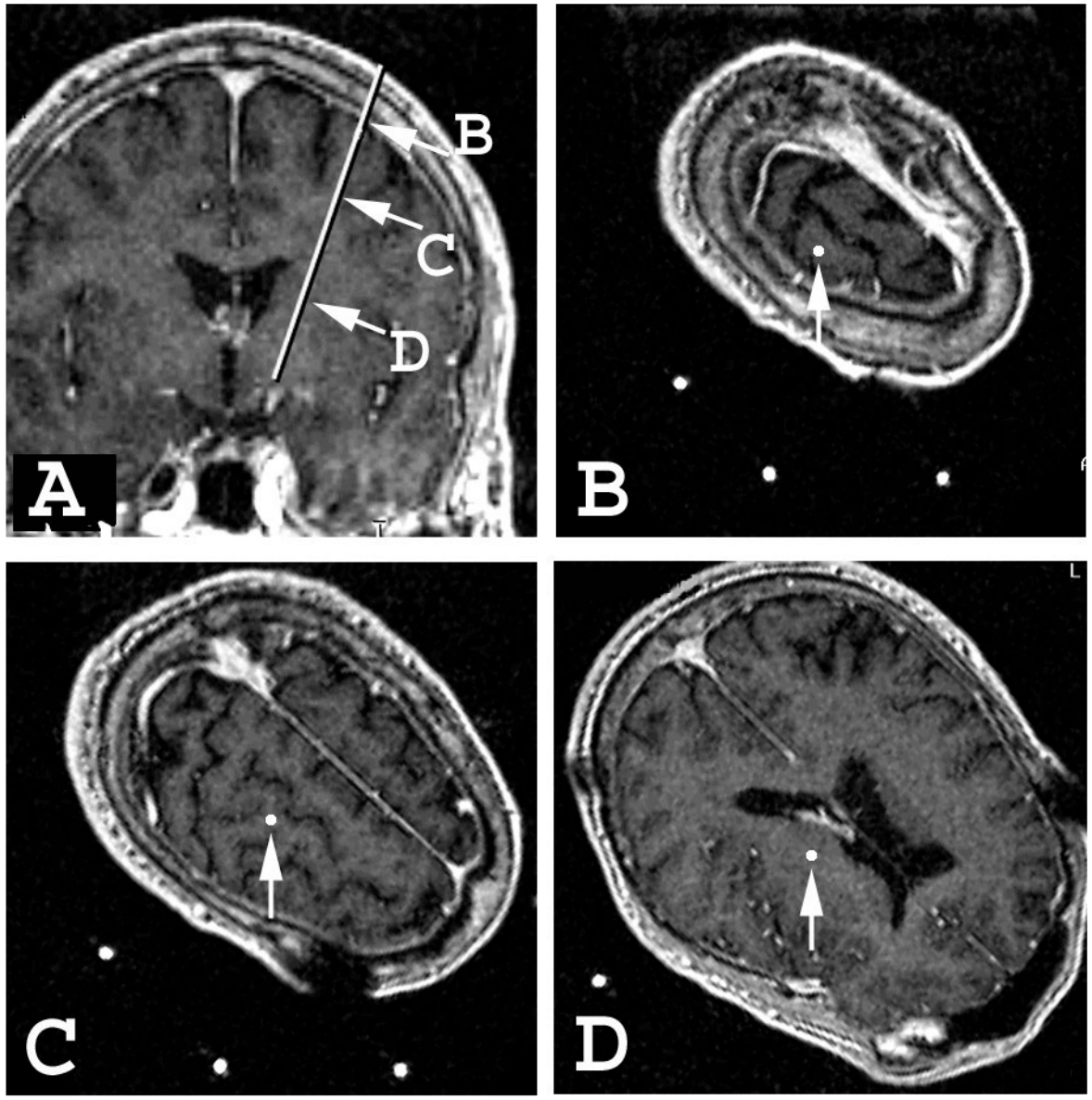


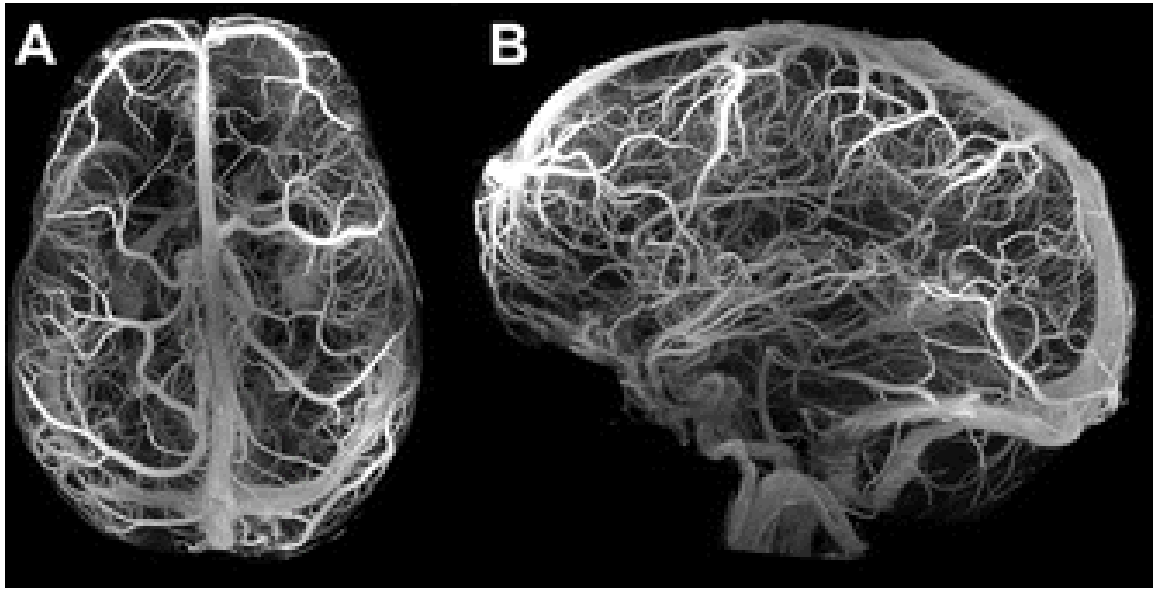


Mirthful Laughter Induced by Subthalamic Nucleus Stimulation

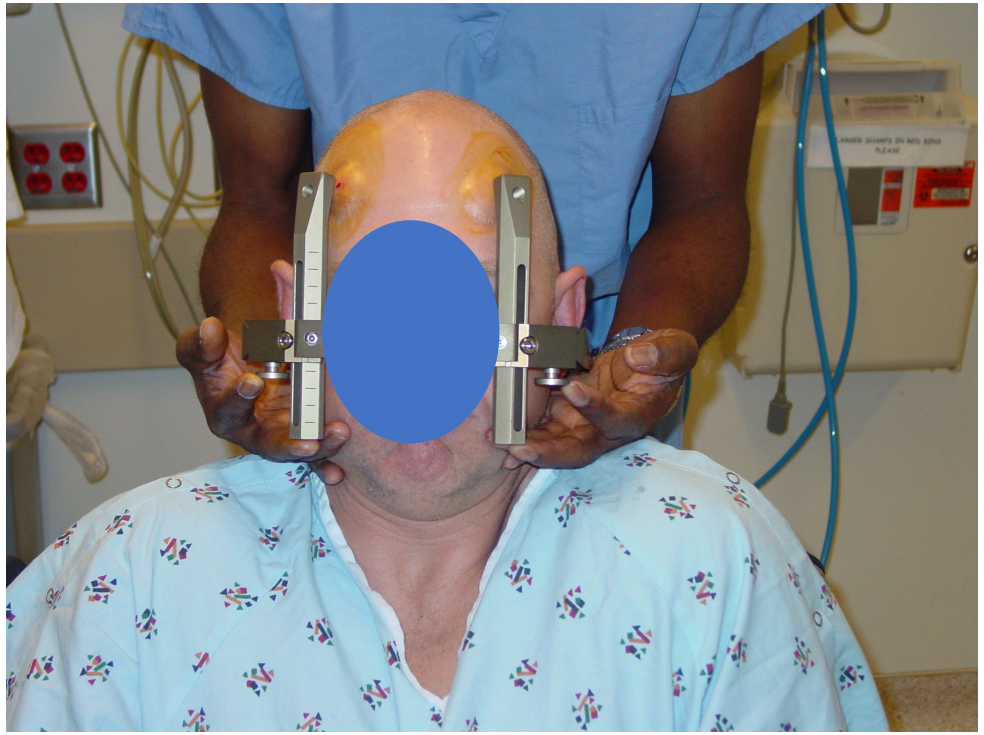
Paul Krack, MD,[1,2*] Rajeev Kumar, MD,[3] Claire Ardouin, PhD,[1] Patricia Limousin Dowsey, MD, PhD,[1,4]
John M. McVicker, MD,[3] Alim-Louis Benabid, MD, PhD,[1] and Pierre Pollak, MD[1]

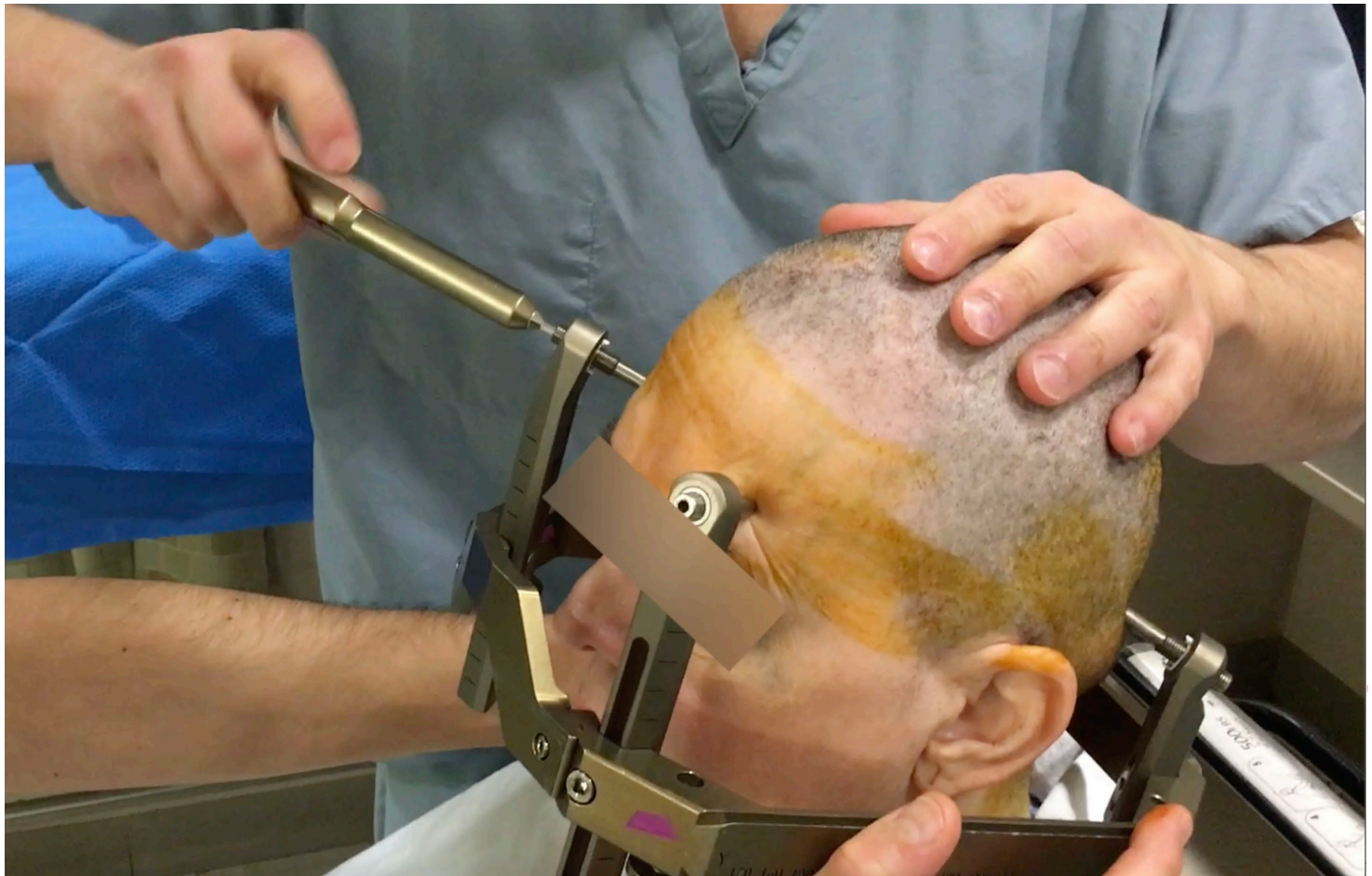
Planning: Vessels



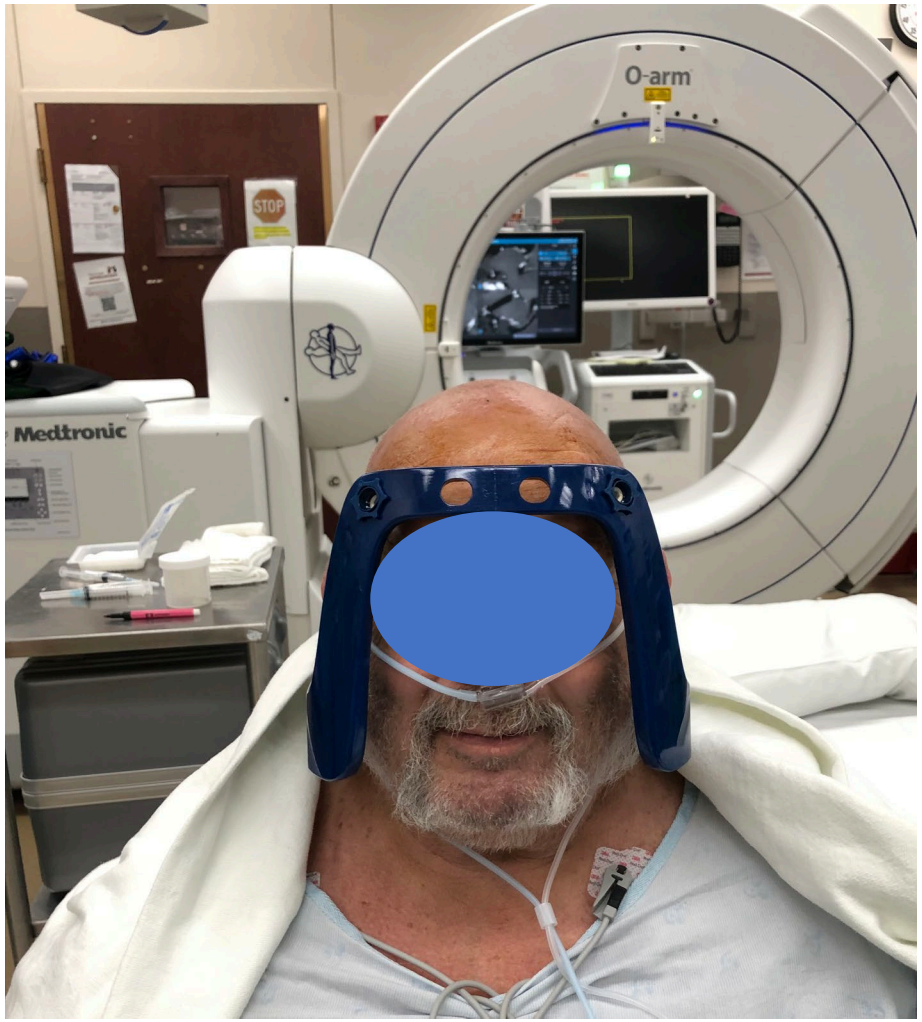


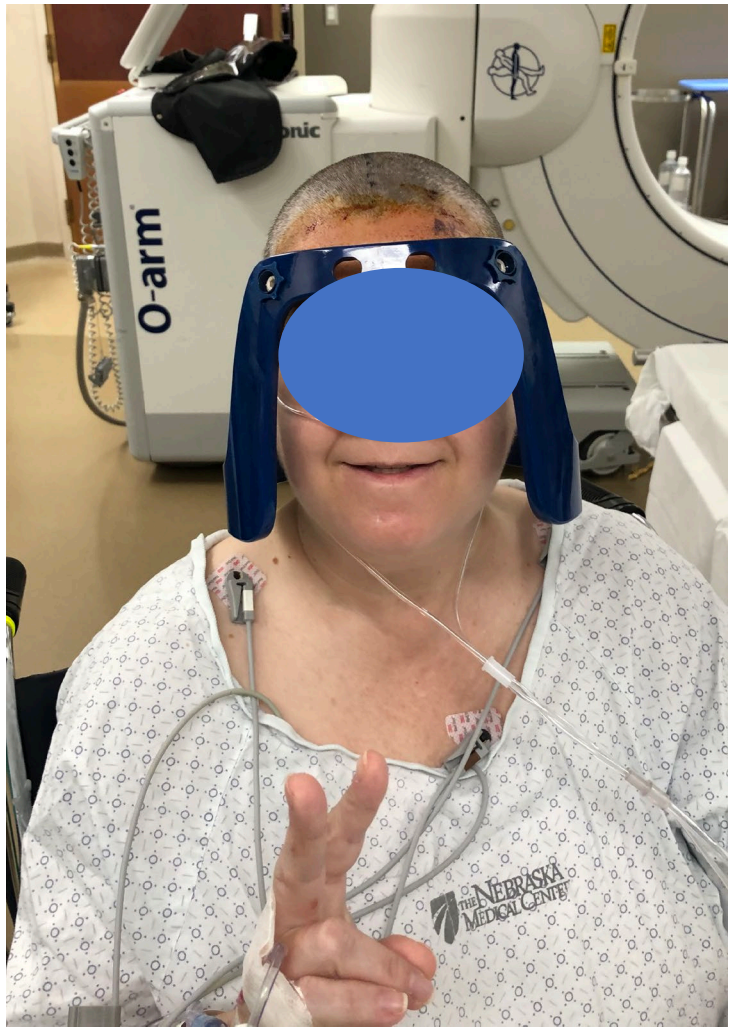
Procedure: Frame placement



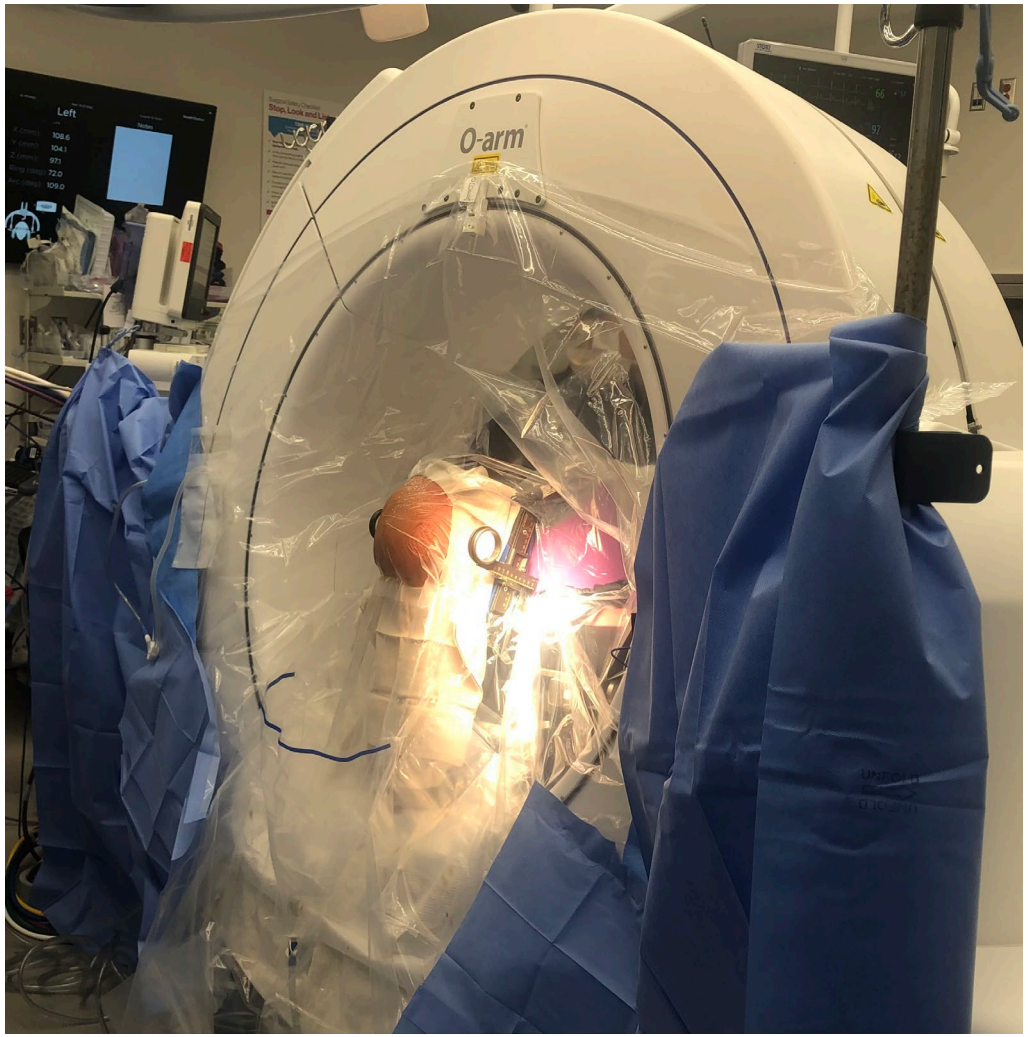


Procedure: Frame placement





Procedure: Set up

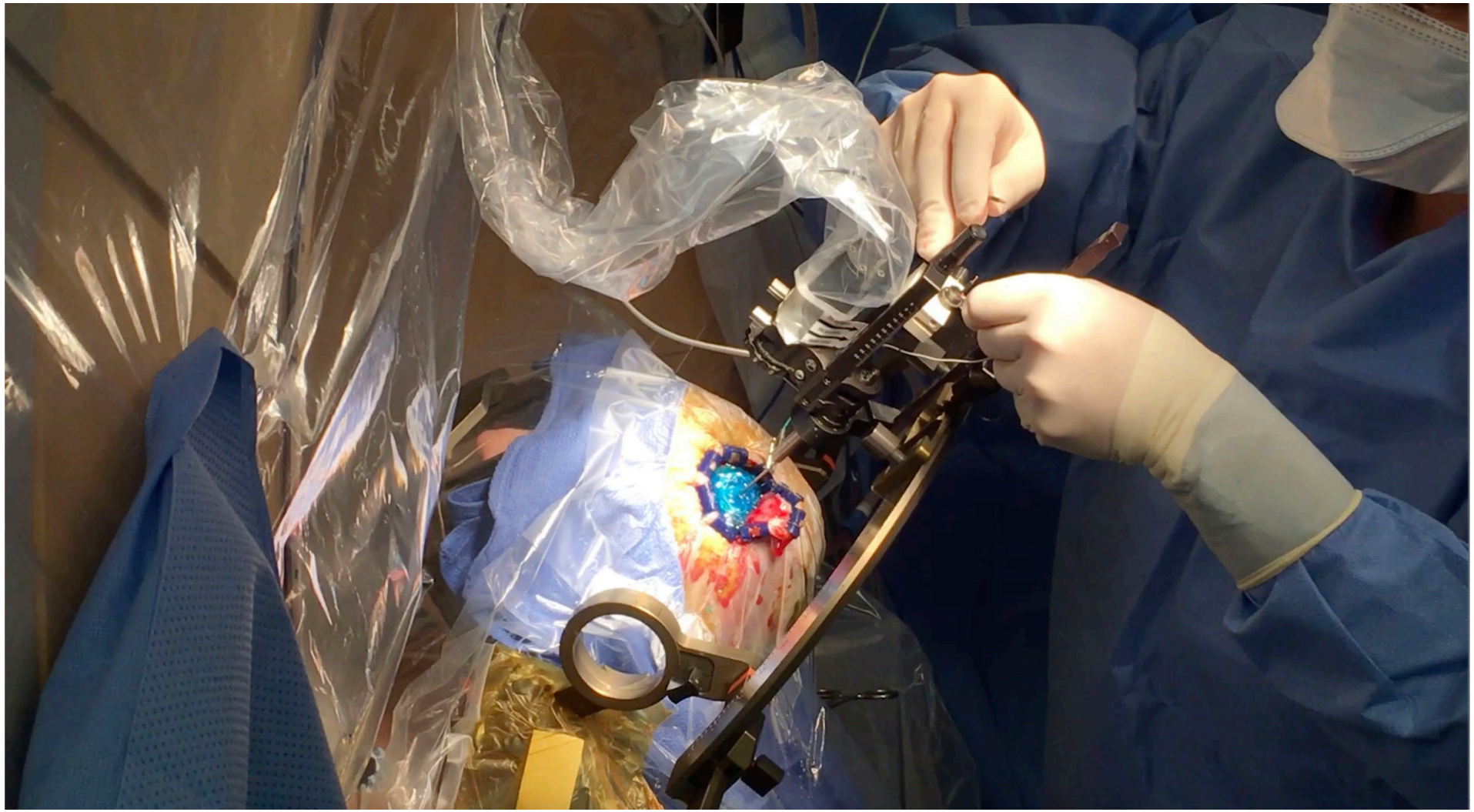


Procedure: Set up

Asleep-Awake-Asleep Surgery

- Patient will be sedated for skin incision and burr hole placement

Procedure: Asleep



Asleep-Awake-Asleep Surgery

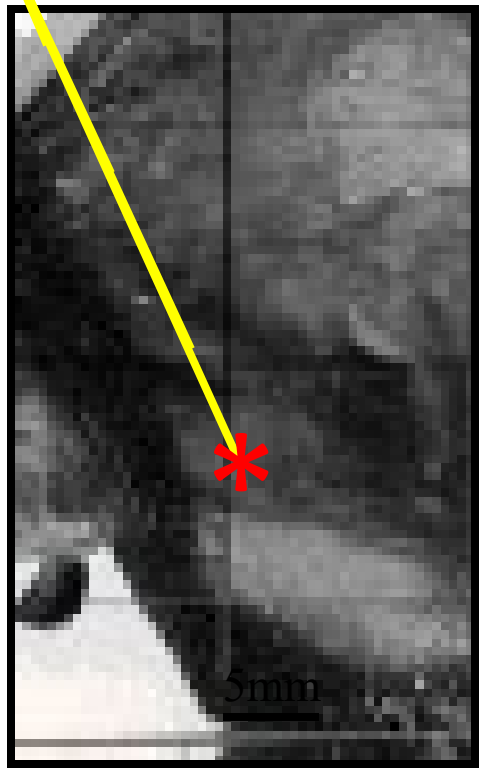
- Patient will be sedated for skin incision and burr hole placement
- Patient will be awakened for brain mapping and electrode insertion

Asleep-Awake-Asleep Surgery

- Patient will be sedated for skin incision and burr hole placement
- Patient will be awakened for brain mapping and electrode insertion
  - Motor symptoms does NOT manifest in the sleeping state

Procedure: Recordings

Position of electrode

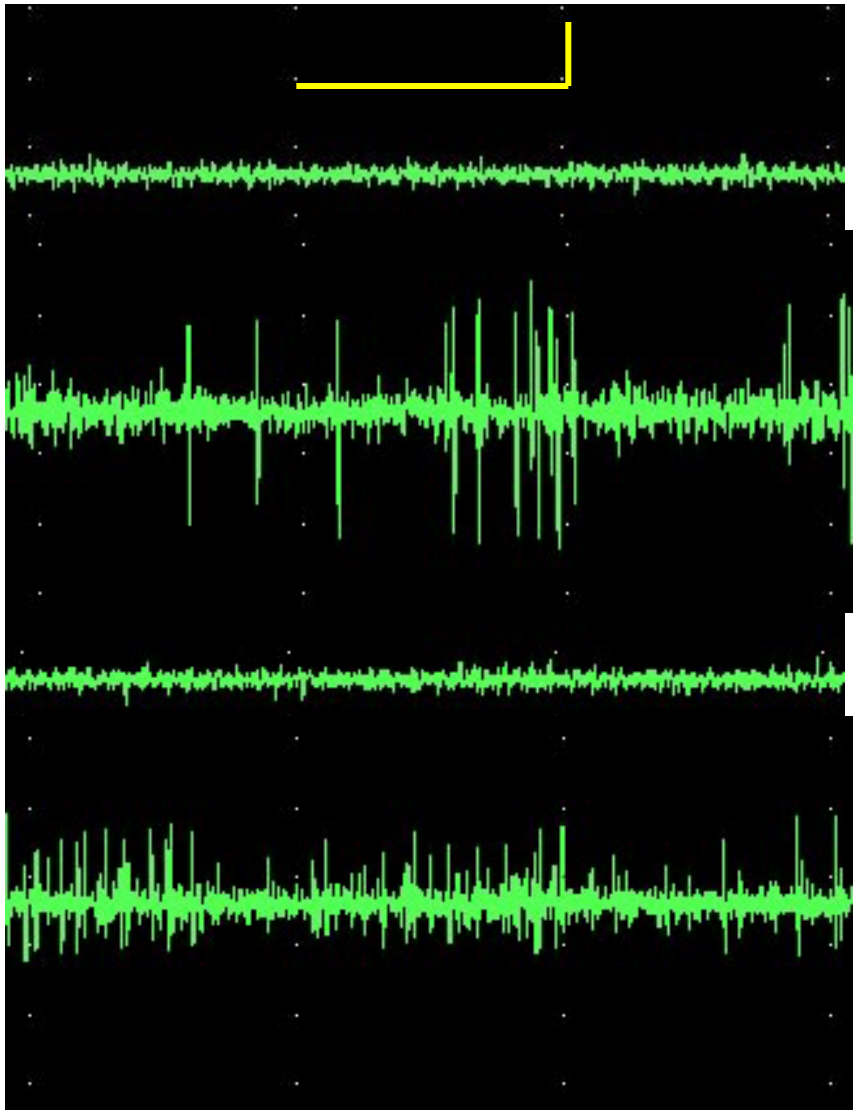


White matter

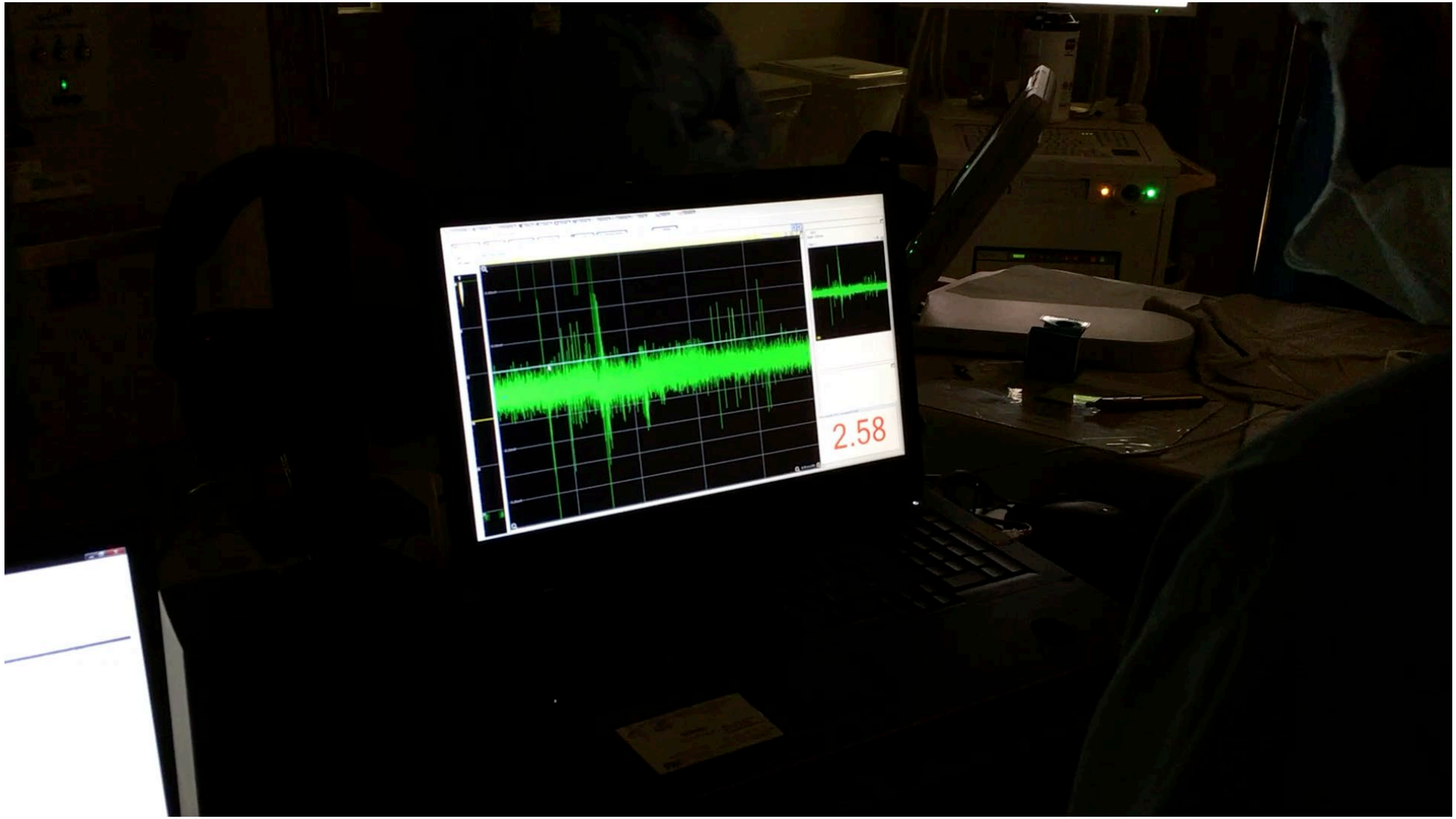
Thalamus

Zona incerta

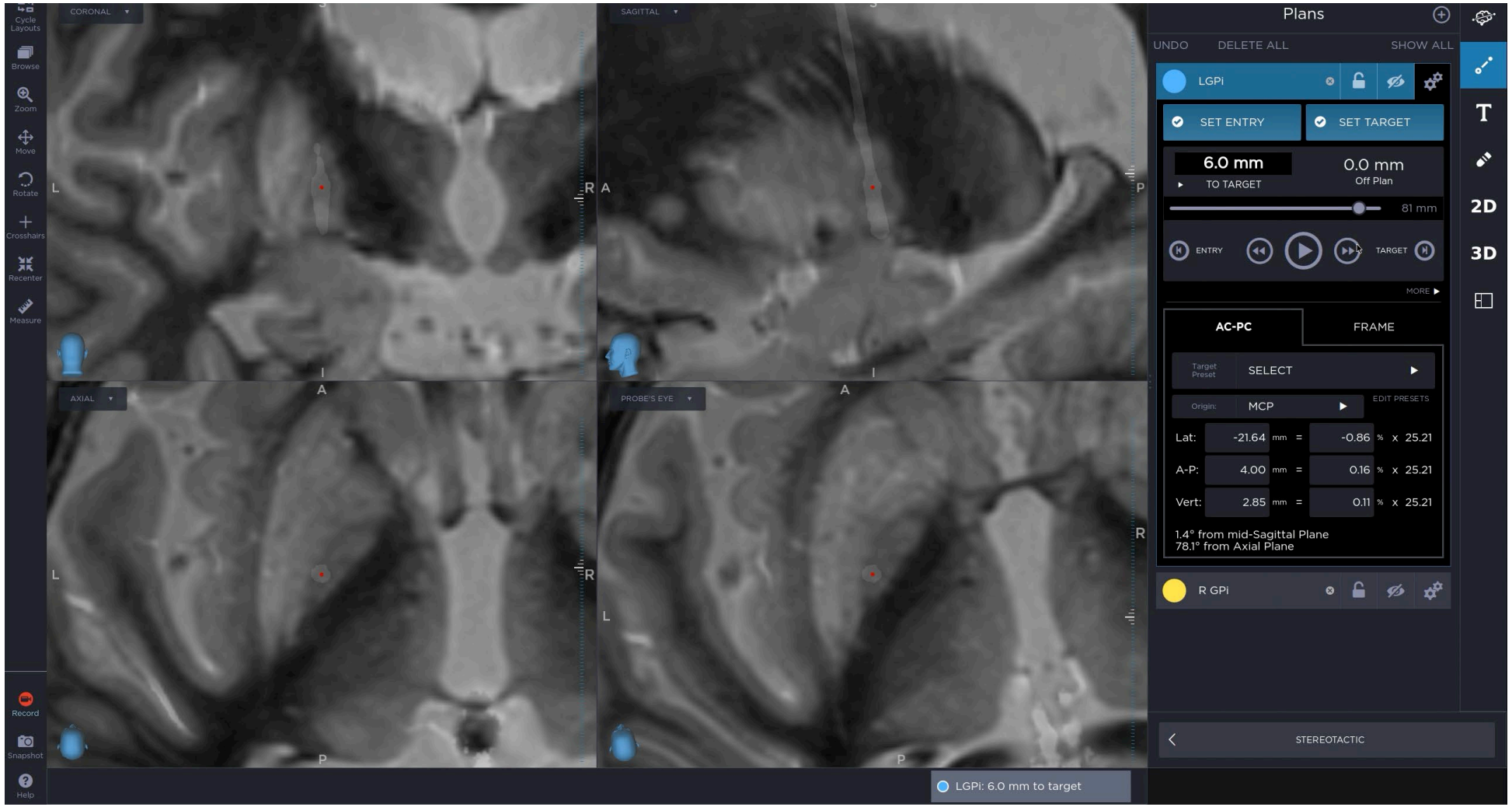
STN



Procedure: Recordings



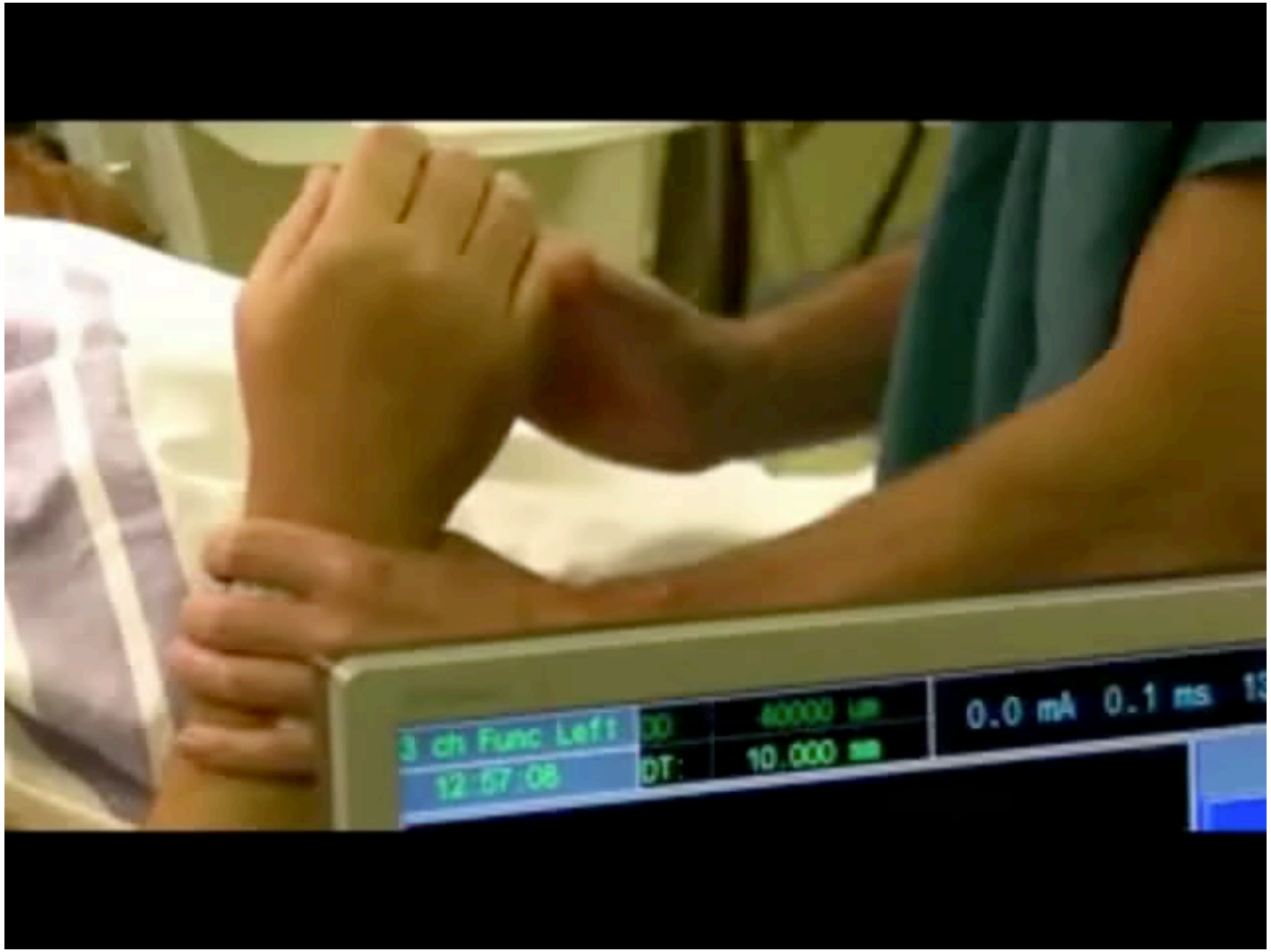
Procedure: Imaging Confirmation



Procedure: Clinical testing

- Clinical benefit at low current: 0.5 mA
- Side effects at high voltages: > 4 mA
- Wider therapeutic window

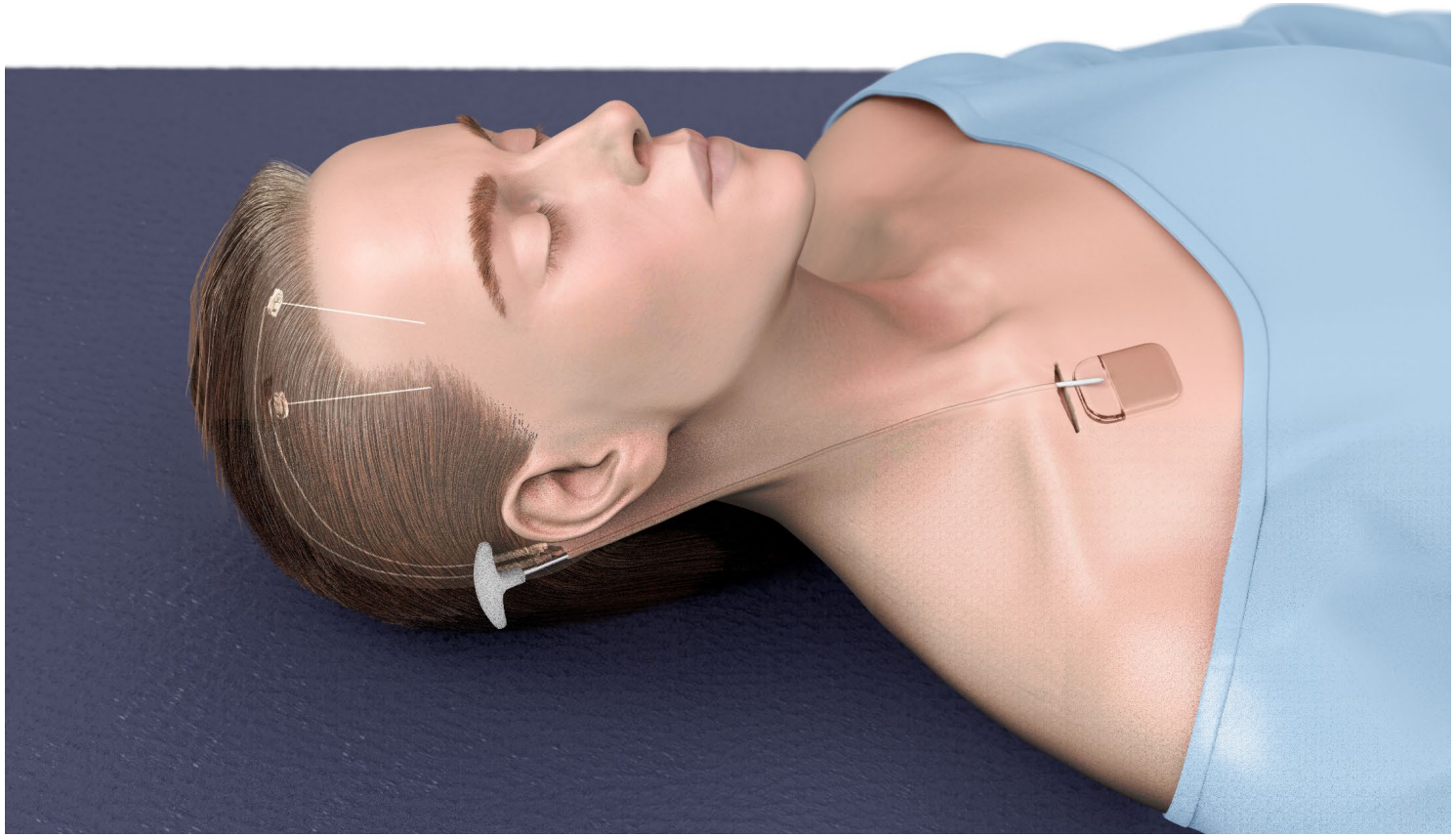
Procedure: Clinical testing

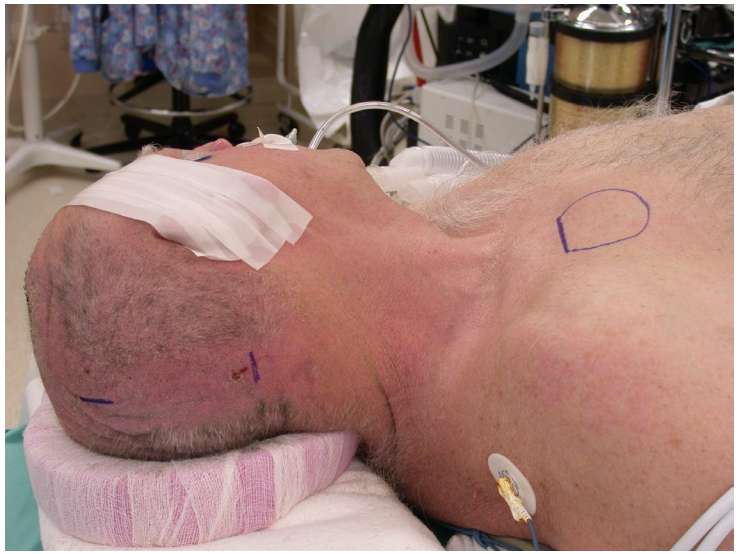


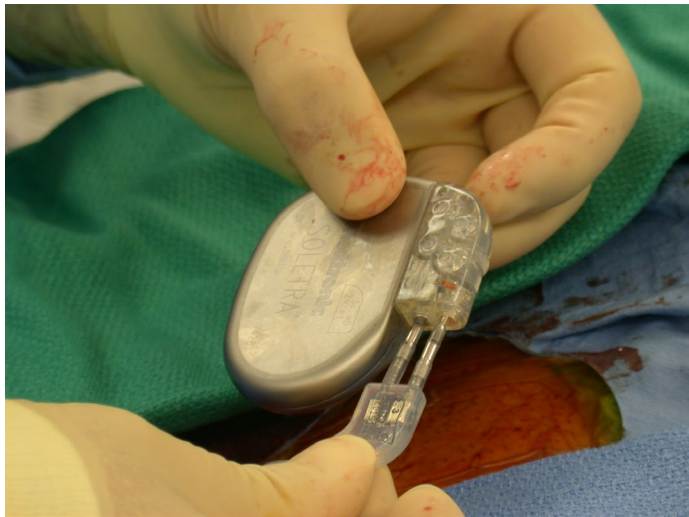
Asleep-Awake-Asleep Surgery

- Patient will be sedated for skin incision and burr hole placement
- Patient will be awakened for brain mapping and electrode insertion
  - Motor symptoms does NOT manifest in the sleeping state
- Patient will go back to sleep for closure

Procedure: generator placement







Complications

- Hemorrhage: 3% Usually minor, no symptoms
- Severe Hemorrhage: 1%

Complications

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- Severe Hemorrhage: 1%
- Infection: 3 %. Leads vs IPG.. Management?

Complications

- Hemorrhage: 3% Usually minor, no symptoms
- Severe Hemorrhage: 1%
- Infection: 3 %. Leads vs IPG.. Management?
- Hardware related: 3%, including misplaced leads.. What to do?

After surgery

What is important after surgery?

- Parkinson's medication
  - DBS is not ON
- Early ambulation
  - Speeds up recovery
  - Discharge next day after surgery

What is important after surgery?

- Communication Communication Communication

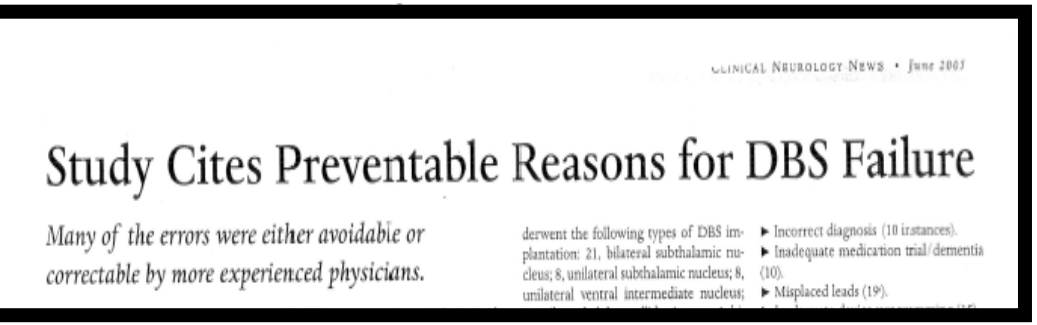
- Check your incisions!

What is happens after surgery?

- Precise Programming
  - Movement Disorder Neurologist
  - Advanced practice provider
  - Nurses

  - Time and patience!

- Medication and stimulation adjustments



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Study Cites Preventable Reasons for DBS Failure

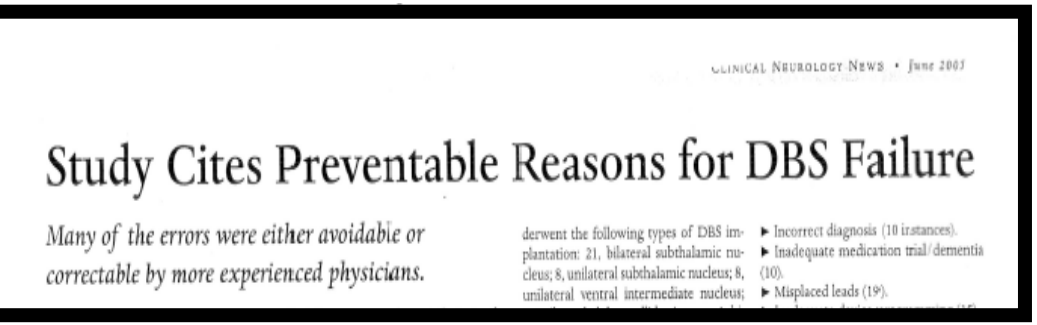
Many of the errors were either avoidable or correctable by more experienced physicians.

derwent the following types of DBS implantation: 21, bilateral subthalamic nucleus; 8, unilateral subthalamic nucleus; 8, unilateral ventral intermediate nucleus;

- Incorrect diagnosis (10 instances).
- Inadequate medication trial/dementia (10).
- Misplaced leads (19).

Conclusions

- Experience counts: More experience > better outcomes
- Proper patient selection



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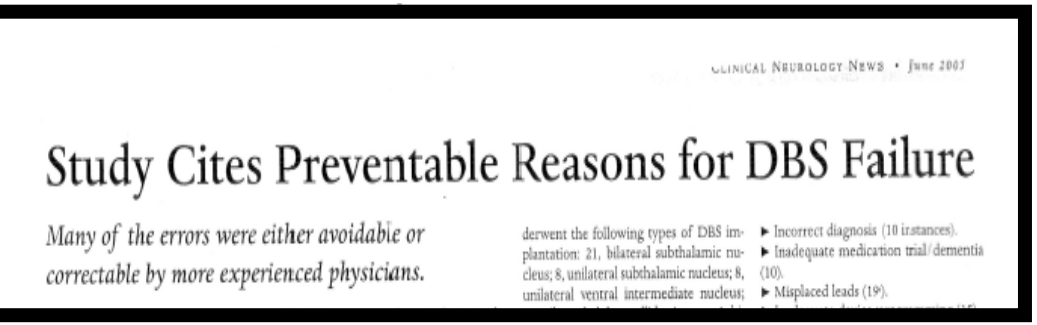
- Minimize complications: Safe surgical technique



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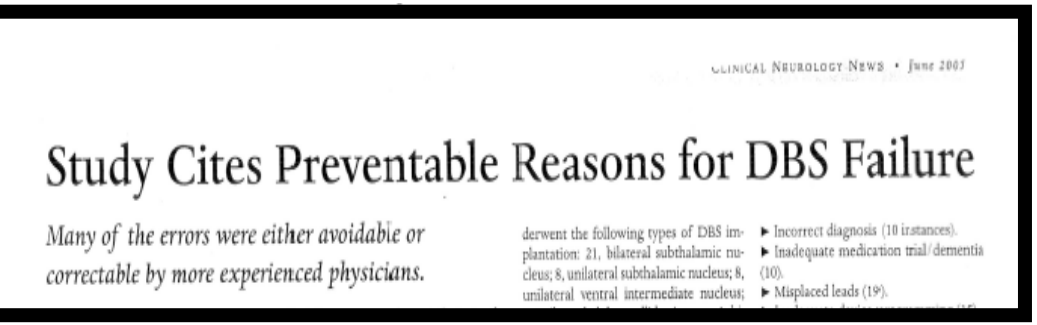
Conclusions

- Experience counts: More experience > better outcomes
- Proper patient selection
- Minimize complications: Safe surgical technique
- Maximize benefit: Accurate electrode placement



CLINICAL NEUROLOGY NEWS • June 2005

Study Cites Preventable Reasons for DBS Failure

Many of the errors were either avoidable or correctable by more experienced physicians.

derwent the following types of DBS implantation: 21, bilateral subthalamic nucleus; 8, unilateral subthalamic nucleus; 8, unilateral ventral intermediate nucleus;

- Incorrect diagnosis (10 instances).
- Inadequate medication trial/dementia (10).
- Misplaced leads (19).

Conclusions

- Experience counts: More experience > better outcomes
- Proper patient selection
- Minimize complications: Safe surgical technique
- Maximize benefit: Accurate electrode placement
- Personalization of therapy based on your goals!

Questions and Answers

Amy Hellman, MD

Parkinson's Disease Symposium 2025

University of Nebraska Medical Center
Nebraska Medicine

Are there any new medications for Parkinson's Disease?

Most recently approved medications

- Onapgo
- Vyalev
- Crexont

Not yet FDA approved but possibly coming soon

- Tavapadon

How many people in Nebraska have Parkinson's Disease

- Over 16,000 people in Nebraska have been diagnosed with PD since 1997

Progression of Parkinson's Disease

- PD is slowly progressive
- The rate of progression varies widely between people
- Life expectancy is reduced, but many live for decades with PD

What do the later stages of Parkinson's Disease look like?

Some of the things we may see include:

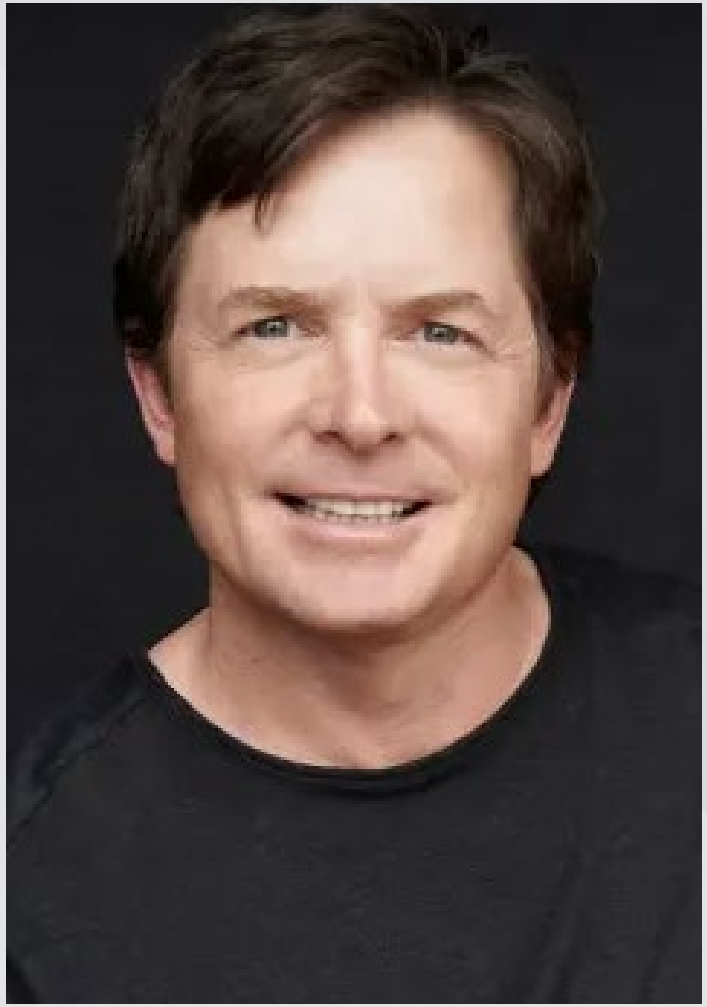
- More severe motor impairment
- Worsening balance
- Swallowing problems
- Cognitive decline
- Worsening non-motor symptoms

How can gait be used to diagnose and monitor PD?

- One piece of the puzzle
- May be improved with medications
- Physical therapy is the best
- Reduce risk of falls

Early Onset Parkinson's Disease

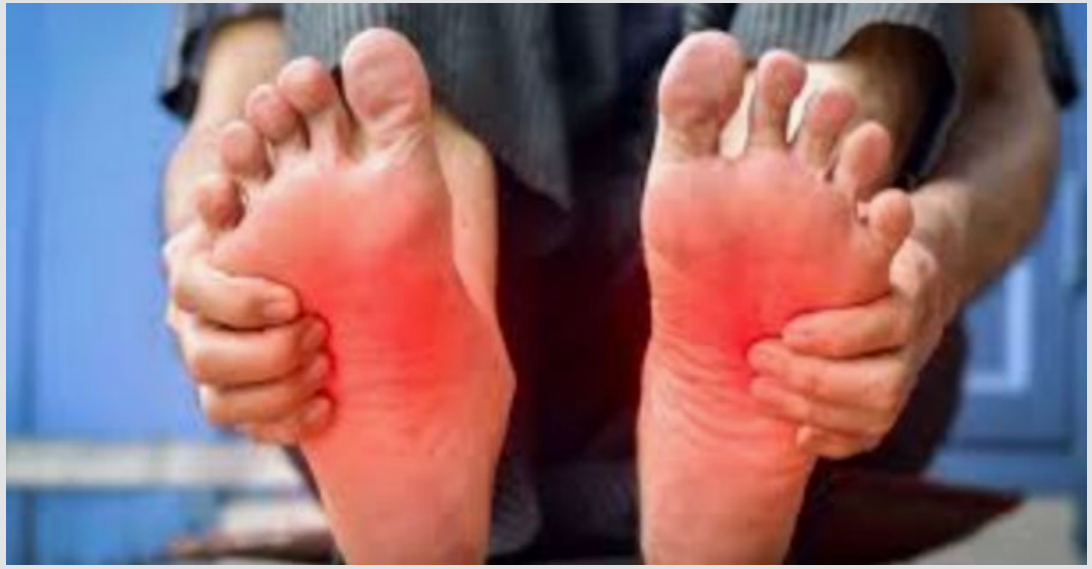
- Before the age of 50
- Symptoms and treatments are the same
- May progress more slowly



My toes have started to lose feeling. Is this normal?

Is progressive neuropathy common in Parkinson's Disease?

- Neuropathy is common in PD



What research is there on microplastics and PD?

Nanoplastics may be an environmental risk factor for PD

- Trigger clumping of alpha-synuclein in test tubes
- Accelerate alpha-synuclein clumping in mouse neurons and brains
- Traces found in brain tissue of people with LBD

What is the latest information on gut health and PD?

- Gut-brain axis
- Gut microbiome
- Role of diet

What can I do to minimize negative effects of PD and keep my lifestyle as normal as possible?

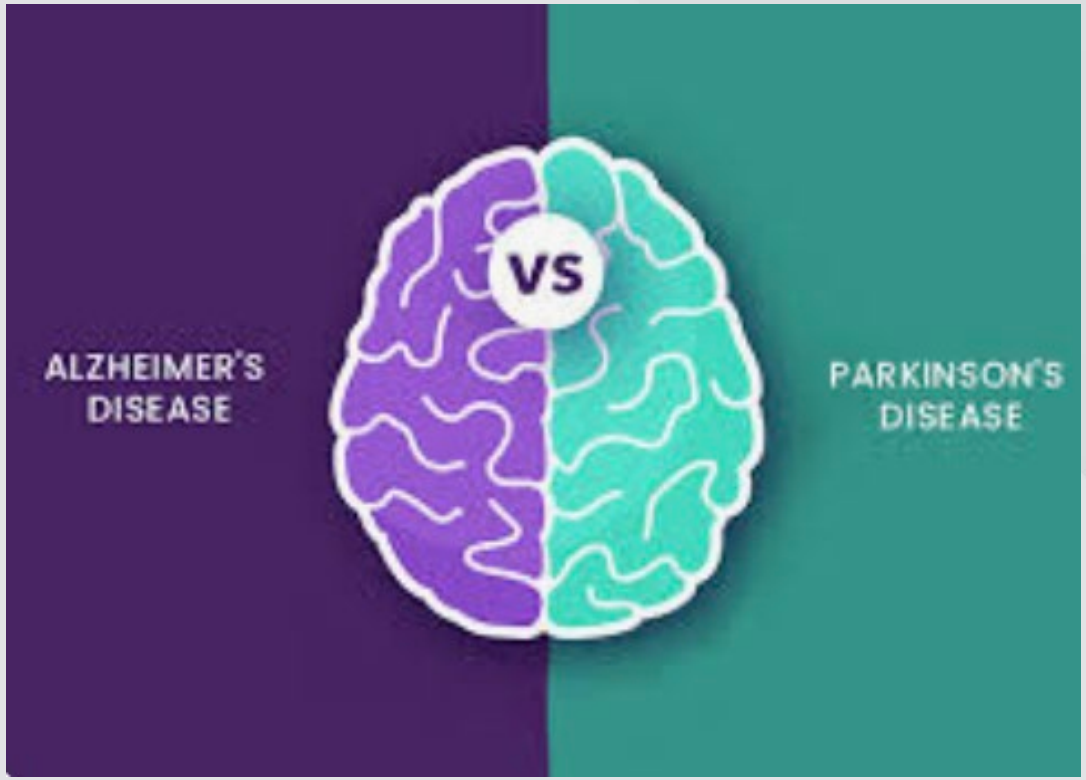
- EXERCISE!!!
- Follow Mediterranean/DASH diet
  - Minimize saturated fats and heavily processed foods
  - Alcohol in moderation for avoid completely
- Get adequate sleep
- Work with your doctors and therapists

Does Parkinson's Disease always lead to dementia?

- Not always
- Risk increases with disease duration

How do Parkinson's and Alzheimer's interact? What are things that will benefit both?

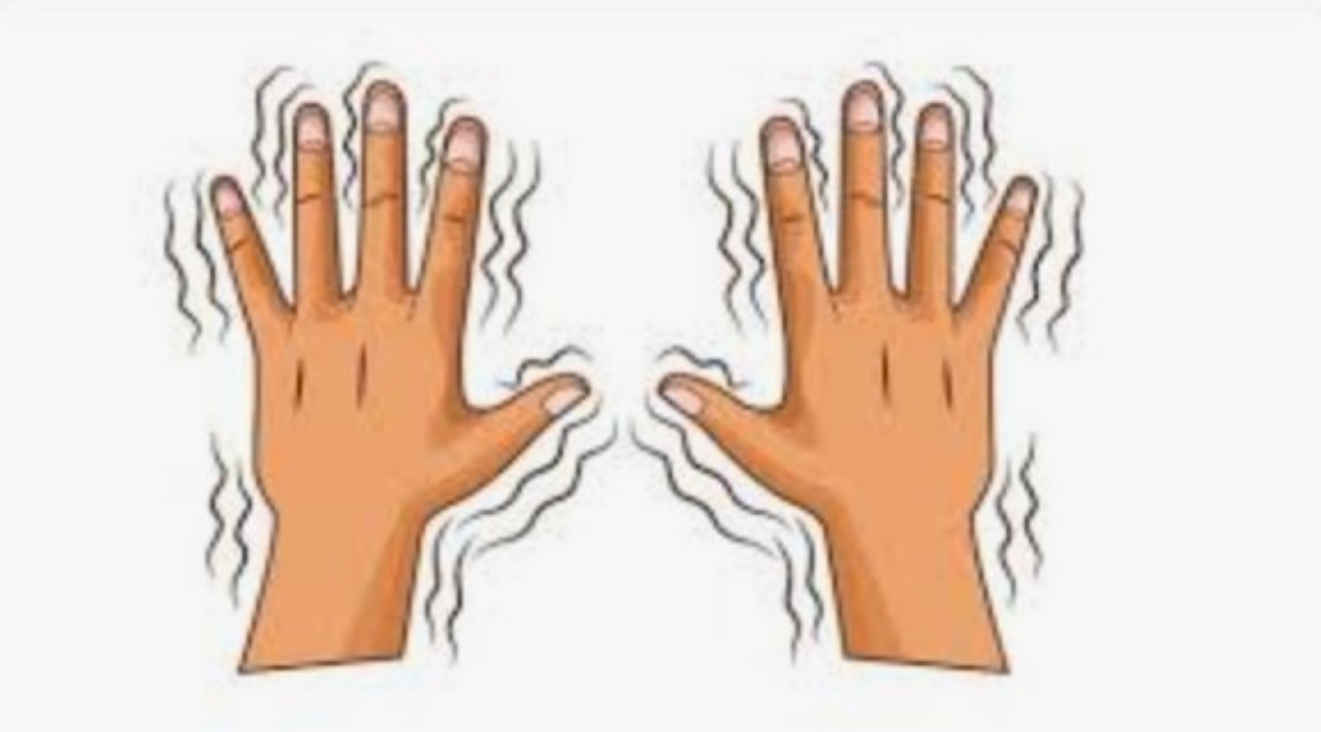
- Different neurodegenerative disease
- Some overlapping symptoms



How does PD fit into the context of other diseases common in seniors such as cardiac or lung issues?

Can levodopa cause tremors?

- No, but it can cause dyskinesias



Should levodopa be taken at bedtime or during waking hours?

- Definitely during waking hours
- Maybe also at bedtime

When is DBS or stem cell treatment most helpful and for how long?

- Stem cells are not currently a treatment for PD
- Deep Brain Stimulation
  - Good response to levodopa
  - Uncontrolled motor fluctuations/dyskinesias
  - Remains effective long term

Focused Ultrasound

What is the most important thing for a caregiver to know?

How to help someone get the help they need?

What is the best way to keep couples together as they experience PD in addition to aging of both spouses?

How can caregivers provide help with reminders to take medications on time?

- Pair medications with habits
- Set up pillboxes
- Automatic pill dispensers
- Smartphone/watch alarms/apps
- Smart speakers

Lower Body Parkinson's

- Vascular parkinsonism – caused by effects of cerebrovascular disease
- Manage risk factors
  - high blood pressure, diabetes, high cholesterol, smoking
- Levodopa less effective
- PT/OT very important

Is there any news about PSP?

University of Nebraska Medical Center

Nebraska Medicine