UF Health
NORMAN FIXEL INSTITUTE FOR NEUROLOGICAL DISEASES

Parkinson's Foundation
CENTER OF EXCELLENCE

On the Horizon: Non-Pharmacologic Advances in Parkinson's Disease and the Multidisciplinary Approach

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ASSISTANT PROFESSOR OF NEUROLOGY

Points of Discussion

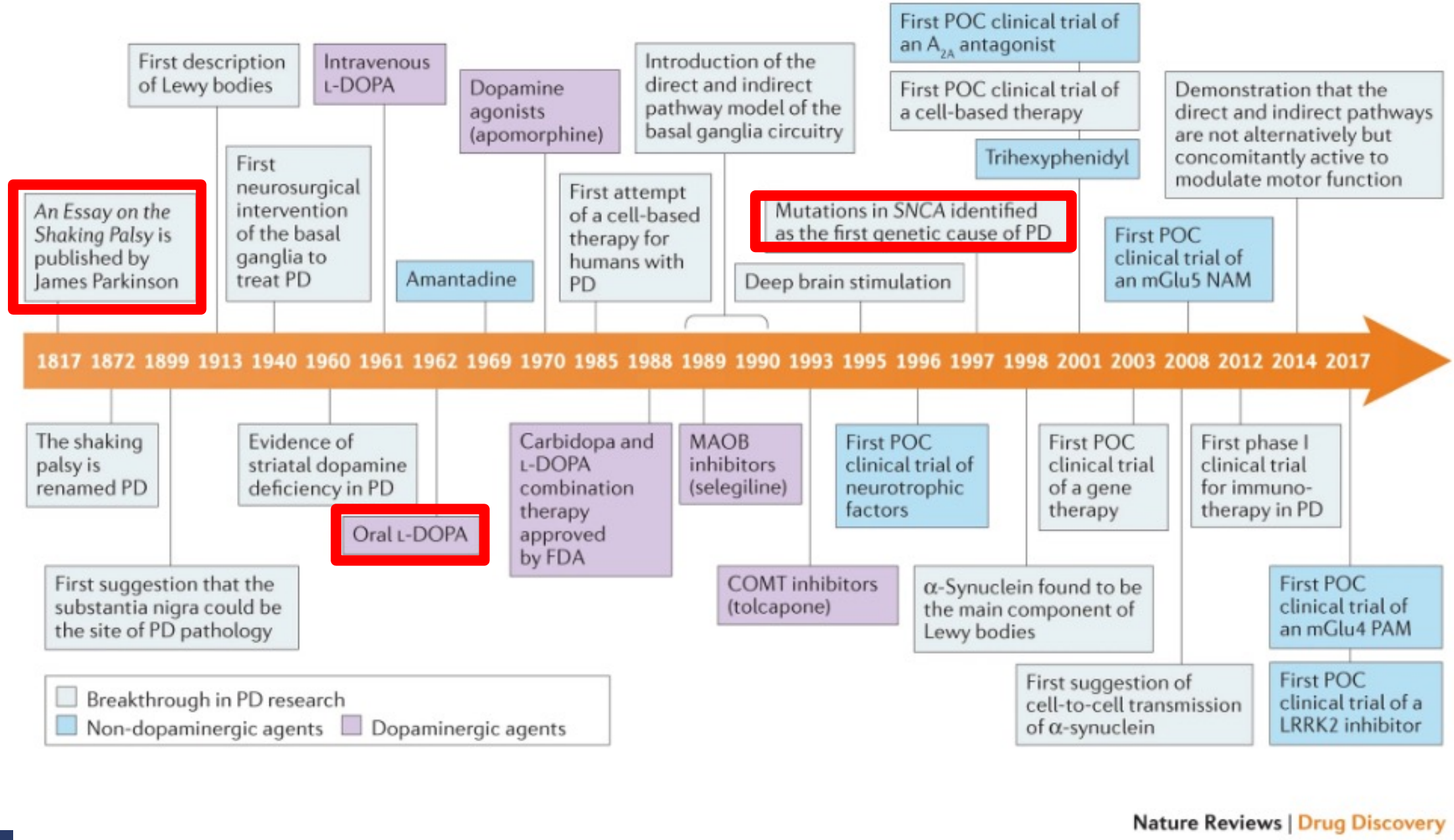
Disclosures

1. What are biomarkers and how are they advancing research and care in Parkinson's Disease
2. What are the advancements in deep brain stimulation and focused ultrasound for Parkinson's Disease
3. The multi-disciplinary approach

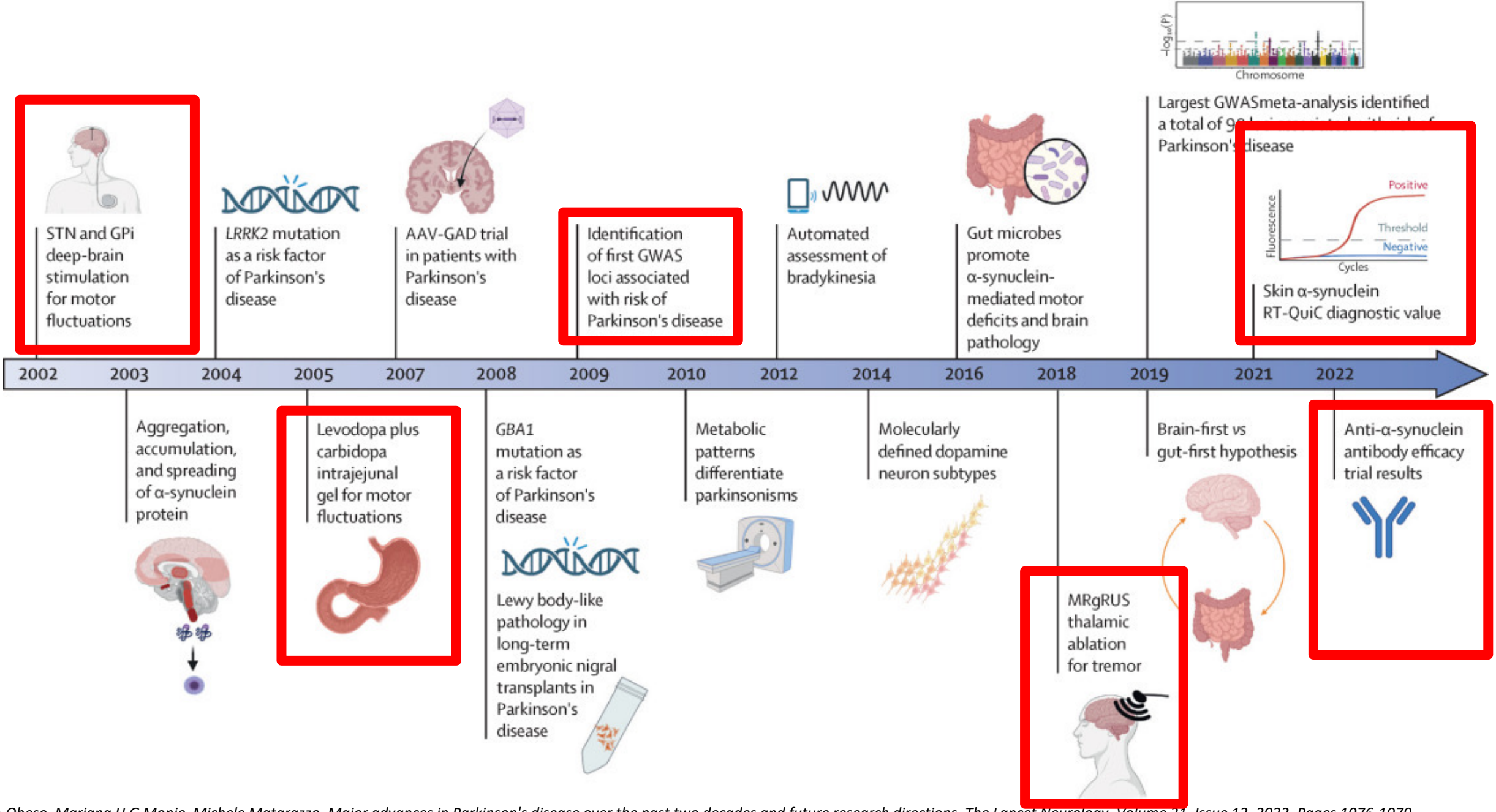
No relevant disclosures to this presentation.

Introduction:

- Parkinson's Disease (PD) is the 2n
  neurodegenerative disorder
  - Affects ~1.2 million in US alone with g
  - ~90,000 people in the US are diagnos
  - ~80,000 people with Parkinson's Disease living in Florida



Hirsch, et al. *Nature Reviews Drug Discovery* (2018).



Jose A Obeso, Mariana H G Monje, Michele Matarazzo, Major advances in Parkinson's disease over the past two decades and future research directions, The Lancet Neurology, Volume 21, Issue 12, 2022, Pages 1076-1079

Points of Discussion

Disclosures

1. What are biomarkers and how are they advancing research and care in Parkinson's Disease
2. Advancements Non-pharmacologic treatment
3. The Multi-disciplinary Approach

Question:

Have you heard of a biomarker?

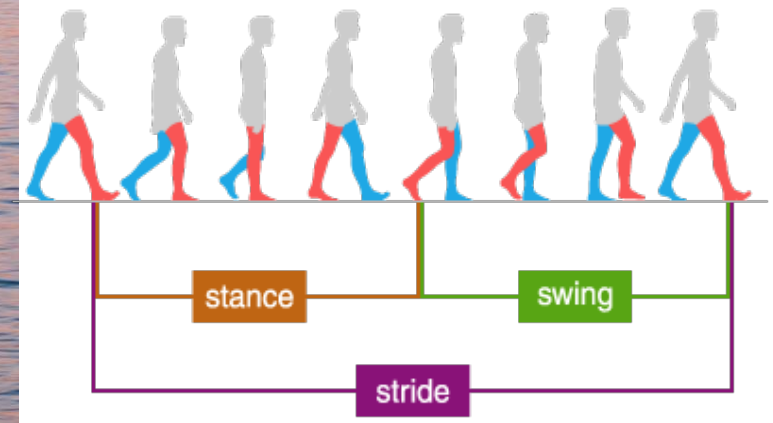
What is a biomarker

- A “biological marker” is a characteristic of the body that can be objectively measured or evaluated AND that provides information about normal biology or a disease process

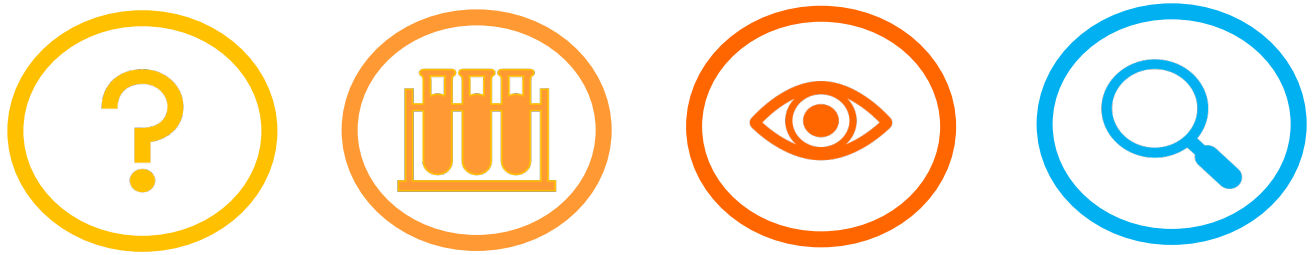
What is a biomarker

Biomarkers include almost anything measurable

- Functional (e.g., gait measures)
- Anatomical (brain or spine imaging)
- Physiological/biochemical (BP, lab tests, tissue pathology, genetics)



Biomarkers - why do they matter?



Risk Diagnostic Prognostic Monitoring

FDA-NIH, 2016

What is a biomarker

Biomarkers include almost anything measurable

- Functional (e.g., gait measures)
- Physiological/biochemical (BP, lab tests, tissue pathology)

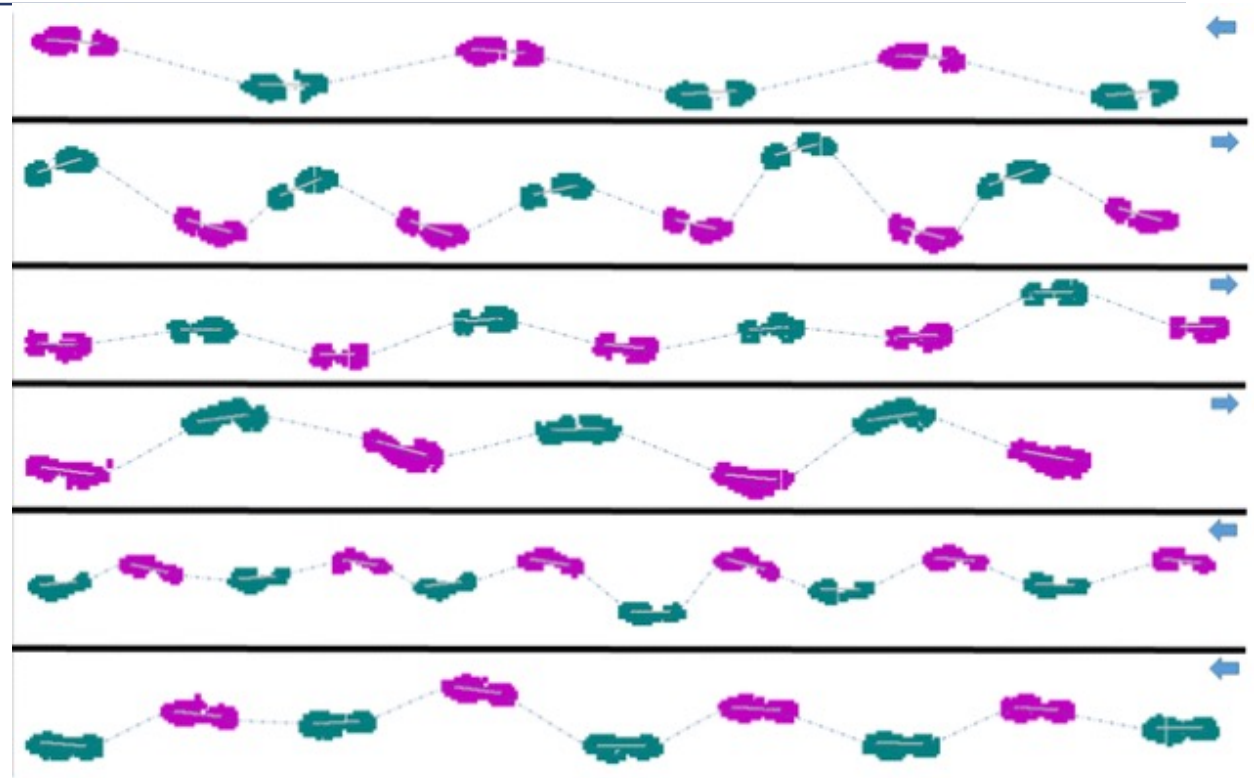
Functional/Clinical biomarkers

Clinical

Objective measures of:

- Gait
- Eye movements
- Acceleration, tremor, dyskinesia
- Facial expression
- Vocal quality

GaitRite

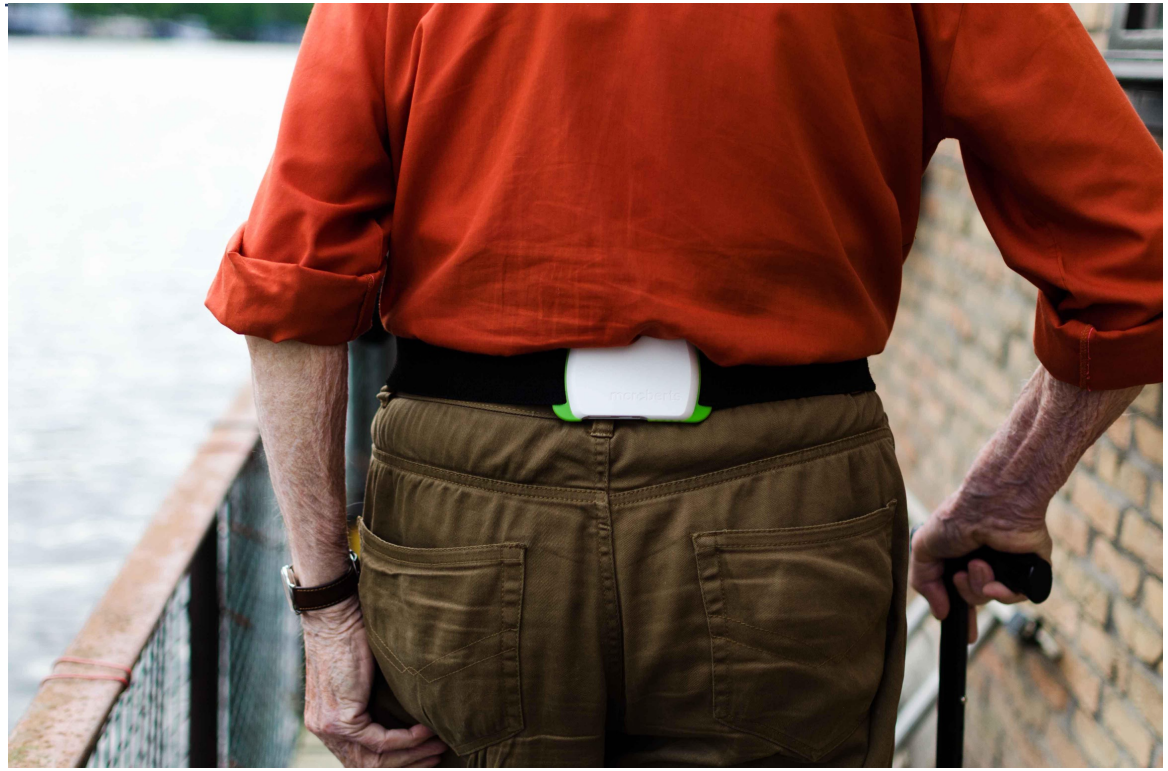


Gimmon, Yoav & Millar, Jennifer & Pak, Rebecca & Liu, Elizabeth & Schubert, Michael. (2017). Central not peripheral vestibular processing impairs gait coordination. Experimental Brain Research. 235.

Detecting Parkinson's Disease from Wrist-Worn Accelerometry in the U.K. Biobank

James R. Williamson,[1,*] Brian Telfer,[1] Riley Mullany,[1] and Karl E. Friedl[2,3]

Antonio Suppa, Academic Editor



Moreau, C., Rouaud, T., Grabli, D. *et al.* Overview on wearable sensors for the management of Parkinson's disease. *npj Parkinsons Dis.* **9**, 153 (2023).

Machine Learning in the Parkinson's disease smartwatch (PADS) dataset

Julian Varghese, Alexander Brenner, Michael Fujarski, Catharina Marie van Alen, Lucas Plagwitz & Tobias Warnecke

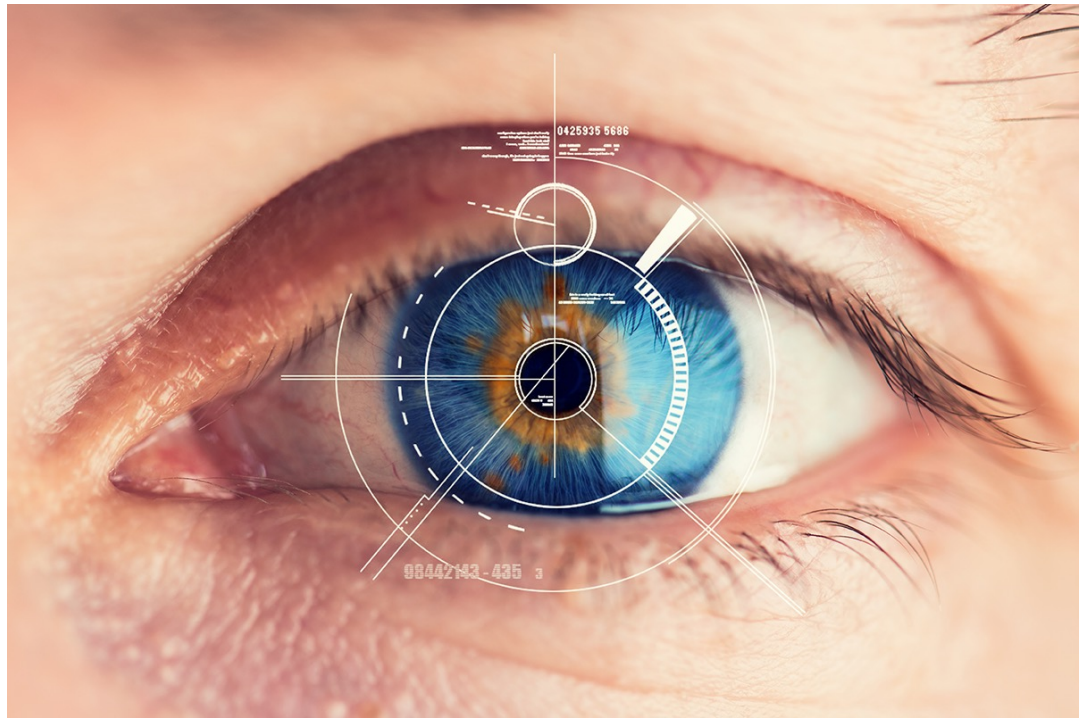
npj Parkinson's Disease **10**, Article number: 9 (2024) | Cite this article

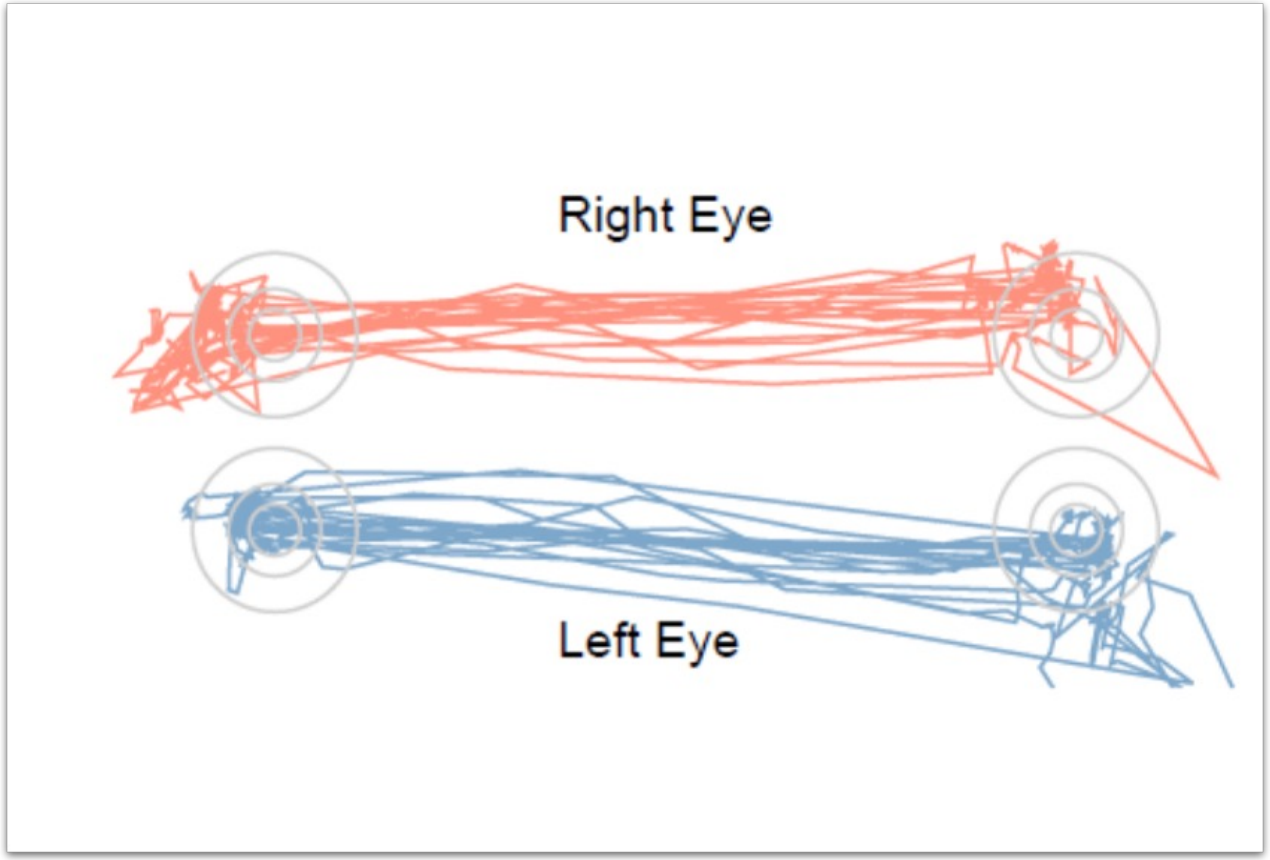
ABOUT

The WATCH-PD study compares clinical assessments with new digital measures including an Apple Watch, an iPhone, and a full-body sensor system.

LEARN MORE

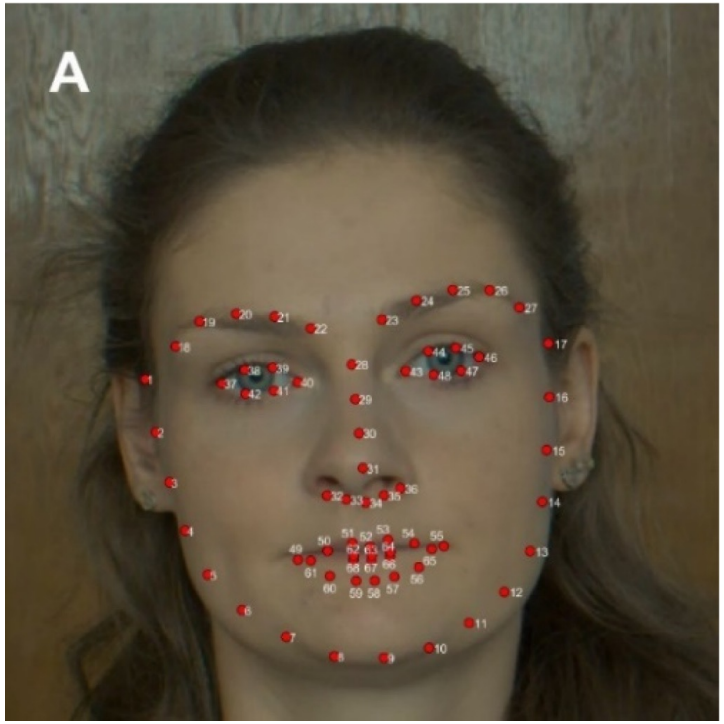
Eye Tracking as a Biomarker for Manifest and Prodromal Parkinson's Disease

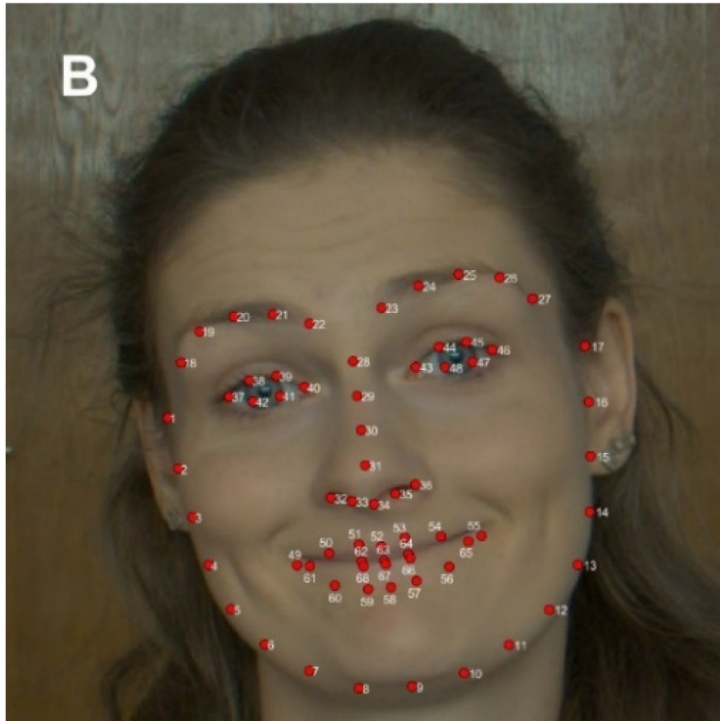


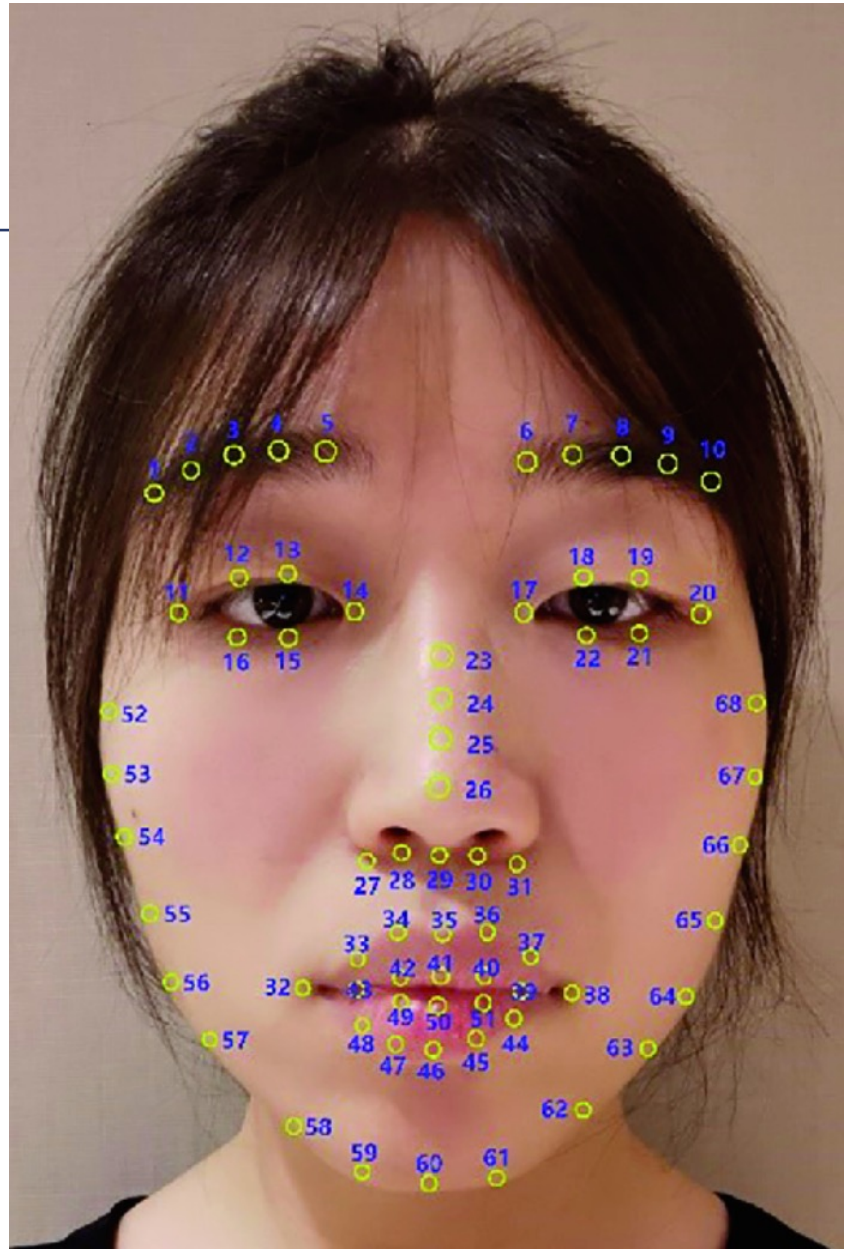


https://righteye.com/
https://www.michaeljfox.org/grant/eye-tracking-biomarker-manifest-and-prodromal-parkinsons-disease

Facial Expressivity



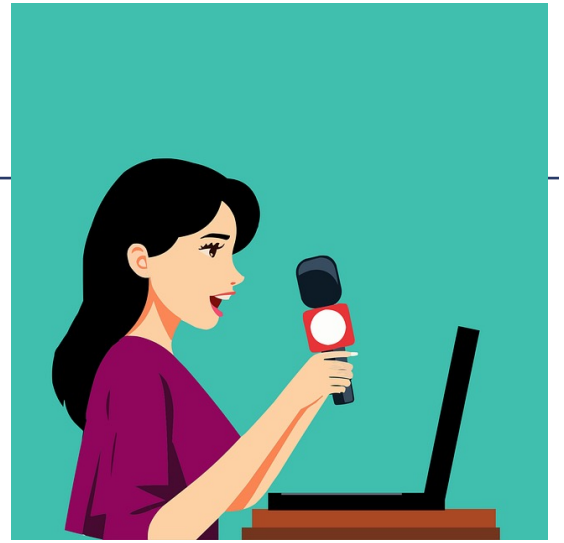




Jakubowski, J.; Potulska-Chromik, A.; Białek, K.; Nojszewska, M.; Kostera-Pruszczyk, A. A Study on the Possible Diagnosis of Parkinson's Disease on the Basis of Facial Image Analysis. *Electronics* **2021**, *10*, 2832.

Ge, Su & Lin, Bo & Yin, Jianwei & Luo, Wei & Xu, Renjun & Xu, Jie & Dong, Kexiong. (2021). Detection of hypomimia in patients with Parkinson's disease via smile videos. Annals of Translational Medicine

Vocal Qualities



Voice in Parkinson's Disease: A Machine Learning Study

Antonio Suppa [1 2], Giovanni Costantini [3], Francesco Asci [2], Pietro Di Leo [3], Mohammad Sami Al-Wardat [4], Giulia Di Lazzaro [5], Simona Scalise [6], Antonio Pisani [7 8], Giovanni Saggio [3]

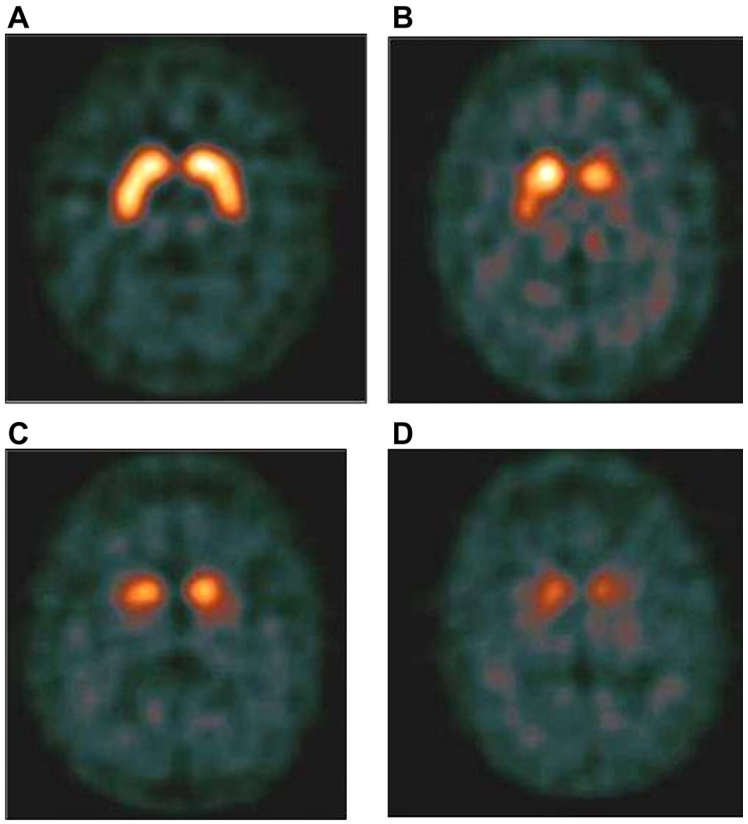
Multilingual evaluation of interpretable biomarkers to represent language and speech patterns in Parkinson's disease

Anna Favaro,[1,*] Laureano Moro-Velázquez, [1] Ankur Butala, [2,3] Chelsie Motley, [2] Tianyu Cao, [1] Robert David Stevens, [4] Jesús Villalba, [1] and Najim Dehak [1]

What is a biomarker

Biomarkers include almost anything measurable

- Functional (e.g., gait measures)
- Physiological/biochemical (BP, lab tests, tissue pathology)



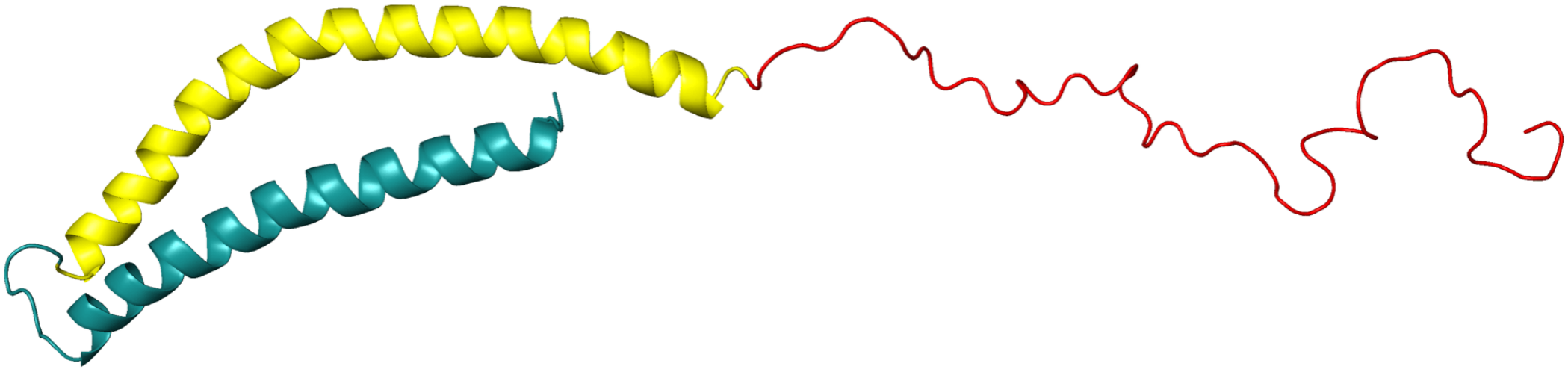
Dopamine Active Transporter Scan (DAT SCAN)

- FDA approved in 2011 “to **assist in the evaluation** of adult patients with suspected Parkinsonian syndromes (PS). In these patients, **DATscan may be used to help differentiate essential tremor from tremor due to PS**.”
- “tags” spots in the brain where dopamine attaches
- Tells information about the function of the brain
- Will not differentiated between the many parkinsonian syndromes

- 95% sensitive for differentiating PD from ET and healthy controls **
- 86.2% sensitive in differentiating PD from drug induced parkinsonism **

Question:

Who has heard about a protein called alpha synuclein (α- synuclein)?



Alpha-synuclein (α- synuclein)

- Alpha-synuclein misfolding leads to loss of dopamine cells in PD
- Abnormal alpha-synuclein in:
  - Parkinson's Disease
  - Multiple system atrophy
  - Lewy body dementia
  - Pure Autonomic Failure

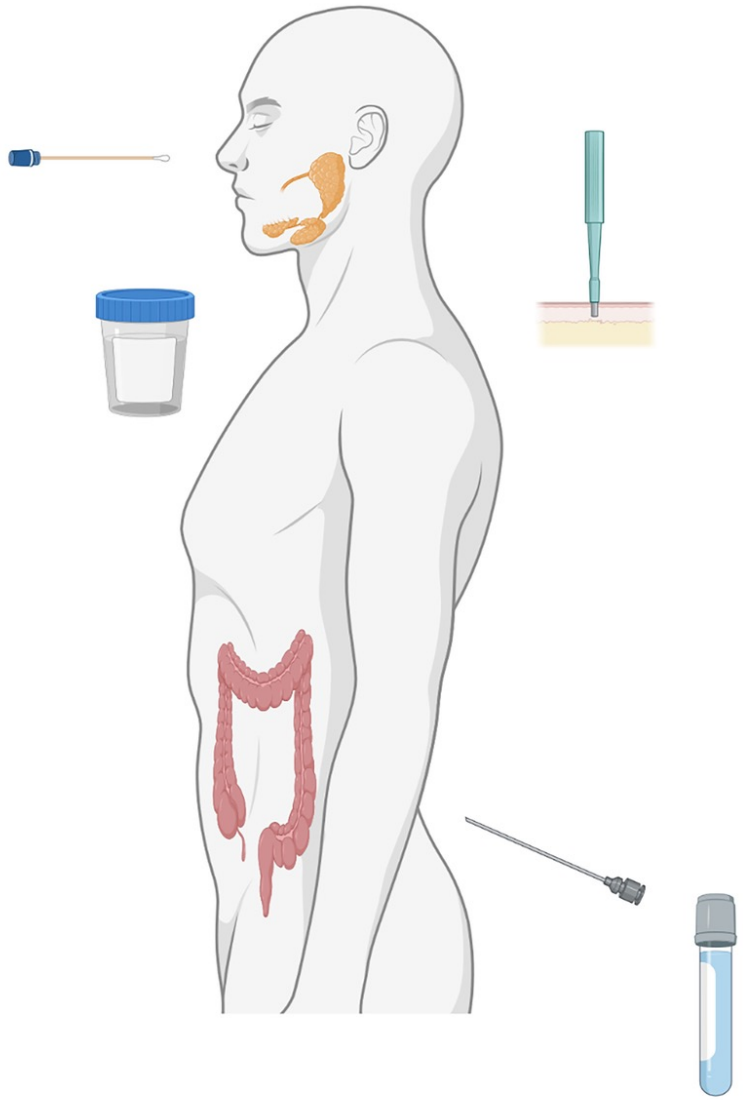
http://www.urmc.rochester.edu/neuroslides/slide199.html

Olfactory Mucosa

Submandibular Gland

Saliva

Colon

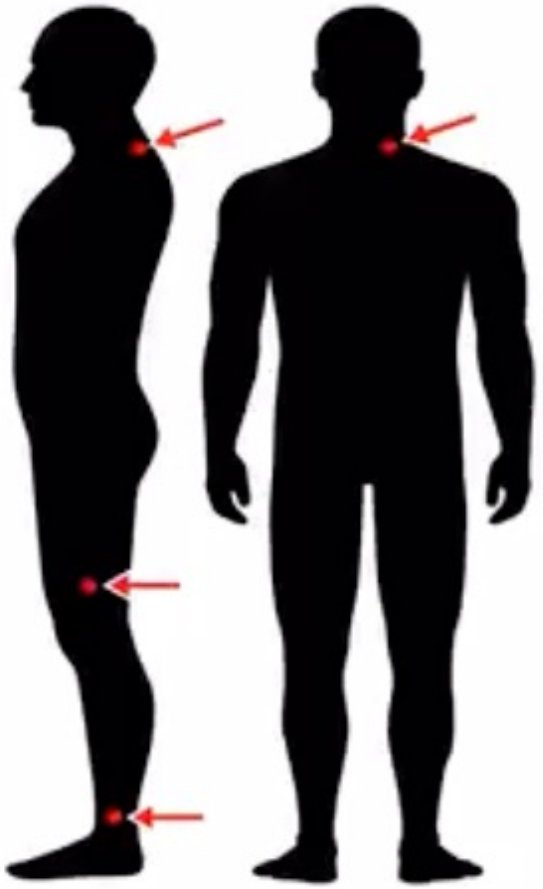


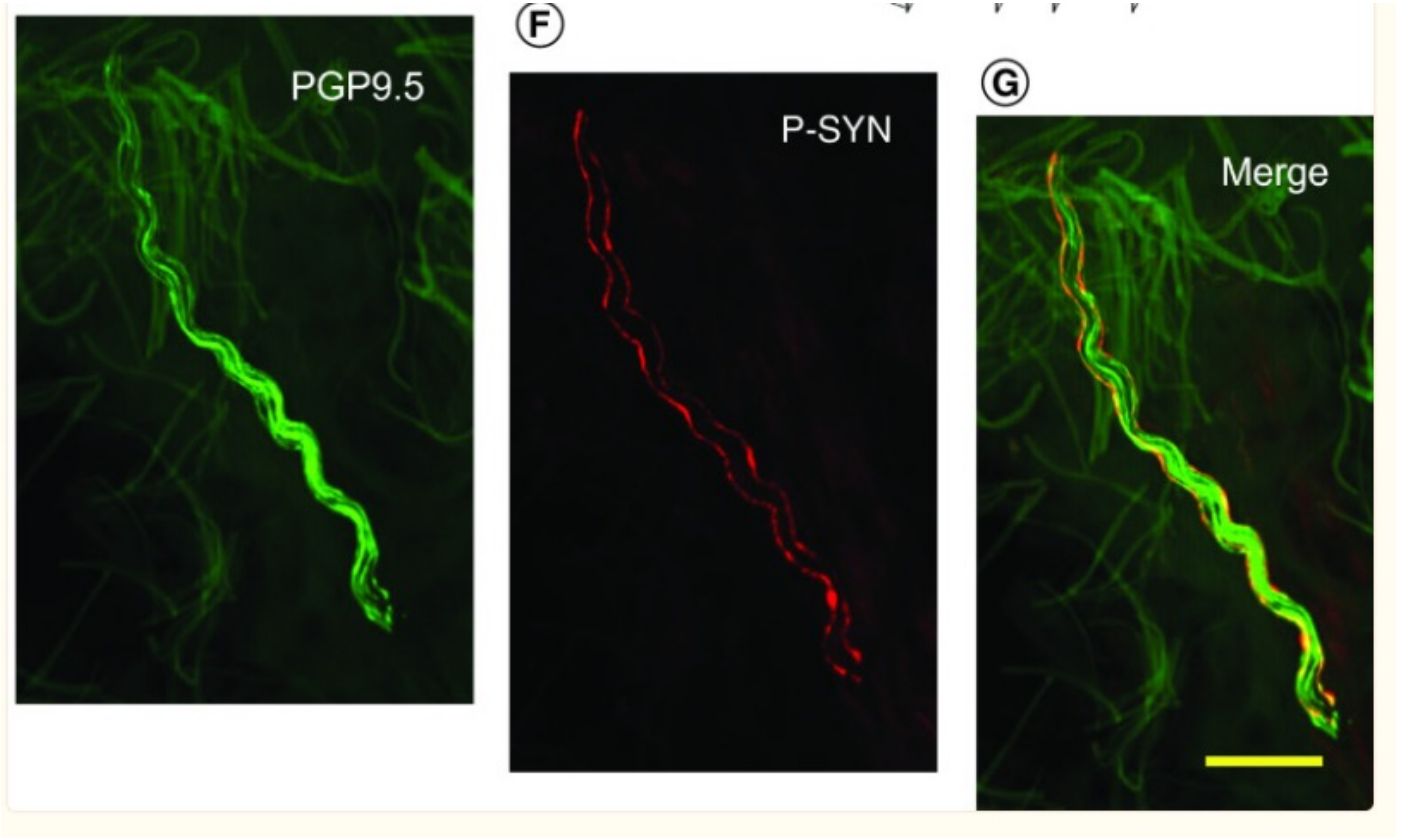
Skin

CSF (Cerebrospinal fluid)

Coughlin, D.G., Irwin, D.J. Fluid and Biopsy Based Biomarkers in Parkinson's Disease. *Neurotherapeutics* **20**, 932–954 (2023)

Skin Biopsy





CND LifeSciences

Skin Biopsy

- Syn-One study included 428 people in total—108 with PD, 69 with MSA, 67 with DLB, 33 with PAF, and 151 healthy controls
- It is available clinically

Diagnosis	Sensitivity	Specificity	Accuracy
Synucleinopathy	**95.5%**	**96.7%**	**95.9%**
PD	92.7%	96.7%	94.9%
MSA	98.2%	96.7%	97.1%
DLB	96.0%	96.7%	96.5%
PAF	100.0%	96.7%	97.2%

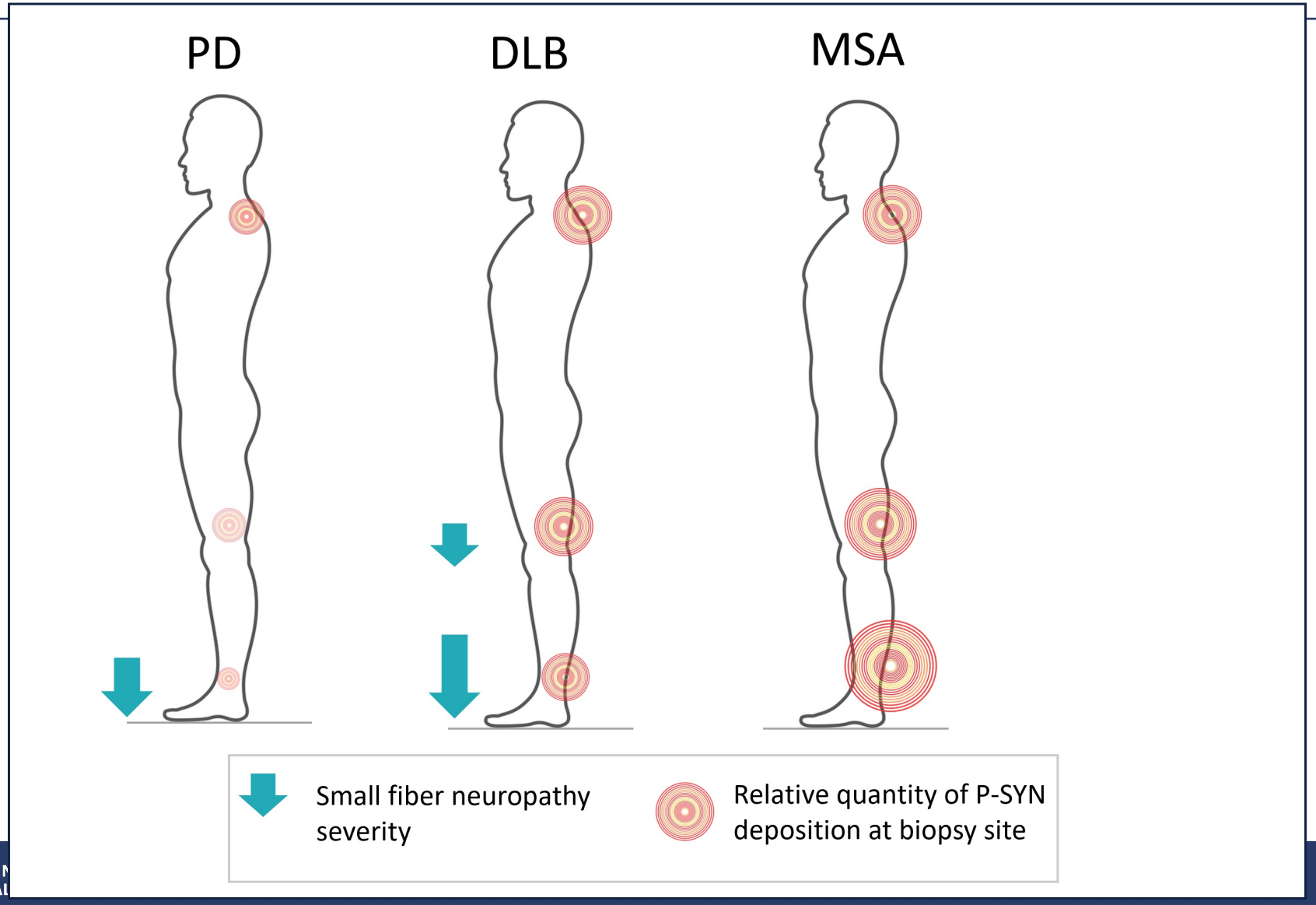
	Grade 1	Grade 2	Grade 3
Adverse events	0.4%*	0%	0%

*minor bleeding from biopsy site

CND LifeSciences

Cutaneous α-Synuclein Signatures in Patients With Multiple System Atrophy and Parkinson Disease

Christopher Gibbons, MD, MMSc,* Ningshan Wang, PhD,* Sharika Rajan, MD, Drew Kern, MD, Jose-Alberto Palma, Horacio Kaufmann, MD, and Roy Freeman, MD



Do I need a skin biopsy or a DAT scan?

- If you meet the criteria for Parkinson's Disease diagnosis and respond to dopaminergic therapy, in most cases further testing isn't needed

Do I need a skin biopsy or a DAT scan?

- If you have been diagnosed with PD and after many years you have symptoms that do not respond as well to dopamine, you do not need skin biopsy or DAT scan

Do I need a skin biopsy or a DAT scan?

- Consider if your team is having a hard time telling if you have Parkinsonism or Essential tremor

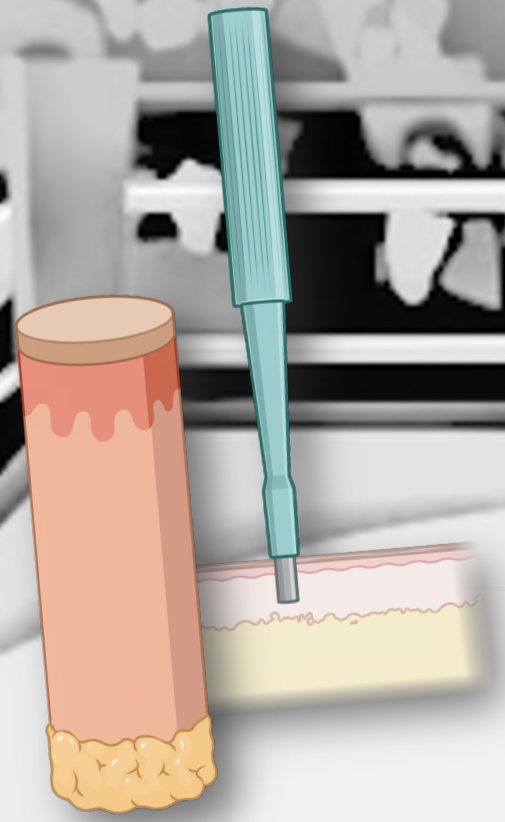
Do I need a skin biopsy or a DAT scan?

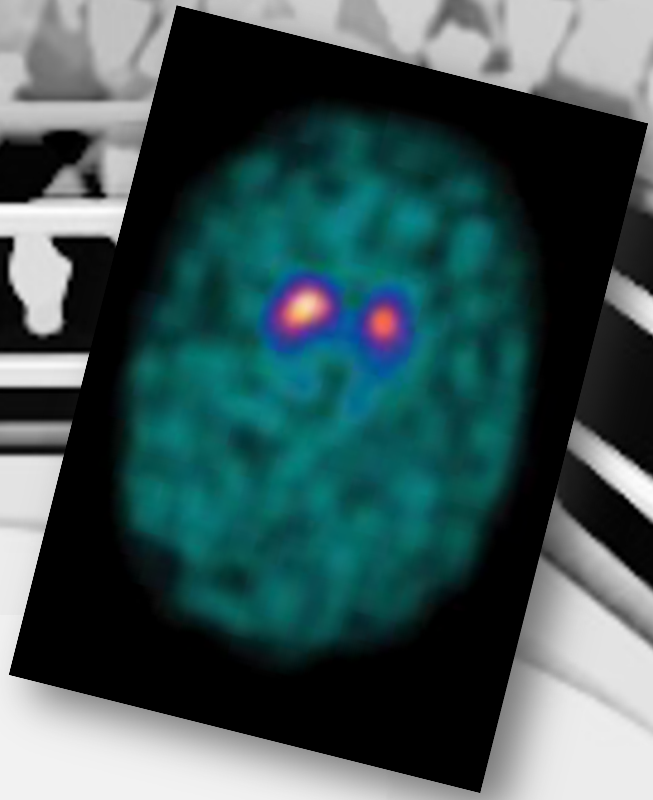
- Consider if your team is trying to determine if you have drug induced Parkinsonism

Do I need a skin biopsy or a DAT scan?

- If you have atypical symptoms and your doctors need help determining if you have a Parkinsonian disorder

Skin Biopsy vs DAT Scan

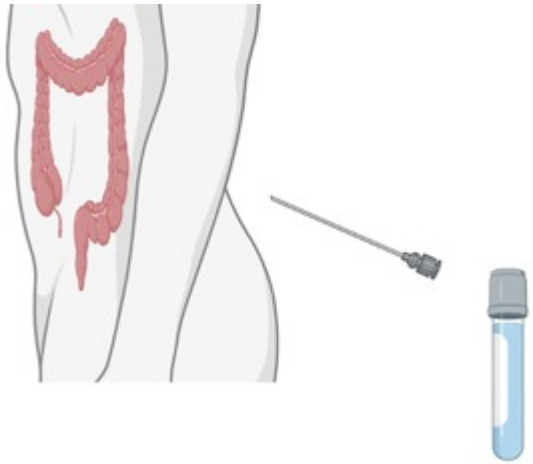




	DaT-Scan	Skin Biopsy
Time for the exam	4-5 hours	20-30 minutes
Medication that needs to be stopped before	Buproprion Stimulants Some antidepressants	Anticoagulants
Time to get the results	A few days	A few weeks
Can help with diagnosis of atypical disorders?	No	Maybe ?
Sensitivity (compared to normal controls)	95% (CAVEAT*)	92.7%
Can help in prodromal PD ?	Maybe	Not enough data

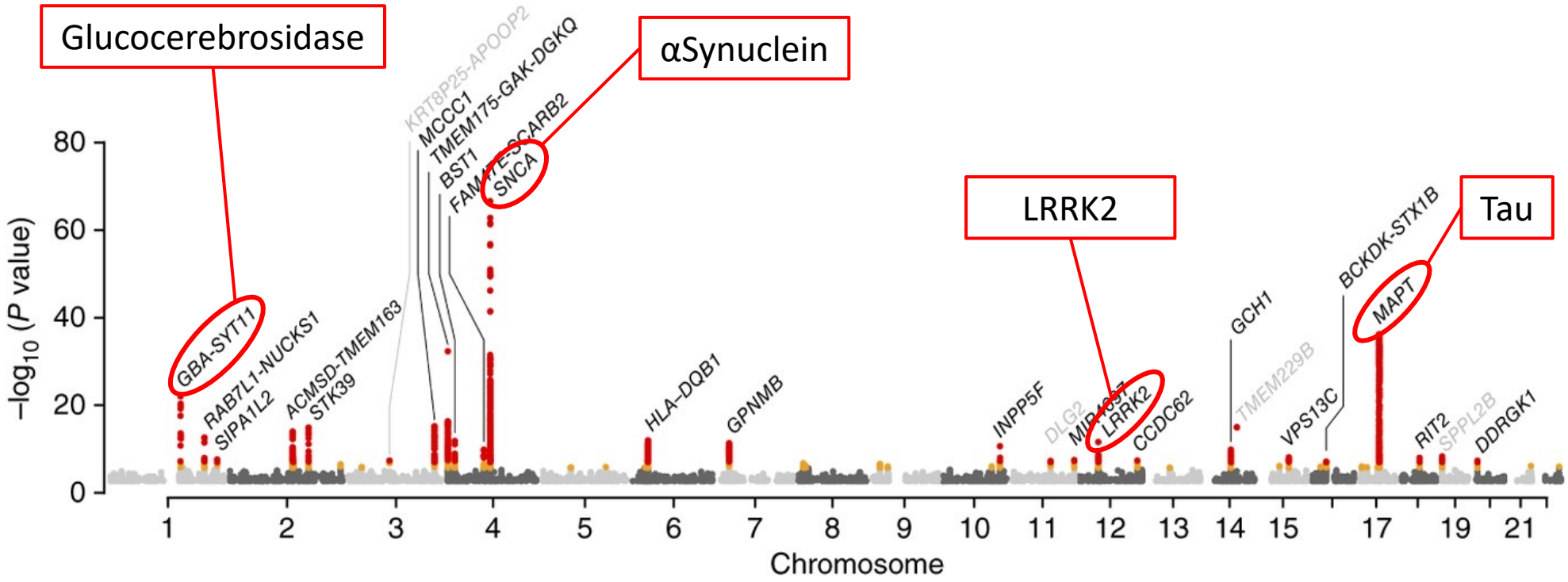
Cerebrospinal Fluid (CSF) Markers

- Alpha-Synuclein seeding amplification assay (SAA) differentiates people with PD from healthy controls, 98.6%
- Was able to identify early Parkinson's
- May eventually be able to help differentiate between PD and MSA
- Currently alpha-synuclein CSF tests are research based only
- CSF biomarkers to help diagnose Alzheimer’s Disease now available



Genetics and PD

nature genetics

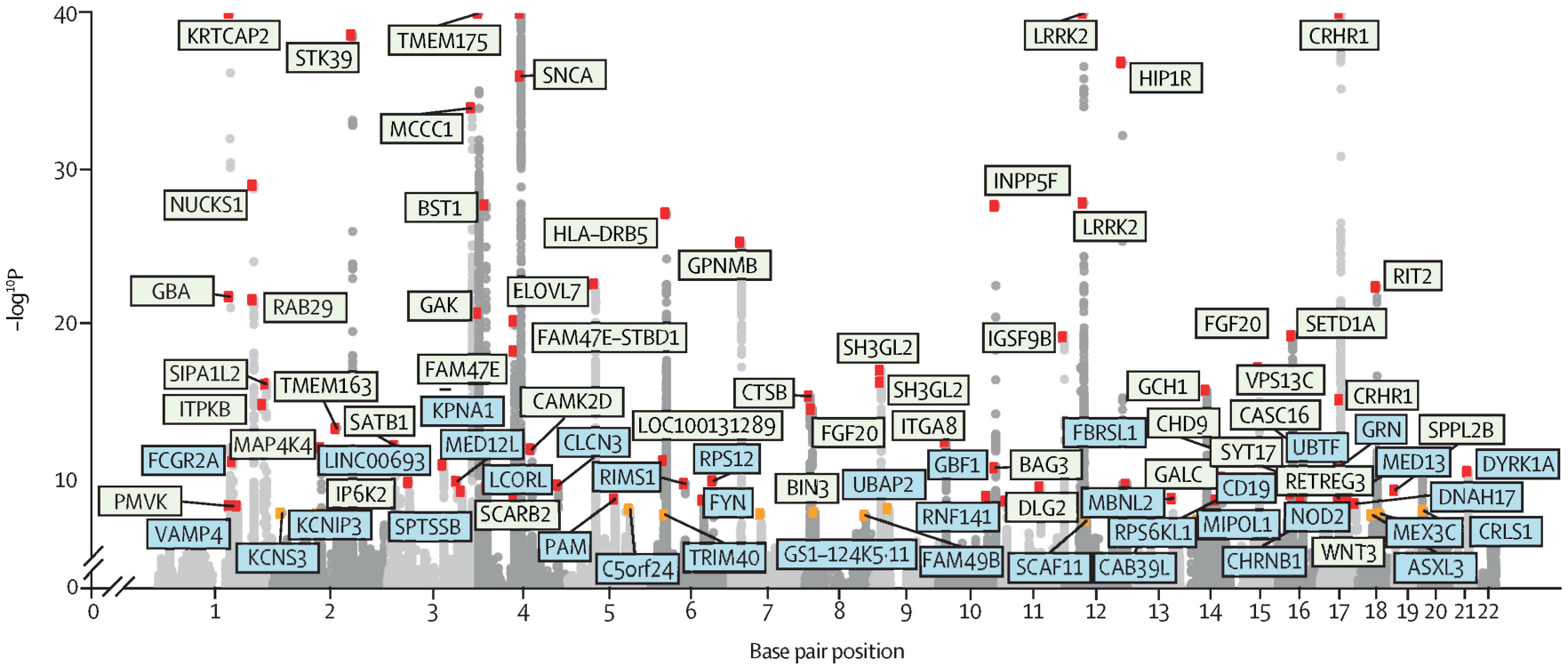


Nalls M, et al. *Nat Genet* **46**, 989–993 (2014). https://doi.org/10.1038/ng.3043

Mov Disord. 2020 Nov; 35(11): 2056–2067.
Published online 2020 Aug 31. doi: 10.1002/mds.28197
PMCID: PMC7754106
PMID: 32864809

The Parkinson's Disease Genome-Wide Association Study Locus Browser

90 independent genome-wide significant association signals identified



The Lancet Neurology 2019 181091-1102DOI: (10.1016/S1474-4422(19)30320-5)

New genetic testing

PD GENEration

National initiative offering **free** genetic testing for clinically relevant PD-related genes and genetic counseling at no cost for individuals with confirmed diagnosis of PD

Participation at Parkinson Foundation Centers of Excellence, Parkinson Study Group sites, or from home through telemedicine visit

For more info: contact Genetics@Parkinson.org or visit Parkinson.org/PDGENEration.

Parkinson's Foundation
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Parkinson's Progression Markers Initiative

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Who may be eligible to participate?

Participants must be at least 30 years of age.

- People with Parkinson's who have been diagnosed within the last 2 years and are not currently taking standard PD medications

- First-degree family members (parent, child, sibling) of a person with Parkinson's

- People with risk factors for the development of PD (known genetic mutation, loss of smell, history of physically acting out dreams during sleep, and others)

- People without Parkinson's and no known risk to act as a comparison group

The study covers the cost of study-related travel, and pays a set amount for each visit to compensate for time and completion of study-related procedures.

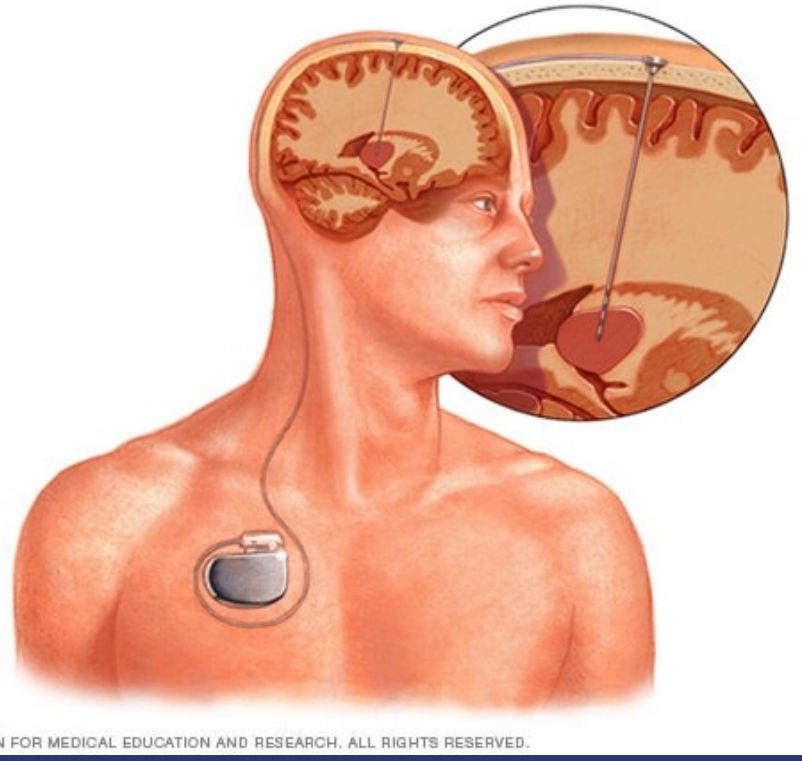
Points of Discussion

Disclosures

1. What are biomarkers and how are they advancing research and care in Parkinson's Disease
2. Advancements Non-pharmacologic treatment
3. The Multi-disciplinary Approach

Deep Brain Stimulation (DBS) and Magnetic Resonance guided Focused Ultrasounds (MRgFUS)

OVERVIEW



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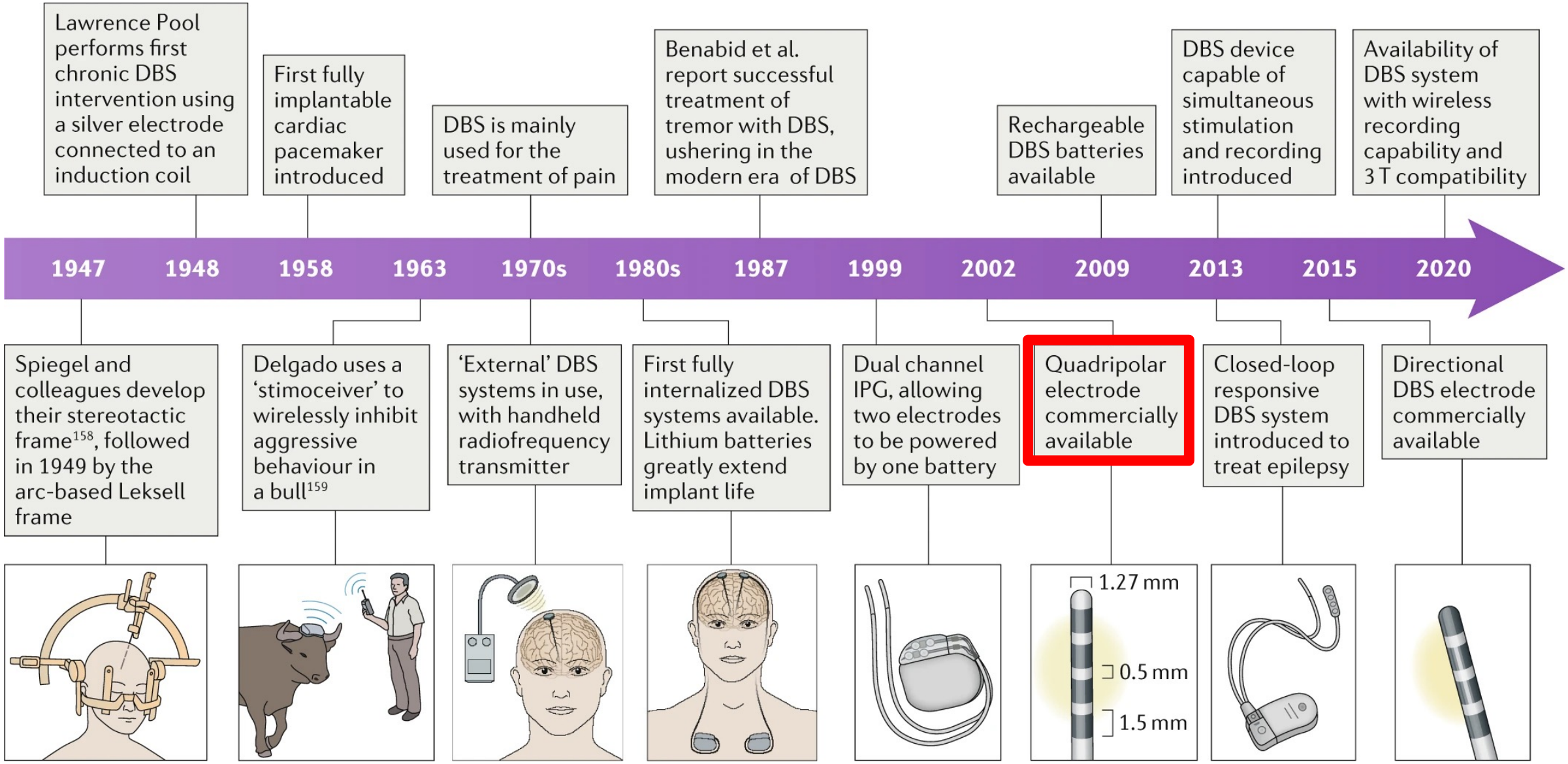
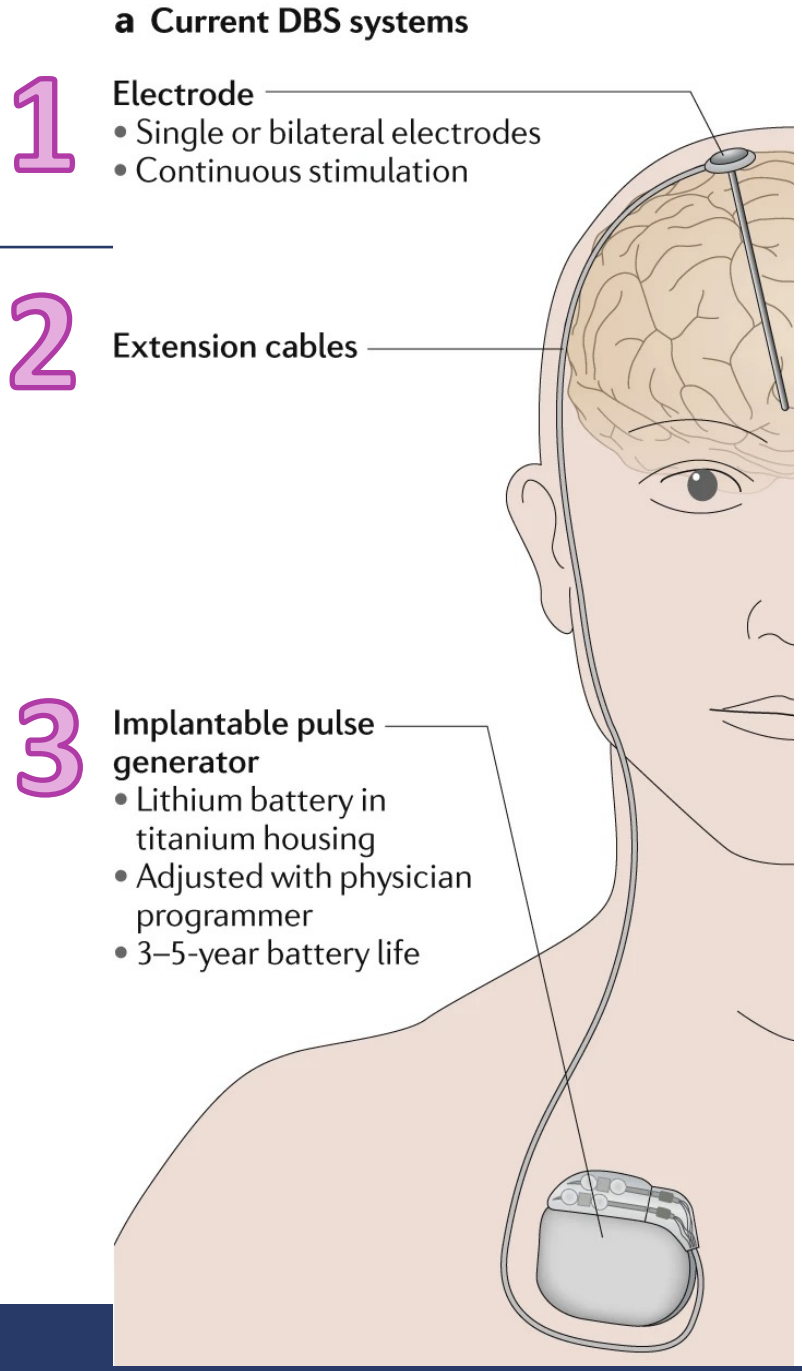
Absen	Deep Brain Stimulation	MRg Focused Ultrasound
Non-invasive	✗	✓
Tremor Control	✓	✓
Bradykinesia, dyskinesia, rigidity	✓	✓
Both sides of the brain	✓	✗
Adjustable	✓	✗
No frequent follow ups required	✗	✓
Not everyone is a good candidate	✓	✓
Covered by Medicare in Florida (for PD)	✓	✗



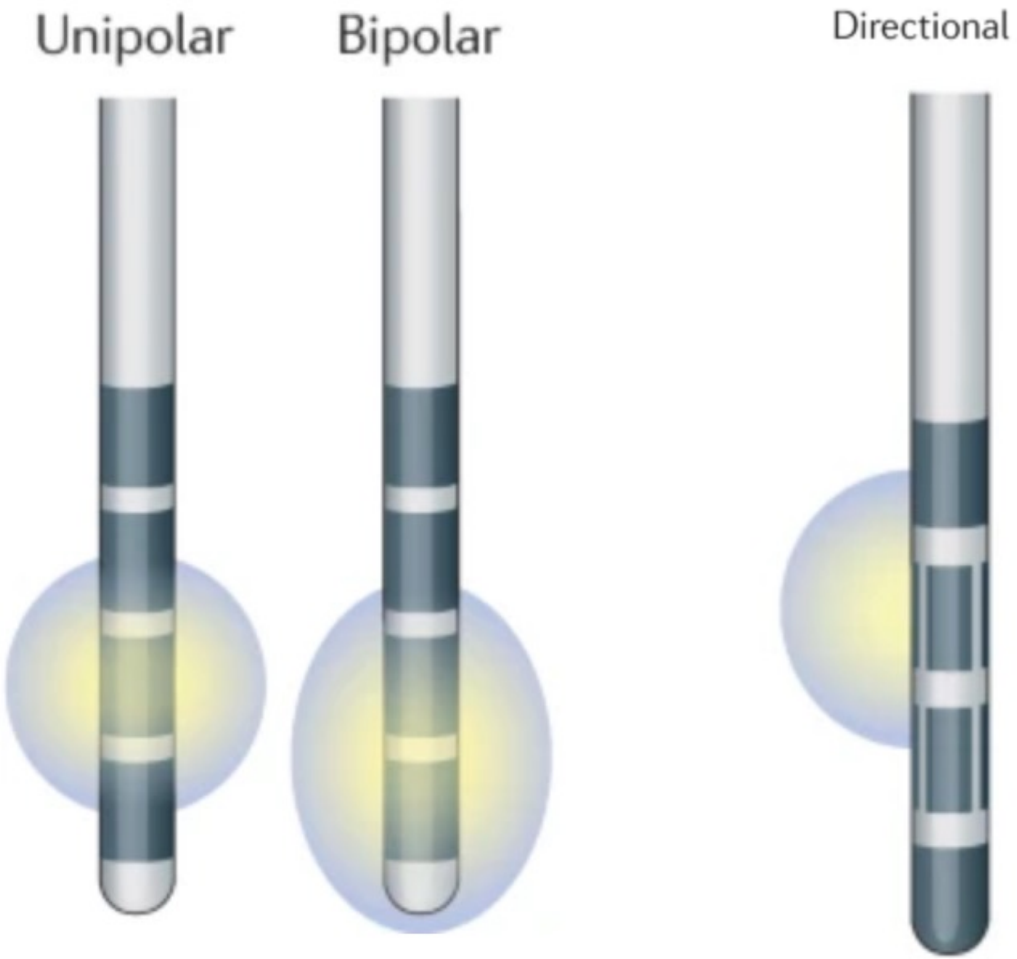
Krauss, J.K., et al. *Nat Rev Neurol 17, 75–87 (2021).*

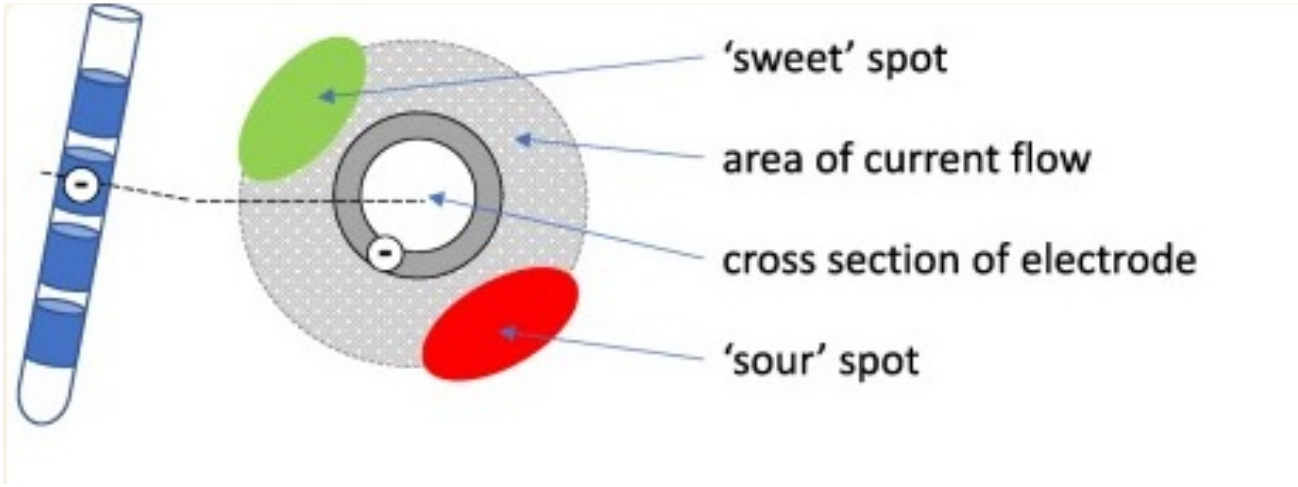
Current Deep Brain Stimulation



Krauss JK, et al.. Nat Rev Neurol 17, 75–87 (2021).

DBS advancements: Electrode configuration





DBS advancements: Implantable pulse generator

Smaller/thinner

Longer battery life

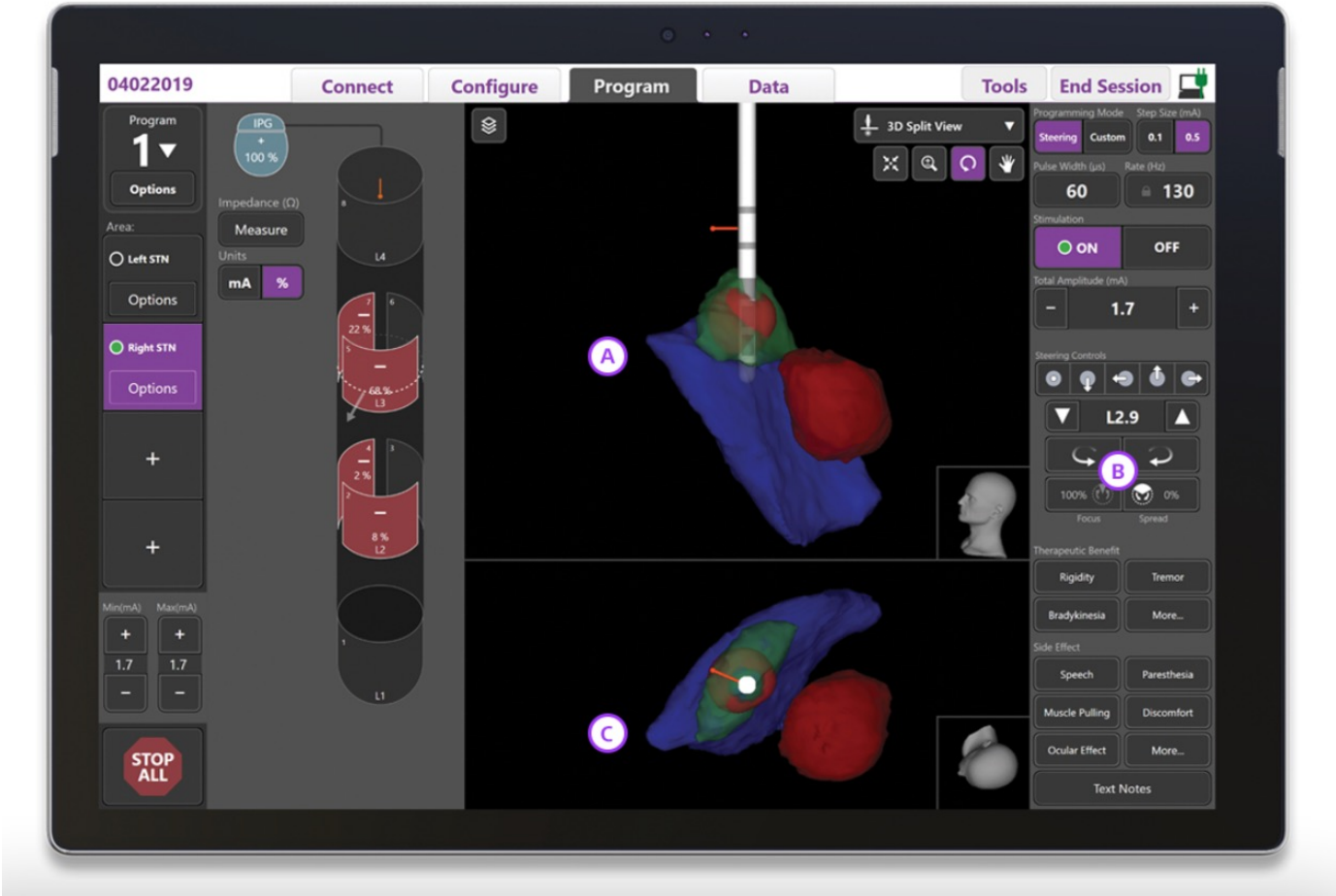
Rechargeable options

MRI Conditional

DBS advancements: Image guided programming

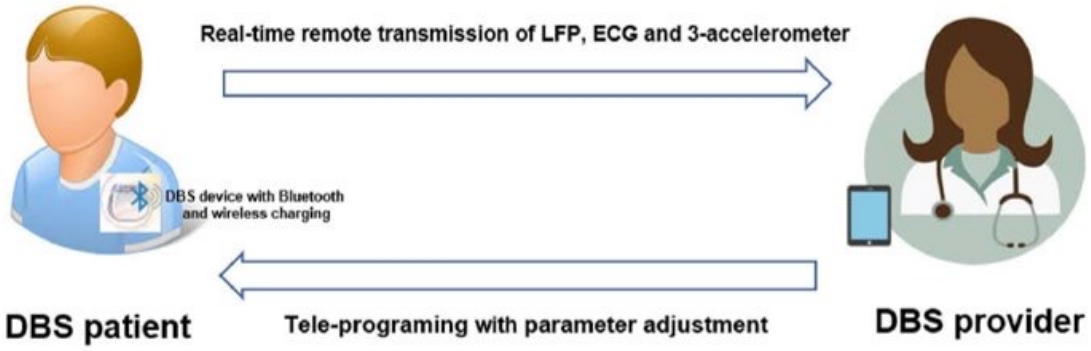
STIMVIEW XT by Boston Scientific

integrates patient's imaging information + programming information to allow the clinicians to see where they are delivering the stimulation

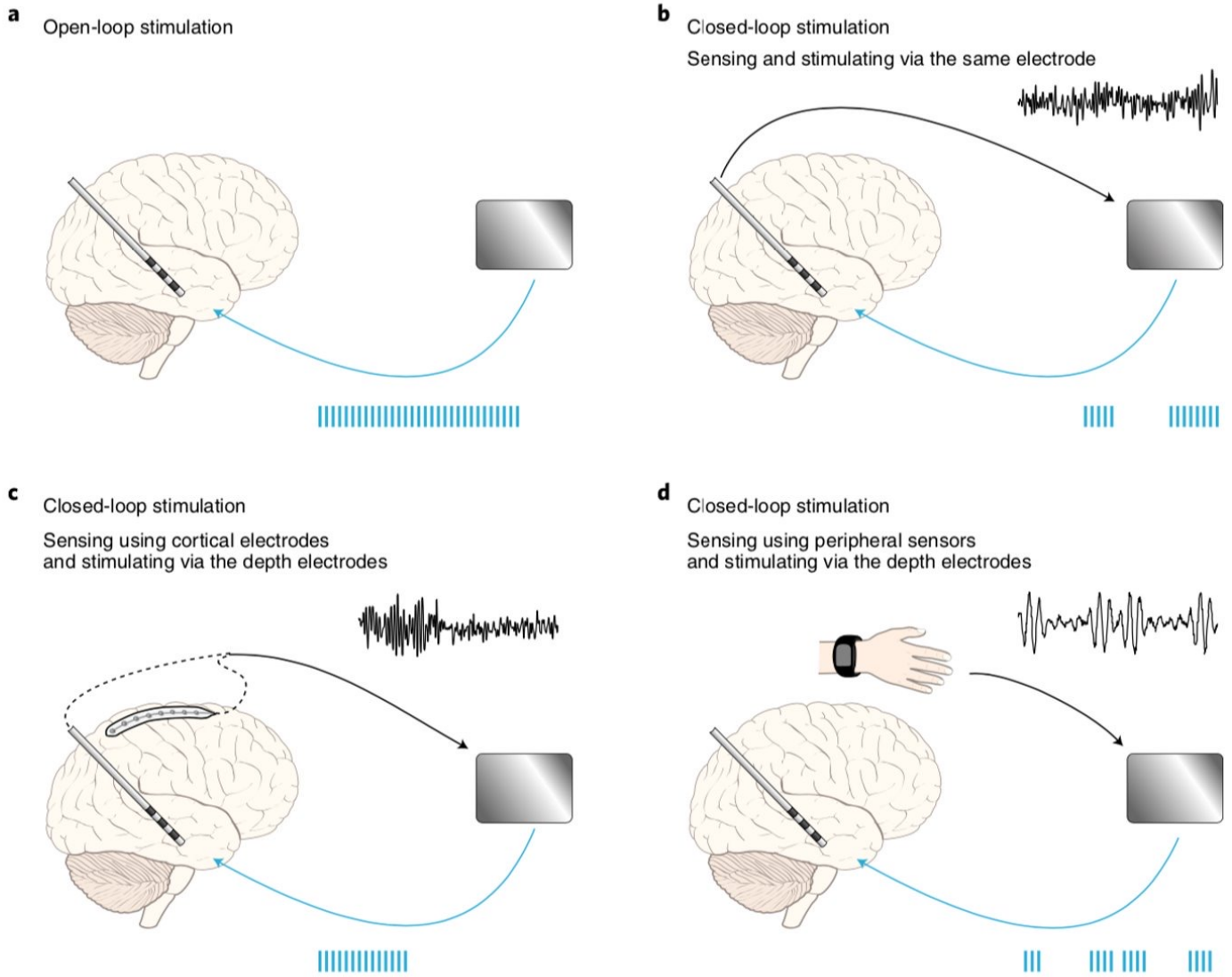


DBS: Remote Programming

Some DBS systems can provide remote programming- no clinic visit required!



DBS: Future directions: Adaptive DBS



NaTurE BIoTECHNology | VOL 37 | SEPTEMBER 2019 | 1024–1033 |

External Devices

CUE1

Cala kIQ

GyroGlove

Points of Discussion

Disclosures

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2. Advancements Non-pharmacologic treatment
3. The Multi-disciplinary Approach

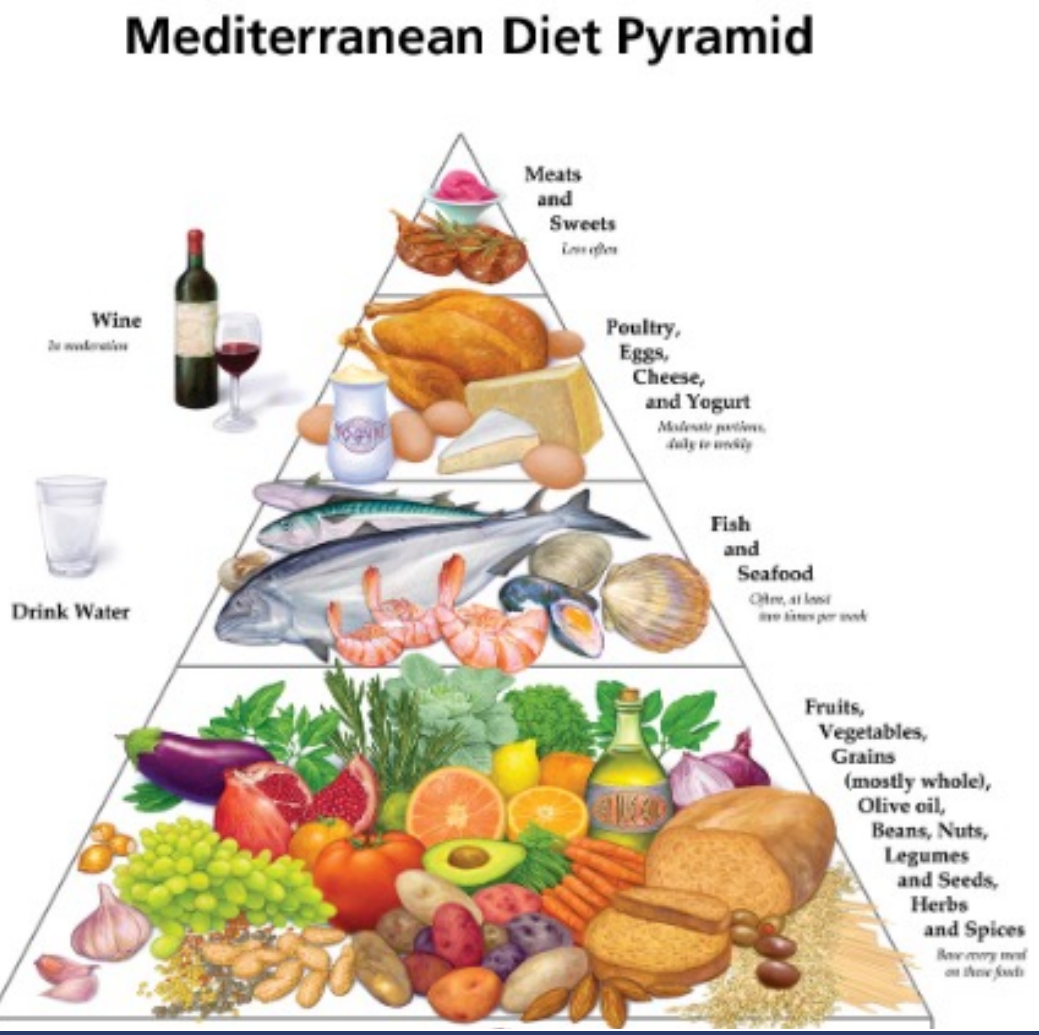
Non-pharmacologic management of PD

Nutrition

Disclaimer:

There is no single diet for PD, and diets should be personalized to the person with PD

Nutrition



Fruits and vegetables
Whole grains and legumes
Healthy fats like nuts and olive oil

Image from Oldwayspt.org

To date studies of various supplements have not demonstrated a meaningful impact on disease progression.

Your doctor may recommend Calcium and Vit D for bone health.

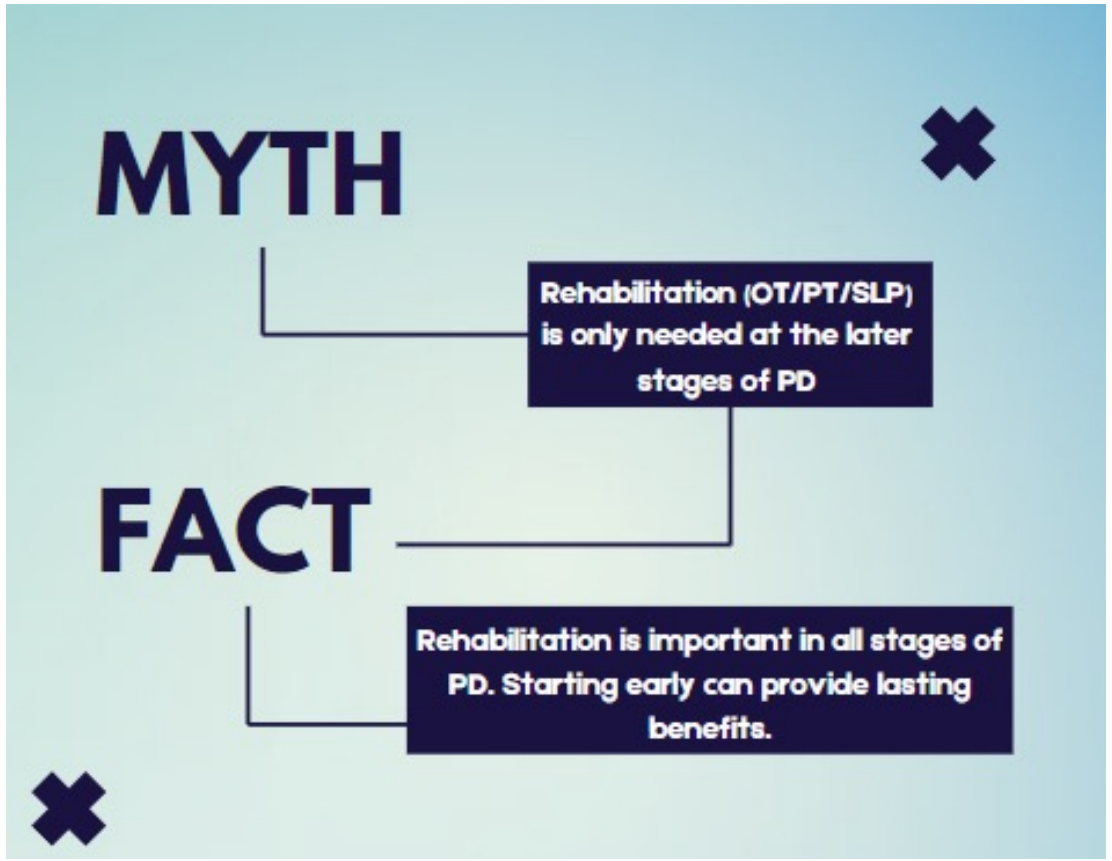
Talk to your doctor before starting any supplements.

Non-pharmacologic management of PD

Physical Therapy

- Gait
- Balance
- Flexibility/Range of Motion
- Posture
- Strength

Early Therapy Critical (Goldman et al., 2024)



People with Parkinson's who participate in rehabilitation care are more likely to experience:

- Decreased Care Partner Strain
- Fewer Hospitalizations
- Prolonged Participation in Meaningful Activity
- Longer Functional Independence

Parkinson's Foundation

Maintenance Therapy

https://www.apta.org/your-practice/payment/medicare-payment/coverage-issues/skilled-maintenance-therapy-under-medicare

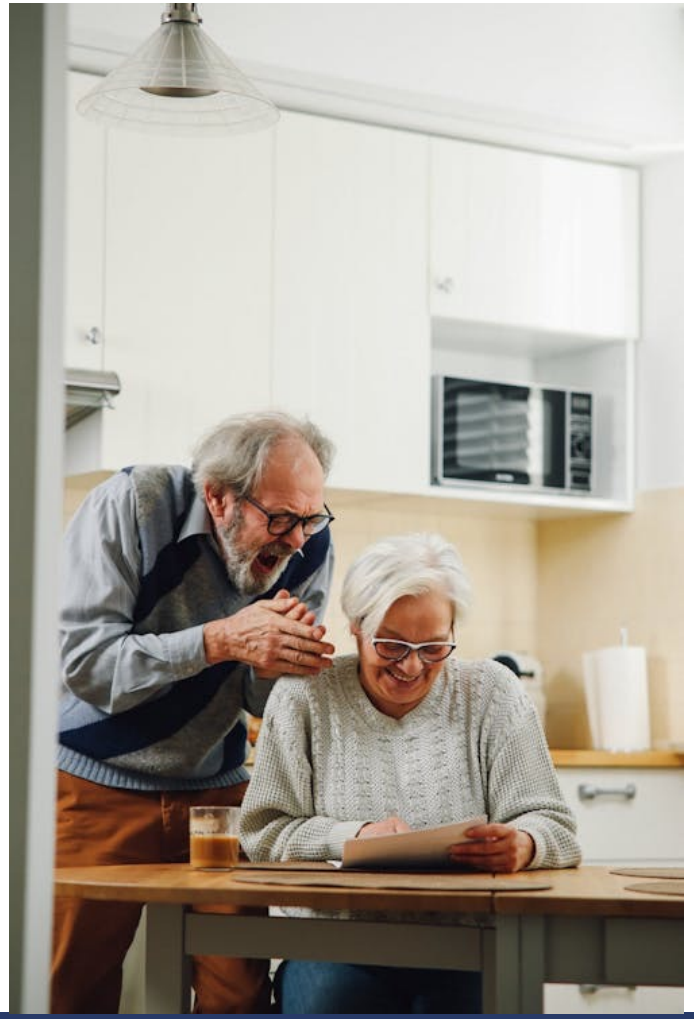
Myth→ Medicare does not cover therapy if expected gains or functional improvement is not accepted

Fact→ *Skilled* maintenance therapy through Medicare is allowed " when (a) the therapy procedures required to maintain the patient's current function or to prevent or slow further deterioration..."

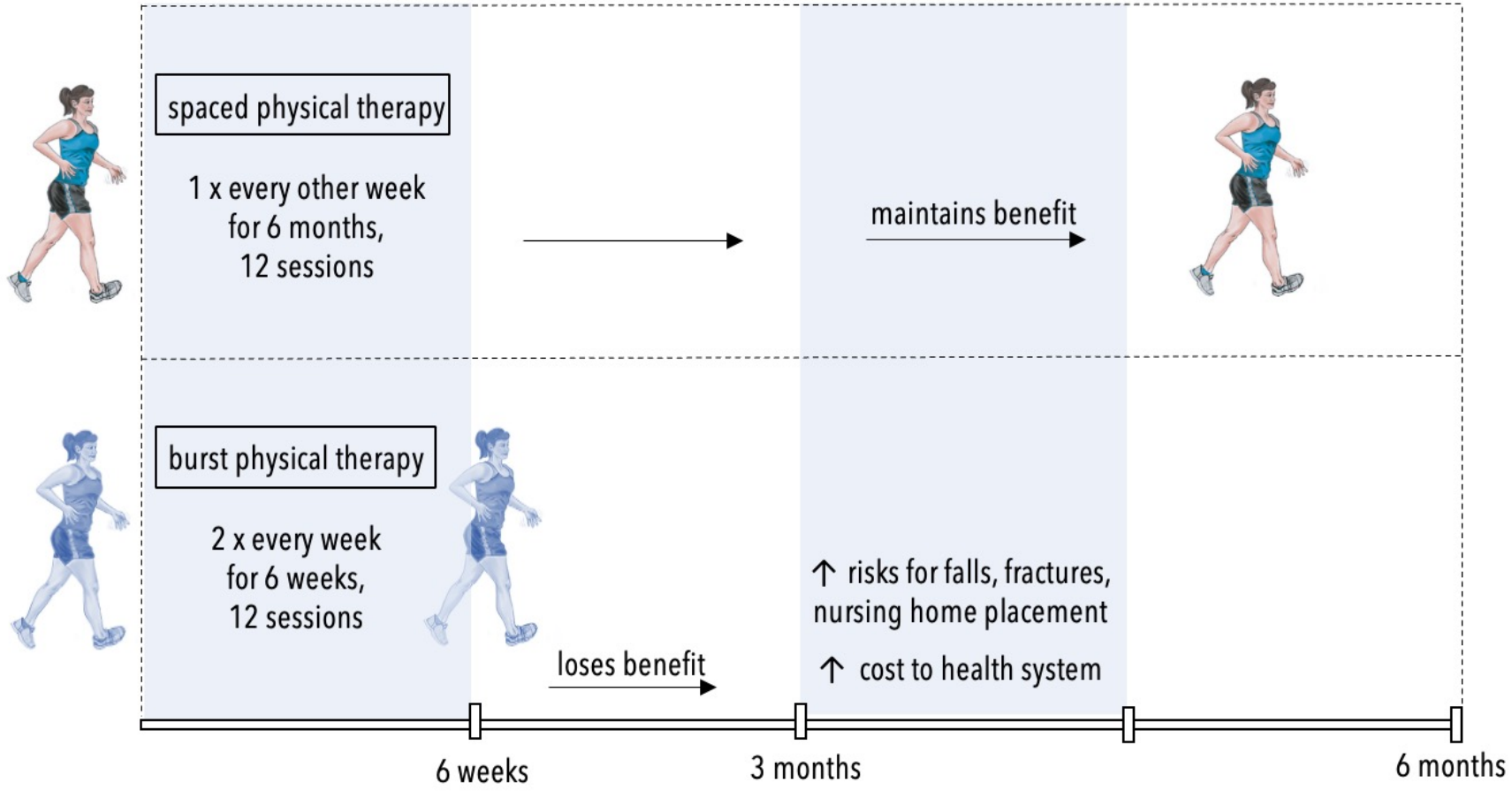
What Does This Mean With Medicare

You do not HAVE to be discharged after a certain number of visits

Medical necessity can be approved despite a progressive condition



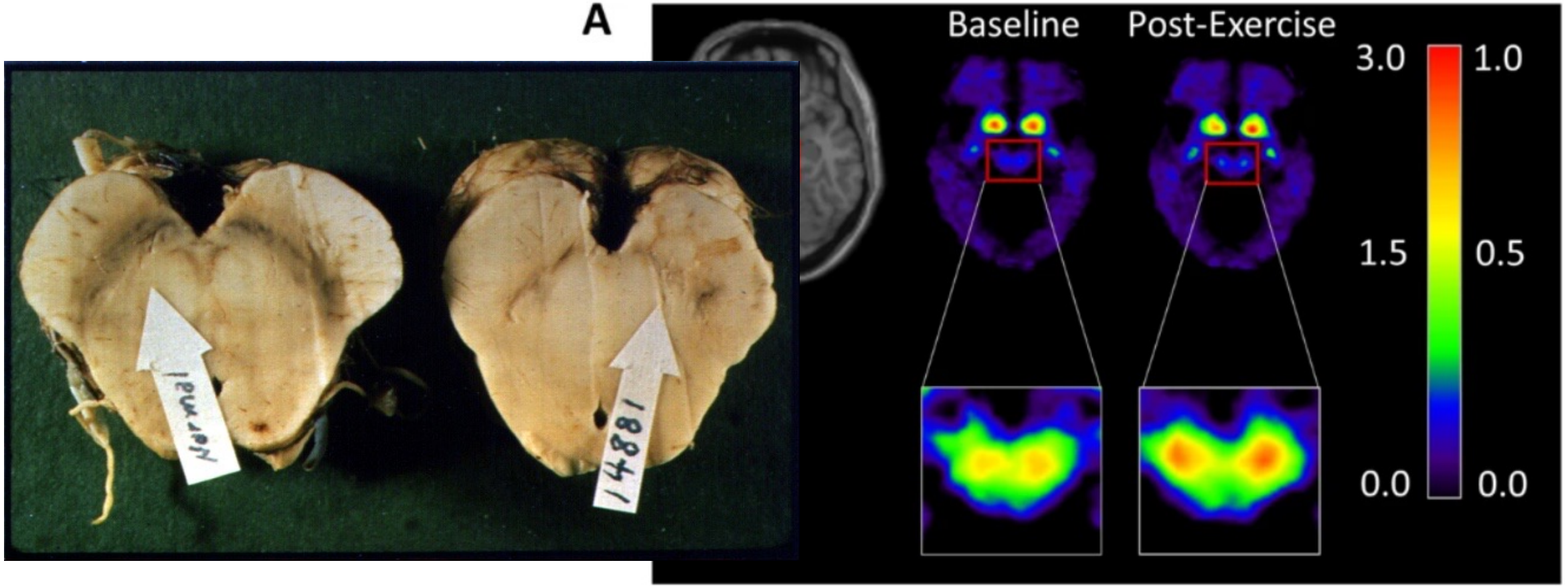
Spaced Versus Burst Therapy (Au et al., 2022) (LeLaurin et al., 2024)



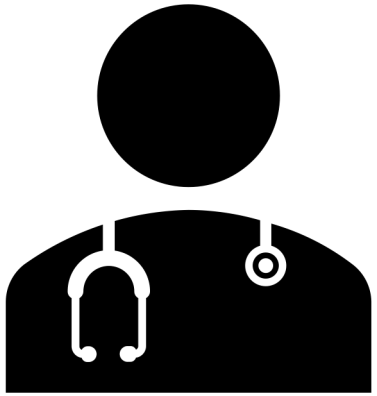
https://www.parkinsonsecrets.com/blog/are-we-writing-prescriptions-for-parkinsons-disease-physical-therapy-wrong

High Intensity Exercise may be neuroprotective

Fig. 1: Dopamine Transporter Levels Pre- and Post-Exercise.



Exercise Resources



Talk to your doctor and physical therapist to help develop a personalized exercise plan.

SPARX3

Study in Parkinson's Disease of Exercise
Phase 3 Clinical Trial

TO TAKE PART IN THIS RESEARCH STUDY

Participants must:

- Be between 40 to 80 years old
- Parkinson disease diagnosis with last 3 years
- Not currently be taking any PD medication or expect to start taking PD medications within the next 6 months
- Be able and willing to do moderate to high intensity exercise on a treadmill 4x/week for 18 months and participate in study visits for 24 months
- Be able to travel to UF periodically for study related visits

Additional details, contact:
Amanda.Fessenden@neurology.ufl.edu

Non-pharmacologic management of PD

Speech Therapy

- A speech and language pathologist will evaluate speech, voice, and swallowing and provide exercises, strategies, and sometimes tools like amplification devices
- Daily practice of therapy exercises leads to more rapid improvement
- Re-evaluation every few years is recommended to stay on track
- Ask your doctor for a referral to an SLP, ideally one with special training in Parkinson's programs like LSVT LOUD or Parkinson Voice Project SPEAK OUT!

Speech Therapy

Epub 2023 Jul 28.

Feasibility and efficacy of video-call speech therapy in patients with Parkinson's disease: A preliminary study

Hee Jin Chang [1], Jiae Kim [2], Jae Young Joo [3], Han-Joon Kim [4]

Affiliations + expand

PMID: 37531838 DOI: 10.1016/j.parkreldis.2023.105772

Research Article

Rehabilitating Cough Dysfunction in Parkinson's Disease: A Randomized Controlled Trial

Michelle S. Troche PhD, CCC-SLP, James A. Curtis PhD, CCC-SLP, Jordanna S. Sevitz MS, CCC-SLP, Avery E. Dakin MS, CCC-SLP, Sarah E. Perry PhD, CCC-SLP ... See all authors

First published: 07 November 2022 | https://doi.org/10.1002/mds.29268 | Citations: 1

Non-pharmacologic management of PD

Occupational Therapy

Goal: Help perform everyday activities safely and if possible independently

Self care (eating, dressing, etc)

Work related tasks

Typing

Writing

Eating

LSVT Big

Driving rehabilitation

Home safety assessments

Sleep hygiene

Non-pharmacologic management of PD

Meditation/Mindfulness

Advocat et al. BMC Neurology (2016) 16:166
DOI 10.1186/s12883-016-0685-1

BMC Neurology

RESEARCH ARTICLE Open Access

The effects of a mindfulness-based lifestyle program for a
a mixed meth
randomised c

Jenny Advocat[1*], Joanne Enticot

Original Investigation

April 8, 2019

Effects of Mindfulness Yoga vs Stretching and Resistance Training Exercises on Anxiety and Depression for People With Parkinson Disease

A Randomized Clinical Trial

Jojo Y. Y. Kwok, PhD, MPH, BN, RN[1]; Jackie C. Y. Kwan, MSocSc, PDMH, BSW

» Author Affiliations | Article Information

JAMA Neurol. 2019;76(7):755-763. doi:10.1001/jamaneurol.2019.0534

npj | parkinson's disease

www.nature.com/npjparkd

ARTICLE OPEN

Check for updates

A randomized clinical trial of mindfulness meditation versus exercise in Parkinson's disease during social unrest

Jojo Yan Yan Kwok[1], Edmond Pui Hang Choi[1], Janet Yuen Ha Wong[2], Kris Yuet Wan Lok[1], Mu-Hsing Ho[1], Daniel Yee Tak Fong[1], Jackie Cheuk Yin Kwan[3], Shirley Yin Yu Pang[4] and Man Auyeung[5]

Non-pharmacologic management of PD

Cognitive Exercises

Neurology® | AMERICAN ACADEMY OF NEUROLOGY®

Cognitive training in Parkinson disease

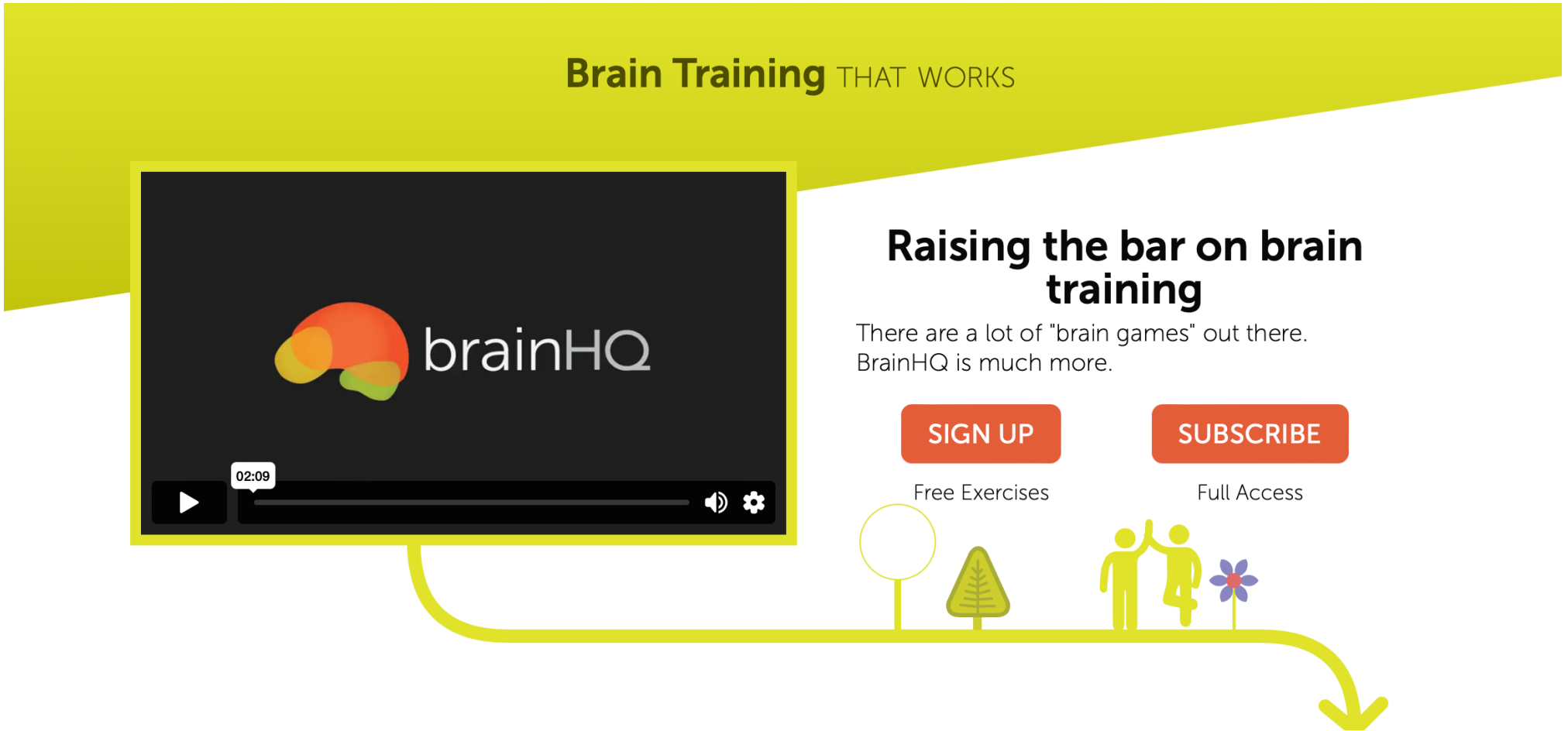
A systematic review and meta-analysis

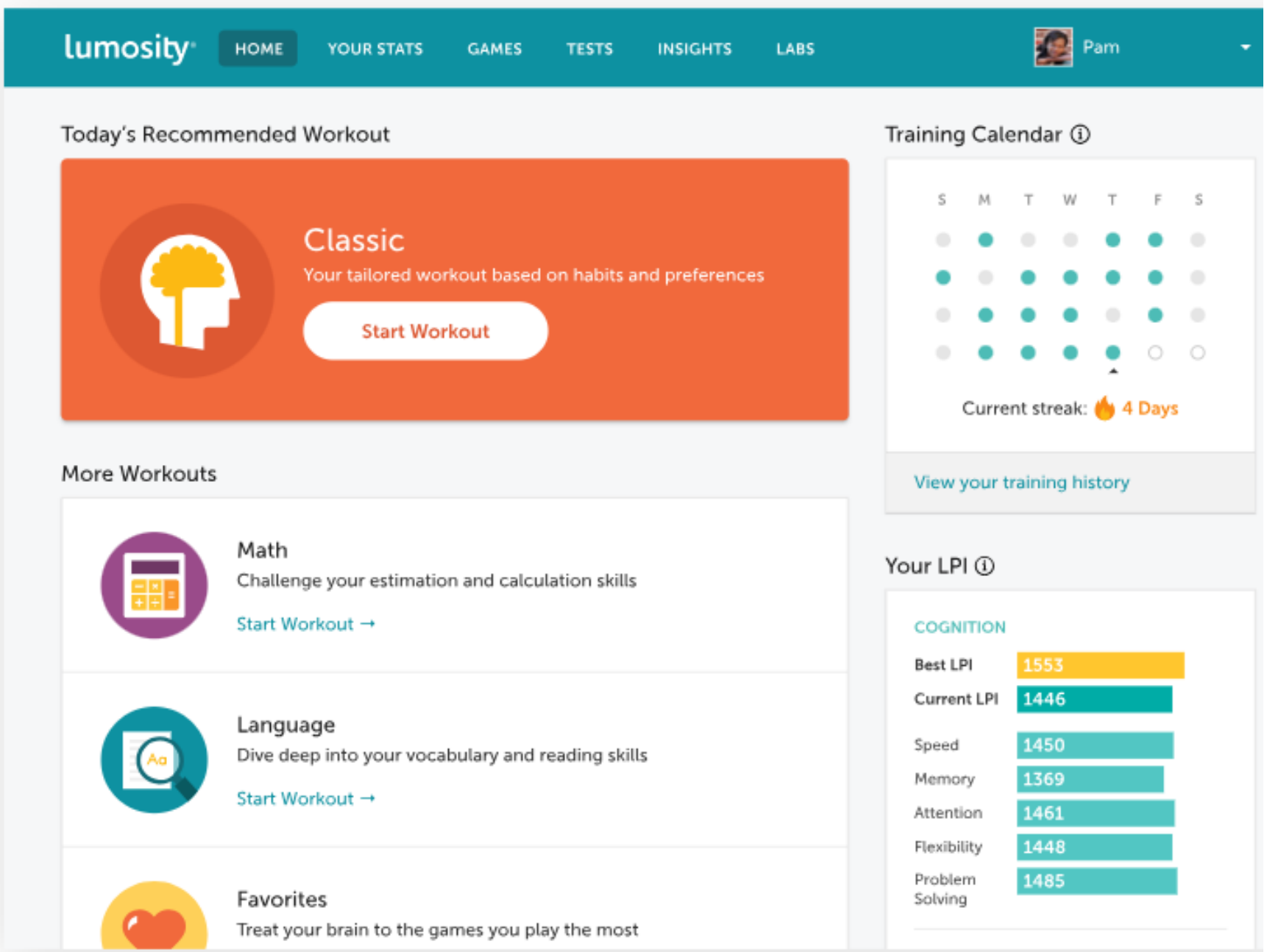
Isabella H.K. Leung, MBMSc,* Courtney C. Walton, BSc (Hons),* Harry Hallock, MBMSc, Simon J.G. Lewis, MD, Michael Valenzuela, MD, PhD, and Amit Lampit, PhD✉

"CT leads to measurable improvements in cognitive performance in individuals with PD, particularly in working memory, executive functioning, and processing speed."

Non-pharmacologic management of PD

Cognitive Exercises




lumosity
HOME
YOUR STATS
GAMES
TESTS
INSIGHTS
LABS
Pam
Today's Recommended Workout
Classic
Your tailored workout based on habits and preferences
Start Workout
More Workouts
Math
Challenge your estimation and calculation skills
Start Workout →
Language
Dive deep into your vocabulary and reading skills
Start Workout →
Favorites
Treat your brain to the games you play the most
Training Calendar
S M T W T F S
Current streak: 4 Days
View your training history
Your LPI
COGNITION
Best LPI 1553
Current LPI 1446
Speed 1450
Memory 1369
Attention 1461
Flexibility 1448
Problem Solving 1485

Non-pharmacologic management of PD

Social support

Impact of Isolation During the COVID-19 Pandemic on the Patient Burden of Parkinson's Disease: A PMD

Neal Hermanowicz[1], Maria C
Jason A Rivera[6], Susan Miller[6],

[1]Christus-St. Vincent Neurology Specialists, S
Hospital, Washington, DC, USA; [4]Scripps Cli
Las Vegas, NV, USA; [6]Parkinson and Moveme
CA, USA

This Issue | Views 13,232 | Citations 2 | Altmetric 65

Medical News & Perspectives

February 9, 2022

How Prolonged Isolation Affects People With Parkin

Melissa Suran, P

Article Informati

JAMA. 2022;327

↑ Social isolation

↑ Non-motor symptoms (mood, cognition)

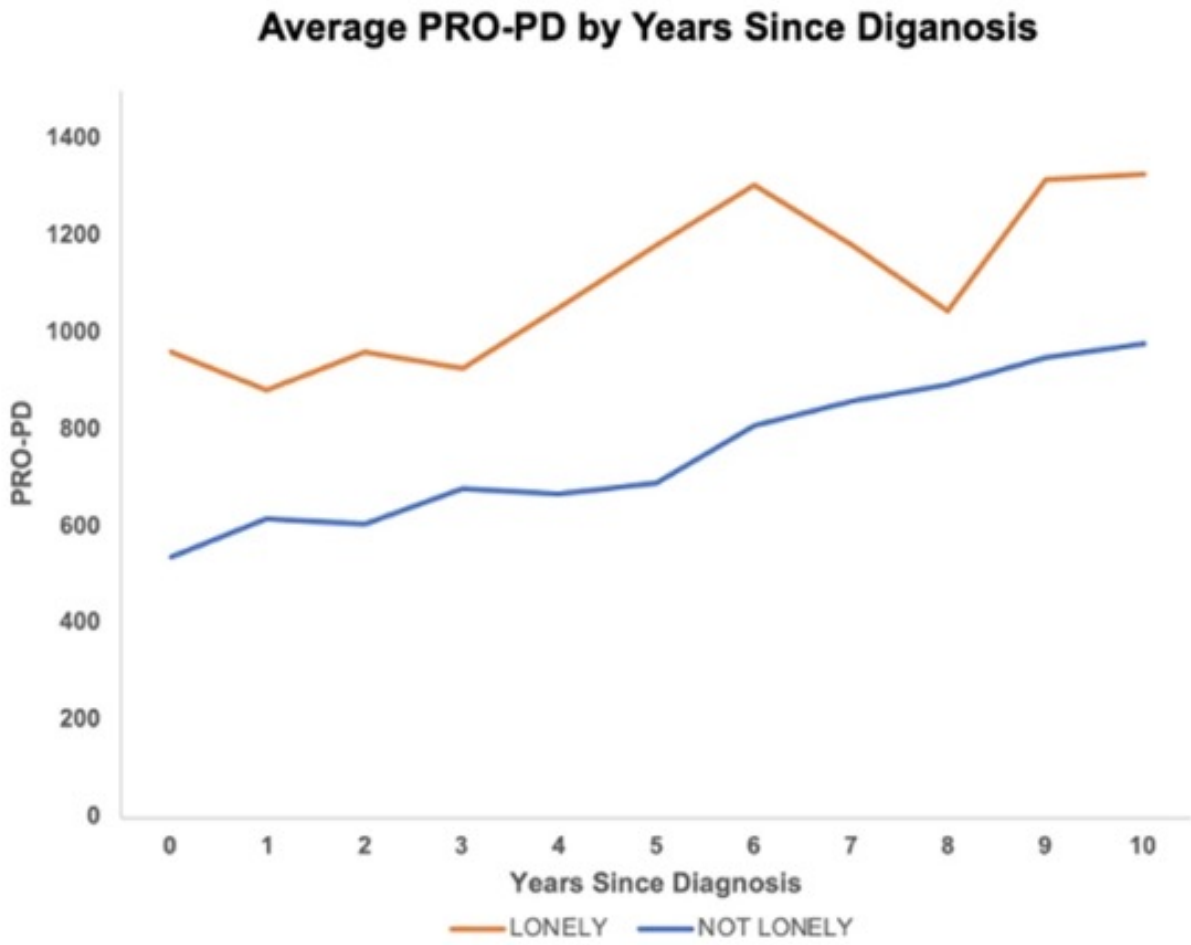
GAPS & CONTROVERSIES

Unmet Needs of Women Living with Parkinson's Disease: Gaps and Controversies

Indu Subramanian, MD,[1,2*] Soania Mathur, MD,[3] Annelien Oosterbaan, MD, PhD,[4] Richelle Flanagan, RD,[5] Adrienne M. Keener, MD,[1,2] and Elena Moro, MD, PhD[6]

Social support

PwP, those who are lonely report greater severity of symptoms of…
Bradykinesia
Pain
Memory
Depression, anxiety
Fatigue



Subramanian, I NPJ Parkinson disease 2020

Social support

Perceived online social support for Parkinson's disease patients: The role of support type, uncertainty, contentment, and psychological quality of life

Surin Chung, Eunjin (Anna) Kim & J. Brian Houston

Pages 259-279 | Published online: 23 Jun 2021

↑ Social isolation → ↑ Non-motor symptoms (mood, cognition)

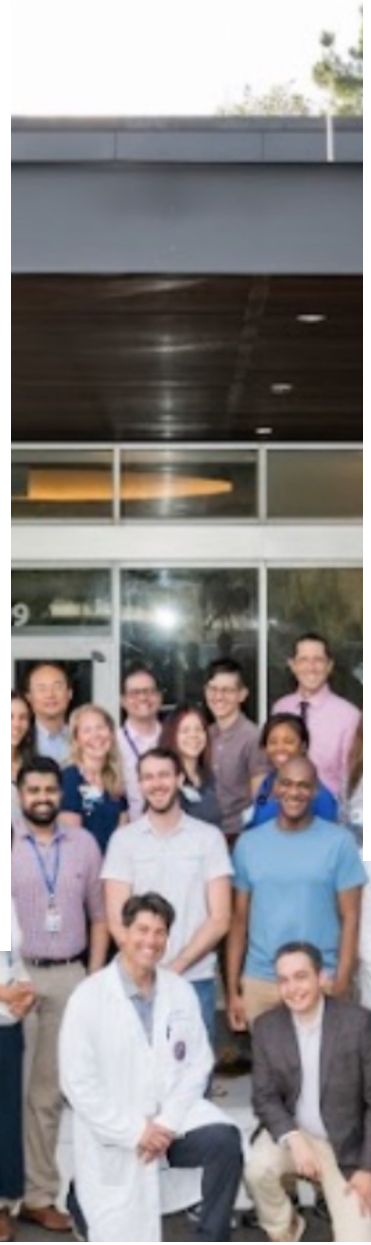
↑ Emotional support → ↓ Non-motor symptoms (mood, cognition)

Build your team!

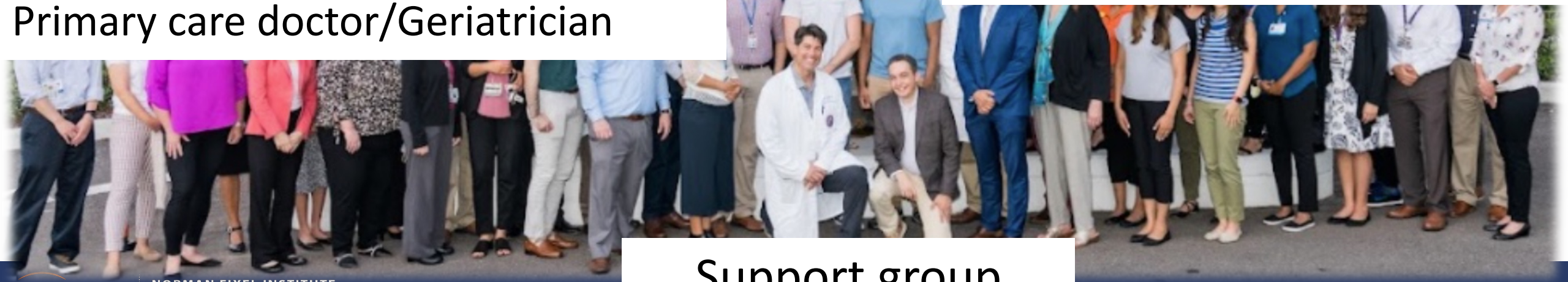
General Neurologist
Movement disorders physician ★
Neurosurgeon ★

Psychiatrist ★
Gastroenterologist ★
Urologist/Urogynecologist
Neuro-Ophthalmologist
Sleep Medicine specialist

Primary care doctor/Geriatrician



Physical therapy ★
Occupational therapy ★
Speech therapy ★
Dietician ★
Neuropsychology ★
Social worker ★
Pharmacist
Counselor/Therapists
Trainer
Research Coordinators ★



Support group

Thank you!