Non-Motor Symptoms Associated with Parkinson Disease

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Disclosures

Nothing to disclose

“I don’t have any choice whether or not I have Parkinson’s, but surrounding that non-choice is a million other choices that I can make.”

–*Michael J. Fox*

Importance of Non-Motor Symptoms in Parkinson disease (PD)

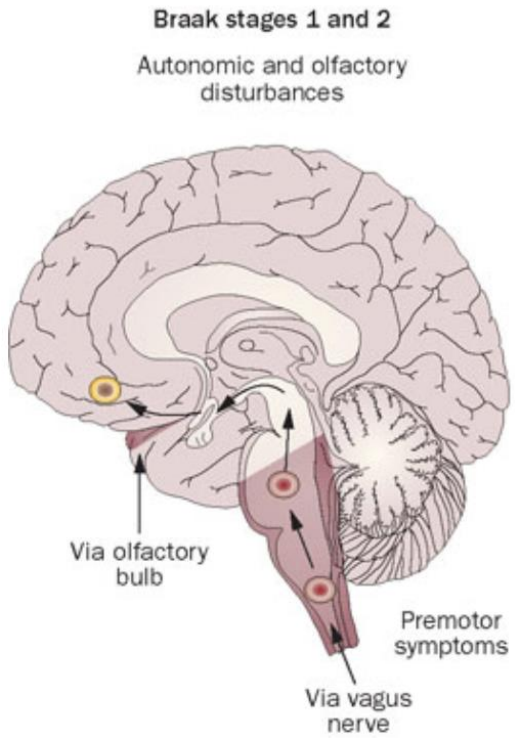
- Non-motor symptoms in PD can be more disabling than motor symptoms
  - Associated with poorer quality of life
  - Some non-motor symptoms are more predictive of nursing home admissions than motor symptoms

(Pfeiffer RF, *Parkinsonism and Relat Dis*, 2016)

Parkinson Disease Prodrome

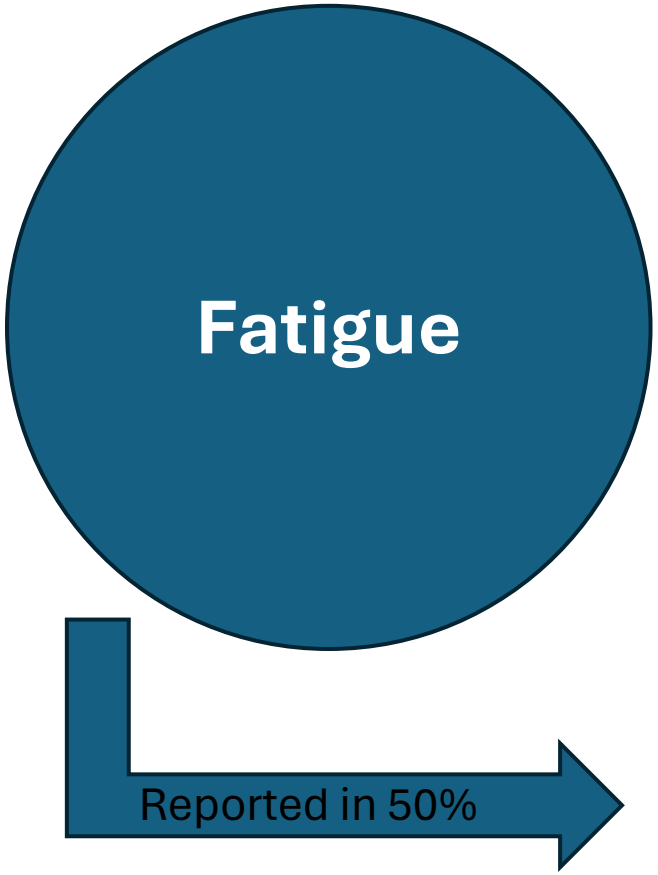
NON-MOTOR SYMPTOMS THAT PRECEDE MOTOR FEATURES OF PARKINSON DISEASE BY MANY YEARS

- Hyposmia (reduced sense of smell), Reduced taste
- Constipation, Postprandial fullness
- REM sleep behavioral disorder (acting out dreams)
- Mood/personality changes



(Pont-Sunyer C et al, *Mov Dis*, 2015)

General symptoms



- Fatigue severity was independent of
  - Depression
  - Cognitive impairment
  - Treated versus untreated people
- Only ½ of studies showed a correlation with disease severity and fatigue
- Fatigue is associated with
  - Older age
  - Co-morbid anxiety
  - Sleep disturbances

(Siciliano M et al., *Mov Dis*, 2018)


Fatigue
Pharmacologic Therapy
-Stimulants
-MAO-B Inhibitors
Non-Pharmacologic Therapy
-Exercise

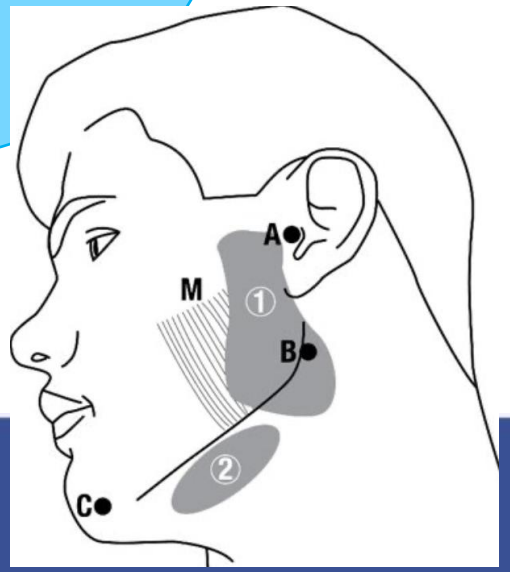
Sensory Changes

- Pain has been reported in about 75% of people with PD
  - musculoskeletal, neuropathic, dystonia-related, central parkinsonian pain, or akathitic discomfort
- Context and physical examination important for treating pain

(Pfeiffer RF, Parkinsonism and Relat Dis, 2016)

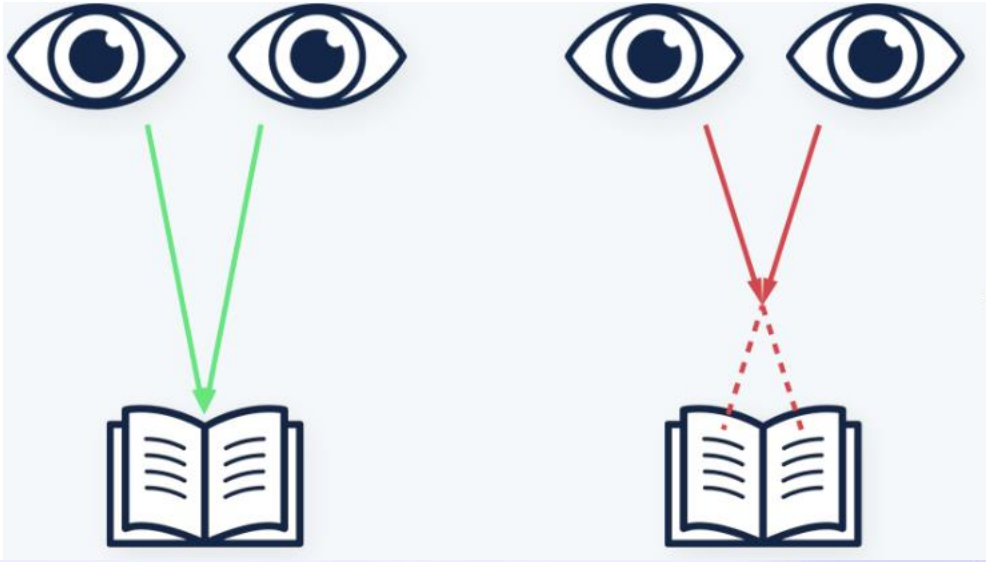
Excess Saliva

- Reported in 32-74% of people with PD
- No necessarily due to increased saliva production
- Treatments
  - Botulinum toxin injections (Typically serotype B)
  - glycopyrrolate
    - Caution recommended due to potential side effects



Eye Changes

- Reduced blinking
  - Dry eye
- Reduced contrast sensitivity
- Reduced near and far visual acuity
- Convergence insufficiency



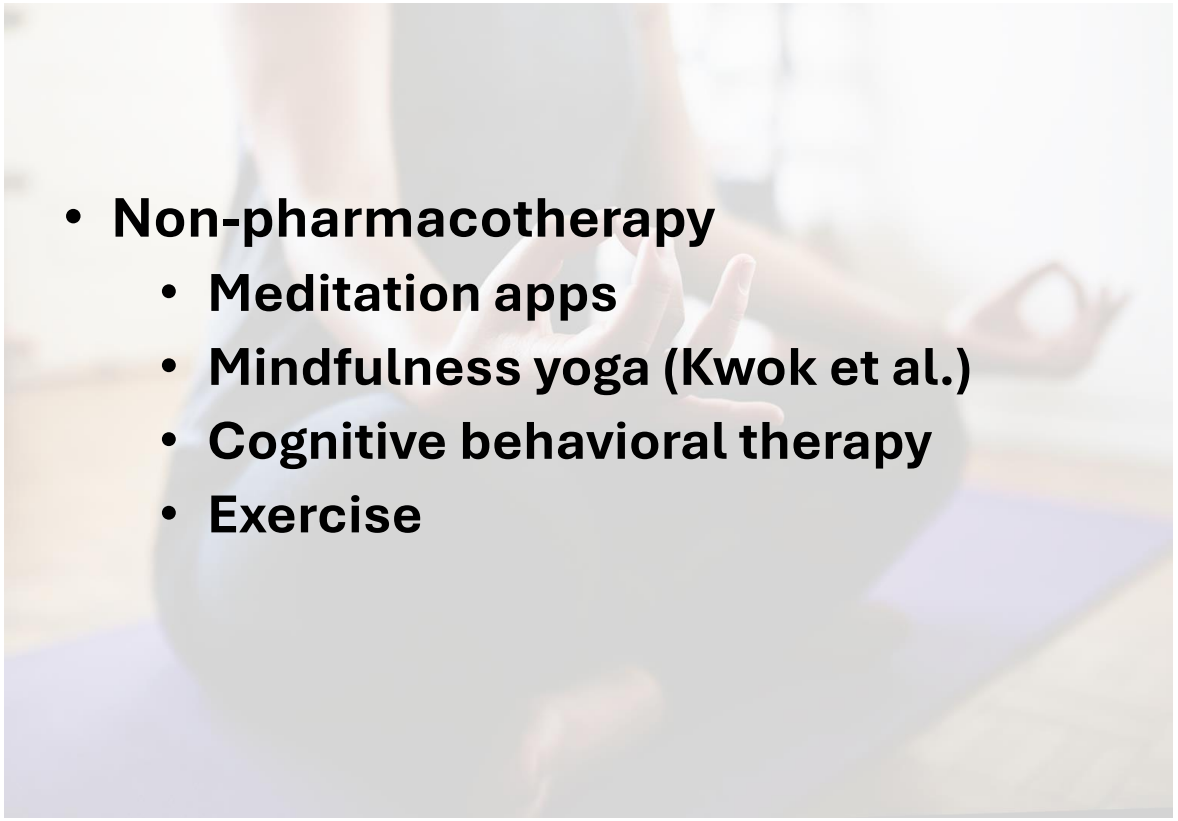
Mood/Personality Symptoms

Parkinson Disease & Mood Disorders

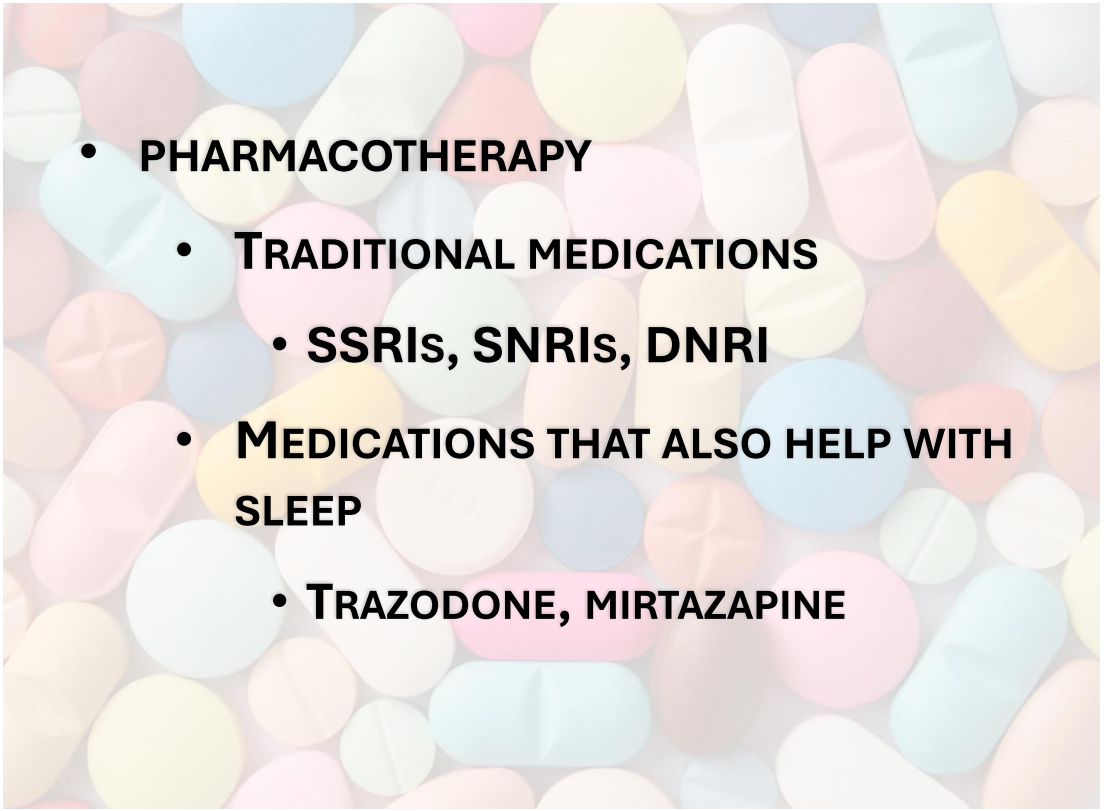
- Anxiety and depression are the most common mood disorders associated with Parkinson disease
  - Affects 30-50% people with PD
  - Can occur before the onset of motor symptoms
  - Let your doctor know if you have depressed mood or anxiety

(Kwok et al, *JAMA Neuro*, 2019)

Therapies for mood changes



- Non-pharmacotherapy
  - Meditation apps
  - Mindfulness yoga (Kwok et al.)
  - Cognitive behavioral therapy
  - Exercise



- PHARMACOTHERAPY
  - TRADITIONAL MEDICATIONS
    - SSRIS, SNRIS, DNRI
  - MEDICATIONS THAT ALSO HELP WITH SLEEP
    - TRAZODONE, MIRTAZAPINE

Personality changes & PD

Apathy

Lack of motivation

Feeling of indifference

Prevalence 40% in people with PD

Impulsivity

Failure to resist a drive or temptation that results in self harm or harm to others

Symptoms: excessive eating, excessive purchases, hypersexuality, hobbyism

Exercise and mindfulness are recommended non-pharmacological treatments

More pharmacological treatments need to be studied

Some evidence for rivastigmine and DA agonists

Treatment: Stop the offending drug
Cognitive behavioral therapy

Opioids antagonist

Symptoms accompanying motor fluctuations

5 years after therapy	%
Smooth, good response	25
Troublesome fluctuations	43
Troublesome dyskinesias	20

- Non-motor symptoms also co-occur with motor fluctuations
  - Anxiety 35%
  - Depressive symptoms 35%
  - Panic 37%

(van der Velden RMJ et al, *Mov Dis*, 2018)

Sleep Disturbances

Sleep complications in PD

- Greatly prevalent, up to 90% people with PD
- Sleep fragmentation is the most common presentation
- Sleep can be impacted by
  - mechanics (difficulty turning)
  - frequent nighttime urination
  - motor/sensory restlessness
  - medication side effects
  - mood disorders

Excessive daytime sleepiness

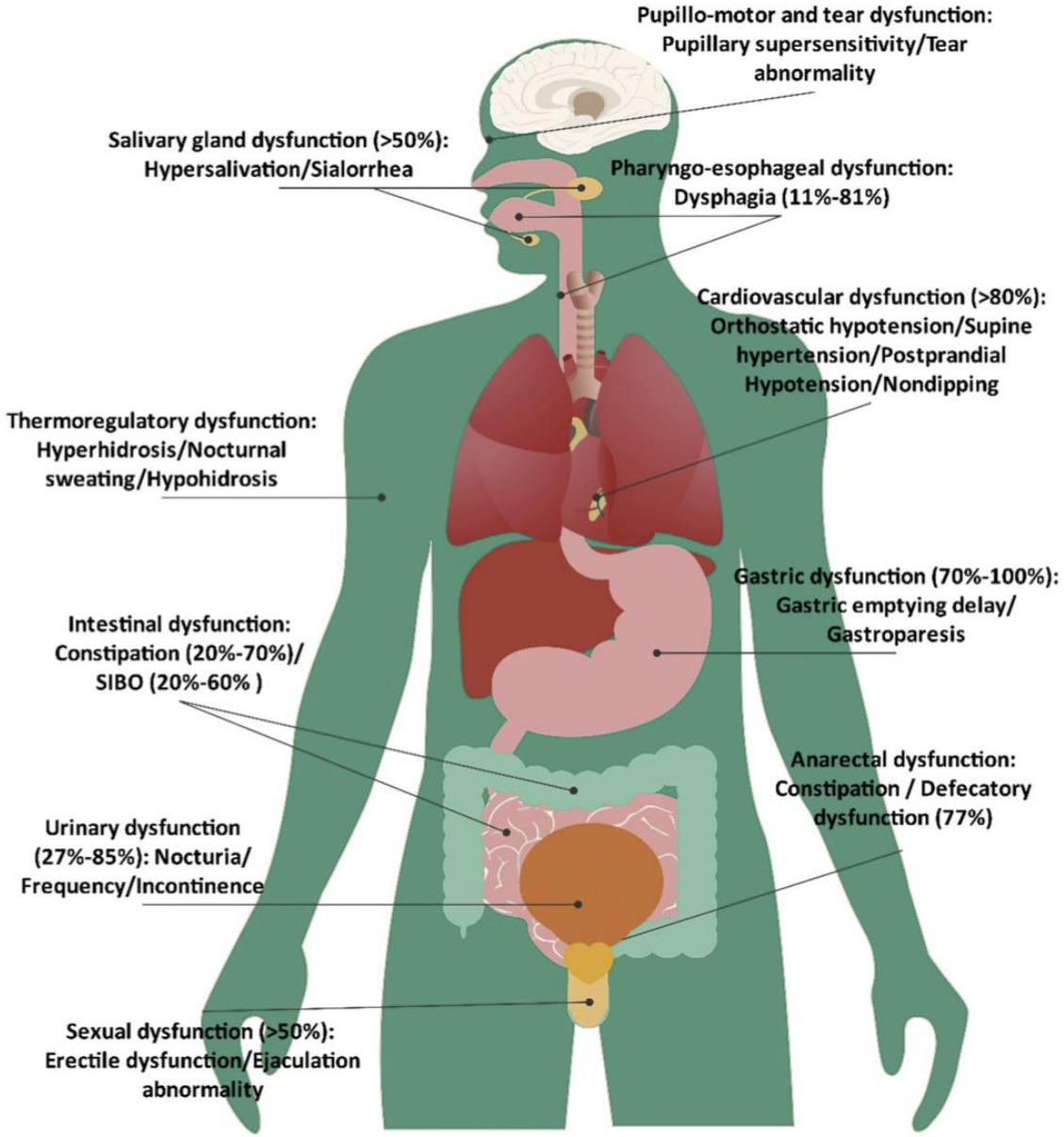
Restless leg syndrome

REM sleep behavioral disorder

Sleep fragmentation

REM sleep behavioral disorder	• Melatonin • Clonazepam
Excessive daytime sleepiness	• Morning caffeine • Exercise • Scheduled naps • Stimulants
Sleep fragmentation	• Evaluate the underlying cause • Mechanical? Motor symptoms? Frequent urination? Sleep apnea? RLS? Anxiety or depression?
Restless leg syndrome	• Dopaminergic medications • Gabapentin

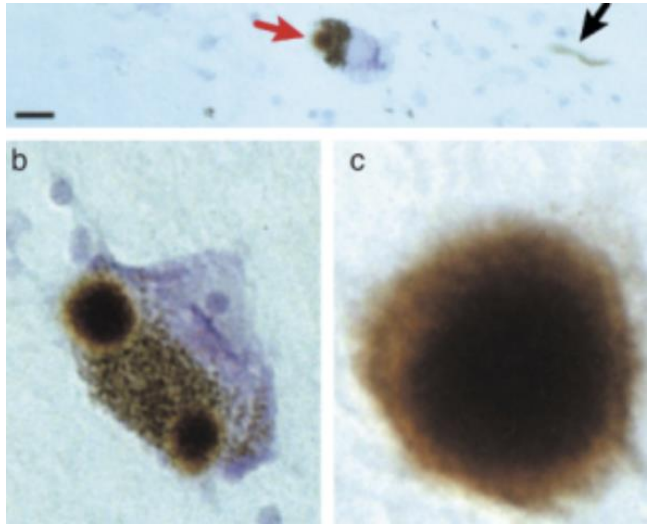
Autonomic system (“flight or fight”) dysfunction

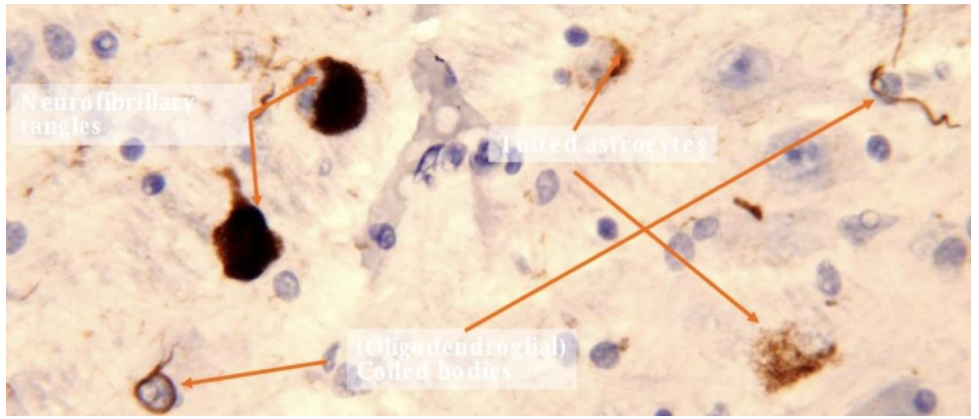


(Chen Z et al, *Neurobiol Dis*, 2020)

Causes of autonomic dysfunction

- Loss of brain cells (neurons) in the brainstem important in autonomic control
- Lewy body deposition in dorsal vagal nucleus, the myenteric plexus of the intestines, and even in the cardiac sympathetic plexus





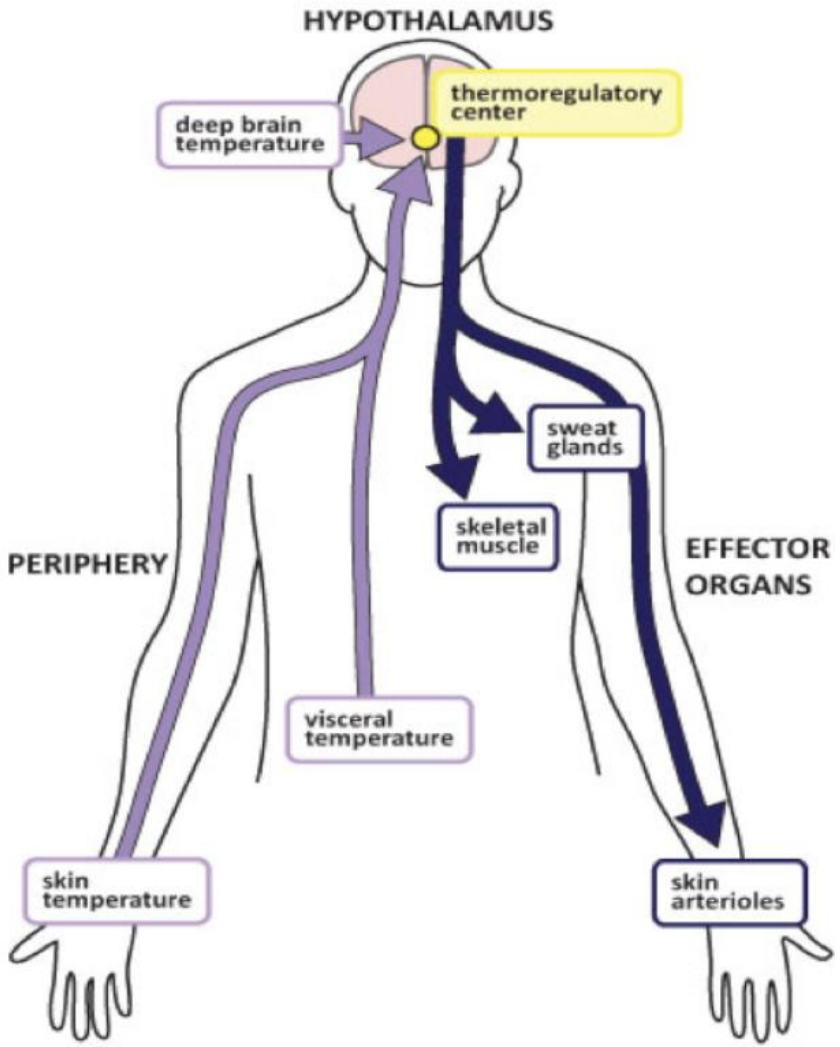
Orthostatic hypotension

- Blood pressure and/or heart rate reduction upon standing
  - Dizziness, passing out, interruptions of cognition
- Occurs in 30-40% of people with Parkinson disease
- Can worsen after meals
- Treatments
  - Increase salt and water intake
  - Eat smaller more frequent meals
  - Compression stockings/abdominal binders
  - Medications

Urinary/sexual Dysfunction

Heat/cold regulation

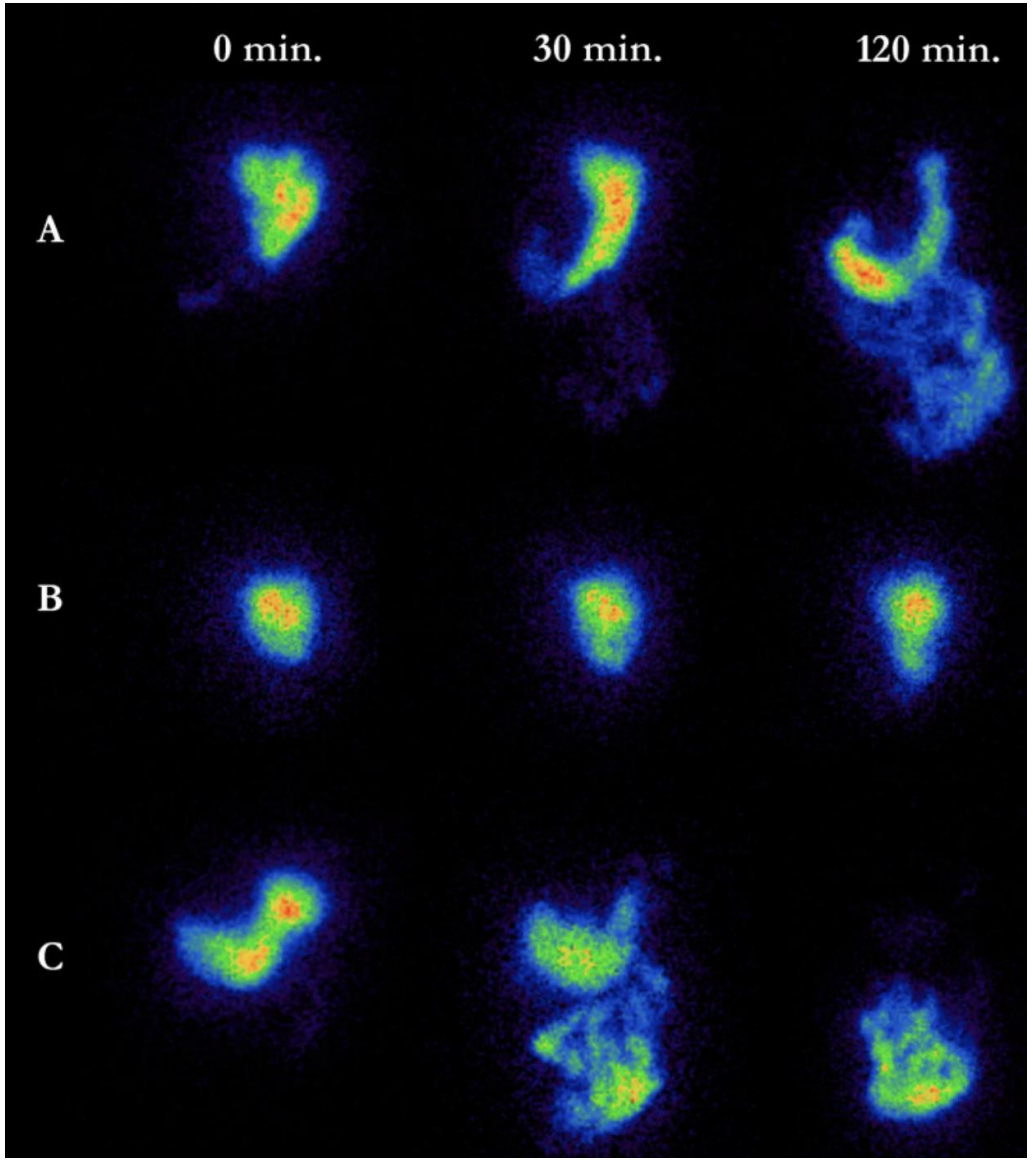
- Excessive sweating
- Nighttime sweating



Gastrointestinal dysfunction

GI dysfunction in PD

- Alpha-synuclein deposition occurs in the GI system → Slower transit time
  - Constipation
  - Feeling of fullness soon after eating
  - Abdominal discomfort
  - Reduced absorption rate of medications
  - Unpredictable ON and/or OFF symptoms
  - May lead to gastroparesis



(Skjærbæk C et al., *J Clin Med*, 2021)

Parkinson Disease & Constipation

- 60-70% of people with PD have constipation
- Treatment
  - Increase dietary fiber
  - Increase water intake
    - > 50 ounces/day
  - Probiotics and prebiotics
  - Medications
    - Sennokot and Dulcolax: stimulant
    - Miralax, milk magnesium: osmotic laxative
    - Docusate: stool softener, usually serves as adjuvant
    - Refractory cases: Linzess

University of Michigan Health System

Constipation Recipe

Mix together:

- 1 cup apple sauce
- 1 cup oat bran or unprocessed wheat bran
- ¾ cup prune juice

https://medicine.umich.edu/sites/default/files/content/downloads/constipation-recipe.pdf

Constipation Fighting Foods

Dried fruits
Fresh fruits

High fiber substances: berries, beans, bran, peas, whole grains
Probiotics: miso, sauerkraut, yogurt, kefir, kombucha
Prebiotics: artichokes, asparagus, bananas, garlic, onions, whole grains

Non-Motor Symptoms in Parkinson disease

- Non-motor symptoms are as important as motor symptoms in pd
- if you are experiencing these non-motor symptoms, please discuss with your physician

Thank you for your attention

What is
Help For Parkinson's?

Jud Eson

www.HelpForPD.org

BOXING FOR PD

It is free for all attendees

because it is funded by Help For PD.

DANCE BEYOND PD

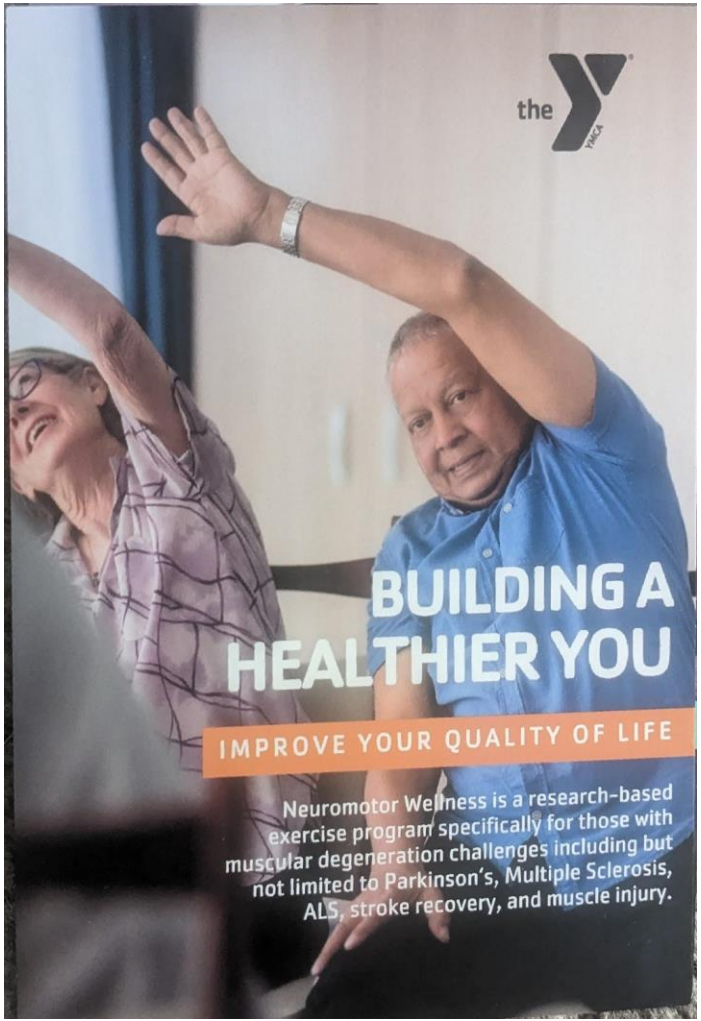
It is free for all attendees

because it is funded by Help For PD.

Ping Pong for PD

It is free for YMCA members, discounted for others

because it is funded by Help For PD.

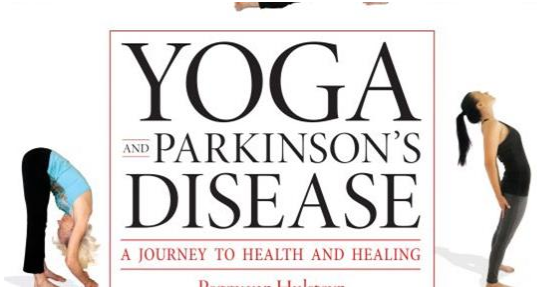


Neuromotor Wellness

It is free for YMCA members

because it is funded by Help For PD.

YOGA FOR PD



It is free for all attendees

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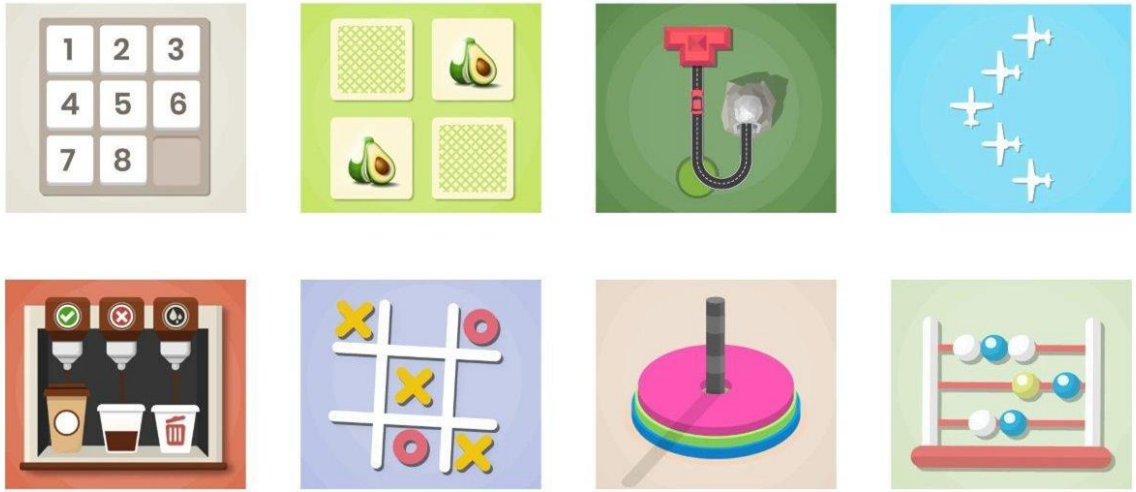
BRAIN TRAINING



It is free for all attendees

because it is funded by Help For PD.

Stand up to Parkinson's will be holding a golf tournament on August 26th at the Colony Country Club.

Community / awareness events like this one held at the Clifton Park YMCA in April

Save the date of October 19th when Help for Parkinson's will host the Hope Soars Gala

www.HelpForPD.org

STAND UP TO PARKINSON'S

Stand Up to Parkinson’s is a 501(c)(3) non-profit organization committed to finding a cure for Parkinson's disease and helping local Parkinson’s patients live more rewarding lives.

STAND UP TO PARKINSON'S

To date.....

Since founded in 2019, Stand Up to Parkinson's has donated over **$250,000** to local Parkinson's research at **Albany Medical Center** and **Capital Region patient support services**, such as **Help for Parkinson's**.

STAND UP TO PARKINSON'S

Our beginning.....

A short time after being diagnosed with Parkinson's Disease in **2017**, **Tim Lange's** focus moved to helping others, as he had done throughout his life in his role as teacher, mentor, coach, administrator, friend, brother, husband, and father. In **2019**, Tim and his wife Dawn founded **Stand Up to Parkinson's**, with the goal of raising funds to assist local researchers in their mission to find a cure.

Tim and Dawn reached out to **my wife Lisa and I,** as well as **Rodger and Kelly Wyland** and asked us to join him as founding officers, and shortly after that in the fall of **2019** the **1st Annual Stand Up to Parkinson's Golf Tournament took place.**

Since that first event, **Stand Up to Parkinson's** has continued to grow as a fundraising organization that not only supports local research at **Albany Medical Center**, but has also begun to support other **regional programming** that assists current Parkinson's patients in the Capital Region live more fulfilling lives.

STAND UP TO PARKINSON'S

The founders.....

STAND UP TO PARKINSON'S

Change……

Upon Dawn's retirement in 2022, Tim and Dawn **relocated to Arizona** where they are currently enjoying the active Arizona lifestyle. They keep **very busy** meeting new friends, playing softball and golf, attending professional sporting events, and **enjoying their time together** in the beautiful Arizona landscape.

In December of **2023**, because of their distance from the Albany area, **Tim (President)** and **Dawn(Secretary)** stepped aside from their active roles with SUTP, and **"passed on"** the organization's leadership to their longtime friends.

STAND UP TO PARKINSON'S

Today and forward….

Today, the current officers and the expanded board of directors **(January 2024 - we added 7 new community leaders were to our board)** are not only **committed to continuing the work** that Tim and Dawn began, but also to **expanding the reach of our organization** in Tim's vision.

Our goals moving forward are to continue to **raise funds in support of local research**, **expand our financial support of patient related programs**, but we also hope to develop **SUTP** into a trusted resource for Capital Region Parkinson's patients to rely on for **information related to local PD programs and services**.

Rodger Wyland - Board Chair & President

Dan Smith - Vice Chair & Vice President

Lisa Smith - Secretary

Board of Directors

Kerry DeWitt

Jon Foshee

Mark L. Fruiterman, M.D.

Donna Goldslager

Matt Phelps

Jeffrey Sperber - *Fundraising Chair & Director of Development*

Greg D. Weitzman, Rabbi

STAND UP TO PARKINSON'S

2024
Stand Up to Parkinson's Pickleball Championship

TRUE PICKLEBALL CLUB

Sponsored By: concord pools & Spas

Raffle Items: $20 per ticket/10 tickets $100

Golf (2)
Colonie Golf & Country Club
- Golf for 4 w/carts
- Dinner for 4 • $1,000 value

Colonie Golf & Country Club

Pickleball True Pickelball
Birthday Party Celebration Package
2 hrs. - Concord Large
2 hrs. - Court time (courts 5/6)
(Court 6 Championship Court)
Pizza/Salad - 16 People
Demo Paddles Included
$600 value

TRUE PICKLEBALL CLUB

Fitness
Metabolic Fitness
6 Month Membership
$1,000 value

METABOLIC FITNESS

5th Annual Stand Up to Parkinson's Golf Tournament

Monday, August 26, 2024

Colonie Golf & Country Club
13 Country Club Lane
Voorheesville, NY 12186

STAND UP TO PARKINSON'S

STAND UP TO PARKINSON'S

Contact.....

Website

standuptoparkinsons.org

Email

standuptoparkinsons@gmail.com

We meet at 7 PM on the second Thursday of most months. Most meetings are in-person at the Glen Eddy Senior Living Community in Niskayuna, NY and by ZOOM.

We welcome new members and guests. Please join us.

Speakers
Support
Activities

Subscribe to our announcement email list using the form at www.cdparkinsons.org in order to receive meeting reminders and other useful links about once a month. Read more at our website

www.cdparkinsons.org

The Importance of Biomarkers in PD

Eric Molho MD

Professor of Neurology

Riley Family Chair in Parkinson's Disease

Disclosures

- **Consulting:** Neurocrine Biosciences (blinded-video rater)
- **Clinical trial grant:** CHDI/HSG, Cerevel Therapeutics, Parkinson Study Group/NIH #U01NS119562, Cerevance Beta inc.,
- **Speaker's bureau:** None
- **Educational grant (fellowship):** Abbott, AbbVie, Amneal, Boston Scientific, Medtronic, Merz North America
- **Sponsors of this symposium:**

What are biomarkers?

- (BY-oh-MAR-ker) A measurable or detectable biological finding that is a reliable sign of a normal or abnormal process, condition or disease.
  - Molecule found in blood, other body fluids
  - Specific finding on microscopic tissue analysis
  - Imaging abnormality

Why are biomarkers useful?

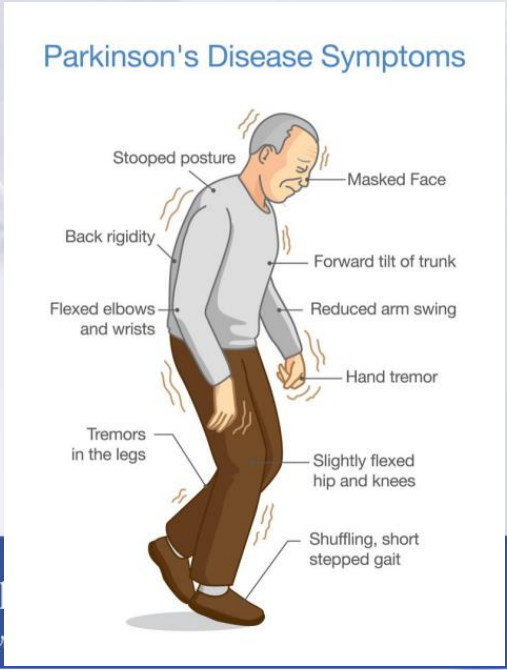
- Diagnosis of disease
- Prediction of disease
- Measuring progression of disease/ detecting response to treatment
- Understanding prognosis
- **Critical for the conduct of valid, rigorous, reproducible clinical trials designed to slow or stop the progression of PD

Why are biomarkers ueful?

- Diagnosis of disease
  - "Hey doc, do I have PD?"
- Prediction of disease
- Measuring progression of disease/ detecting response to treatment
- Understanding prognosis

How is PD diagnosed now?

- Taking a careful history
  - Gradual onset of slowness, stiffness, shaking
- Performing a careful examination
  - Bradykinesia, rigidity, tremor, posture changes
- Confirming the presence of the parkinsonian syndrome
- Ruling out imitators of PD
- Observation over time
  - Response to Ldopa
  - Typical progression

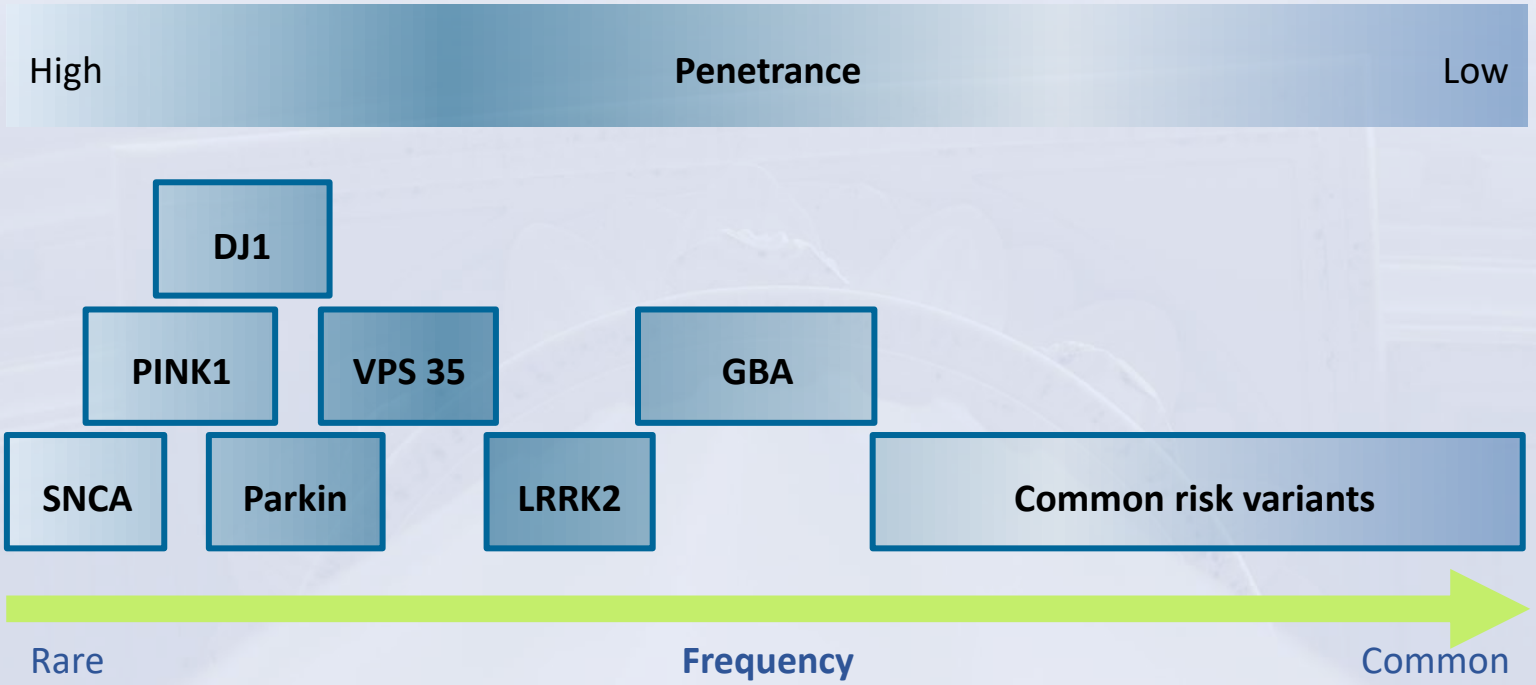


What's new in PD diagnosis?
(Biomarkers)

- Genetic testing
- Brain dopamine imaging (DaTscan)
- Alpha-synuclein assays
- Man's best friend?

  (don't worry Asher..)

Sporadic PD vs Genetic PD



Cherian A and Divya KP. Acta Neurol Belg. 2020;120:1297–1305

PD GENEration

- Sponsored by Parkinson Foundation (PF) and Parkinson Study Group (PSG)
- Tests for 7 most common genetic causes of PD:
  - SNCA, GBA, LRRK2, PRKN, VPS35, PINK1, PARK7
- No cost to study participants
- Large scale effort to expand knowledge about genetic forms of PD and enrich the population of potential research subjects for development of new disease slowing treatments

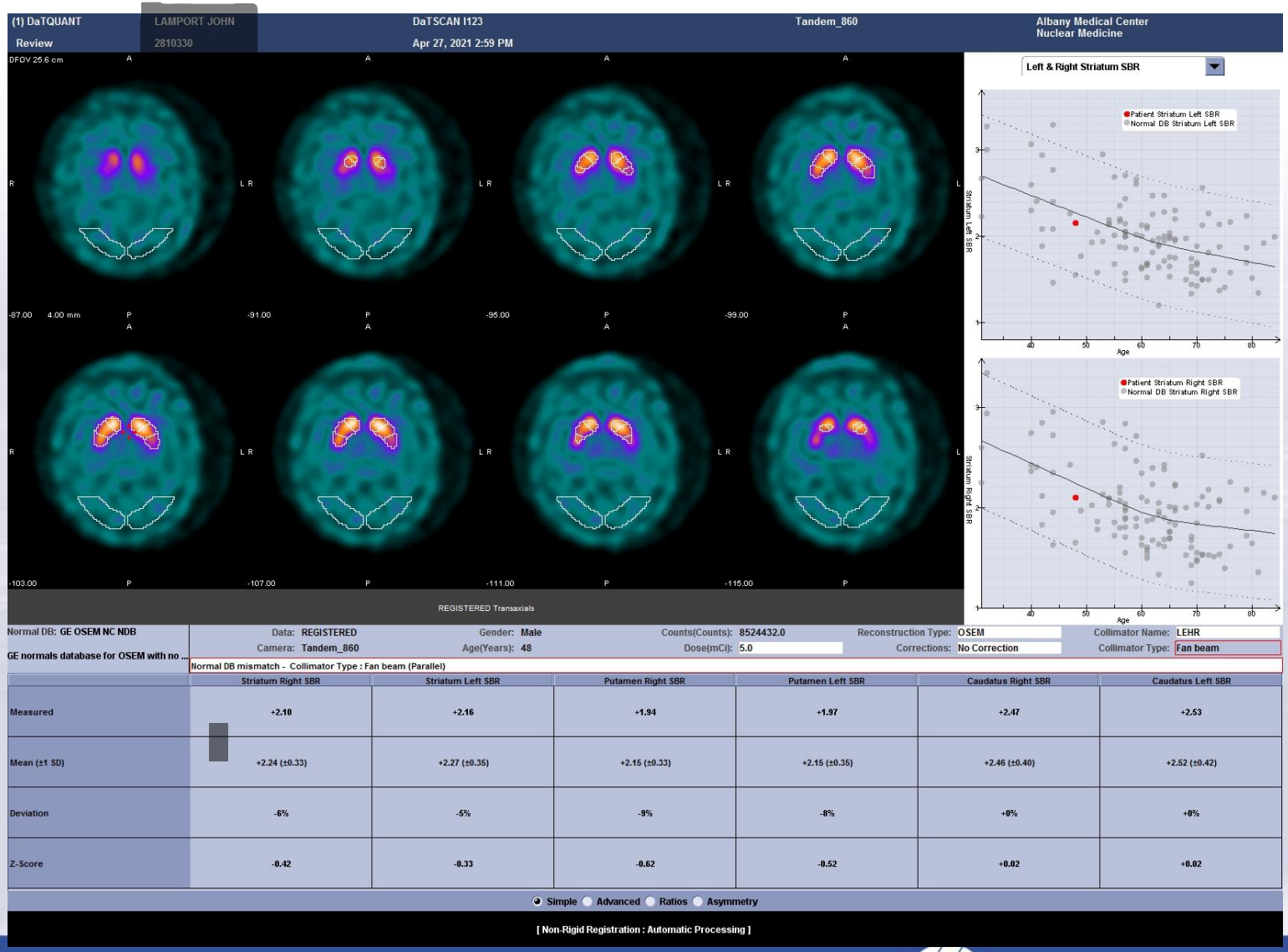
Can we use genetics to diagnose PD?

- The 7 genes tested for only account for a small percentage of cases of PD (depending on population <5% - 30%)
- We don’t know who to test in presymptomatic/prodromal disease
- Having a gene mutation doesn’t reliably predict disease

DaTscan (dopamine transporter scan)

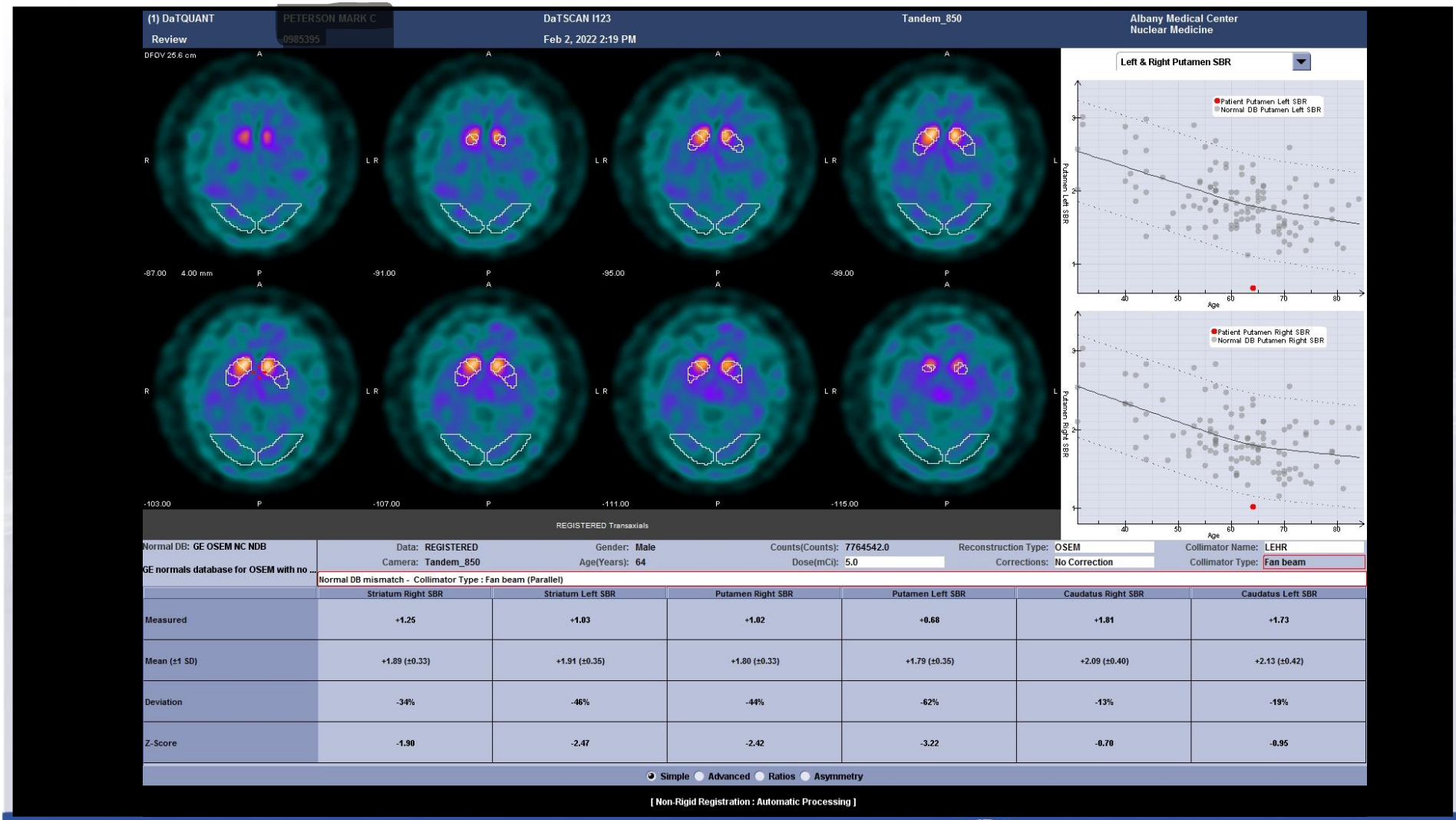
- Nuclear medicine imaging of dopamine activity in the brain region most effected by PD
- Reflects the integrity of the dopamine producing brain cells
- Abnormal scan confirms a degenerative cause of PDism
- Does not separate PD from atypical forms of PDism (MSA, PSP, DLB)
- Can still have PDism with normal scan (drug-induced PDism
- Not a reliable way to predict prognosis or measure progression

DaTscan - normal

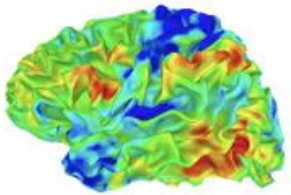


DaTscan

-reduced DA activity = loss of DA brain cells
-doesn't distinguish between PD, DLB, MSA or PSP



Web-based Automated Imaging Differentiation of Parkinsonism

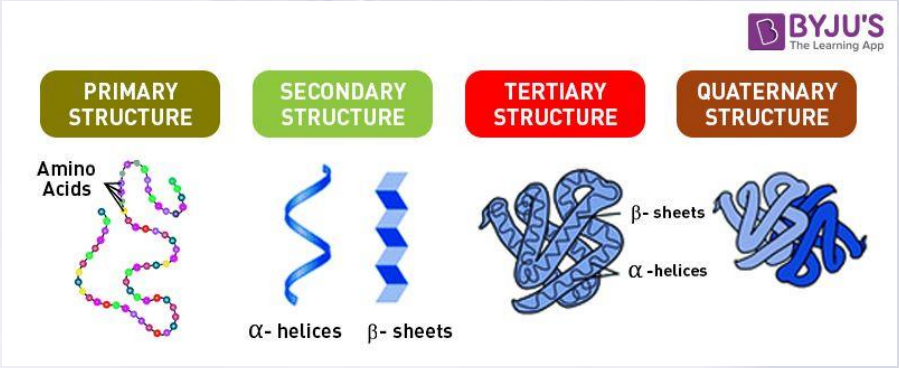


- Multicenter study developed by UF Gainesville/ sponsored by NIH
- AMC is one of 21 study sites in USA*
- Clinical examinations/video exam = clinical best diagnosis (PD vs MSA vs PSP)
- Brain MRI with special imaging sequences and computer analysis (machine learning) = imaging diagnosis
- Hopefully will be accurate, non-invasive way to diagnose different forms of PDism

* Most awesome site!

What is alpha-synuclein?

- A complex protein used throughout the brain
- Abnormal forms are part of PD pathology
- 2 genetic causes of PD involve the alpha-synuclein gene
- Abnormal forms seem to be toxic to brain cells and can spread from sick cells to healthy cells
  - Phosphorylated
  - Aggregated/clumped



Where is abnormal alpha-synuclein found outside the brain?

- Peripheral nervous system (PNS)
  - GI tract - colonoscopy biopsies
  - Salivary glands
  - Skin
- Cerebrospinal Fluid (CSF)
- Blood???

REVIEW ARTICLE

EJN European Journal of Neuroscience FENS WILEY

How close are we to a breakthrough? The hunt for blood biomarkers in Parkinson's disease diagnosis

Cheng Liu | Yang Su | Xiaolong Ma | Yao Wei | Rui Qiao

Peking University Third Hospital, Beijing, China

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Funding information
: This work was supported by the National Natural Science Foundation of China (program no. 82072352).

Edited by: Yoland Smith

Abstract

Parkinson's disease (PD), being the second largest neurodegenerative disease, poses challenges in early detection, resulting in a lack of timely treatment options to effectively manage the disease. By the time clinical diagnosis becomes possible, more than 60% of dopamine neurons in the substantia nigra (SN) of patients have already degenerated. Therefore, early diagnosis or identification of warning signs is crucial for the prompt and timely beginning of the treatment. However, conducting invasive or complex diagnostic procedures on asymptomatic patients can be challenging, making routine blood tests a more feasible approach in such cases. Numerous studies have been conducted over an extended period to search for effective diagnostic biomarkers in blood samples. However, thus far, no highly effective biomarkers have been confirmed. Besides classical proteins like α-synuclein (α-syn), phosphorylated α-syn and oligomeric α-syn, other molecules involved in disease progression should also be given equal attention. In this review, we will not only discuss proposed biomarkers that are currently under investigation but also delve into the mechanisms underlying the disease, focusing on processes such as α-syn misfolding, intercellular transmission and the crossing of the blood–brain barrier (BBB). Our aim is to provide an updated overview of molecules based on these processes that may potentially serve as blood biomarkers.

Submandibular gland needle biopsy for the diagnosis of Parkinson disease

Conclusions: This study demonstrates the feasibility of performing needle core biopsies of the submandibular gland in living patients with PD to assess LTS. Although this was a small study, this tissue biopsy method may be important for tissue confirmation of PD in patients being considered for invasive procedures and in research studies of other PD biomarkers. *Neurology®* 2014;82:858-864

Figure 1 Needle biopsy of the submandibular gland

JAMA | Original Investigation

Skin Biopsy Detection of Phosphorylated α-Synuclein in Patients With Synucleinopathies

Christopher H. Gibbons, MD, MMSc; Todd Levine, MD; Charles Adler, MD, PhD; Bailey Bellaire, BS; Ningshan Wang, PhD; Jade Stohl, BA; Pinky Agarwal, MD; Georgina M. Aldridge, MD, PhD; Alexandru Barboi, MD; Virgilio G. H. Evidente, MD; Douglas Galasko, MD; Michael D. Geschwind, MD, PhD; Alejandra Gonzalez-Duarte, MD; Ramon Gil, MD; Mark Gudesblatt, MD; Stuart H. Isaacson, MD; Horacio Kaufmann, MD; Pravin Khemani, MD; Rajeev Kumar, MD; Guillaume Lamotte, MD, MMSc; Andy J. Liu, MD, MS; Nikolaus R. McFarland, MD, PhD; Mitchell Miglis, MD; Adam Reynolds, MD; Gregory A. Sahagian, MD; Marie-Helene Saint-Hillaire, MD, PhD; Julie B. Schwartzbard, MD; Wolfgang Singer, MD, PhD; Michael J. Sofleau, MD; Steven Vernino, MD, PhD; Oleg Yerstein, MD; Roy Freeman, MD

Table 2. Primary Outcomes

Diagnosis	Participants, No.		Proportion of participants positive for P-SYN, % (95% CI)
	P-SYN positive[a]	P-SYN negative[b]	
Synucleinopathy	213	10	95.5 (91.9-97.8)
Parkinson disease	89	7	92.7 (85.6-97.0)
Multiple system atrophy	54	1	98.2 (91.7-99.9)
Dementia with Lewy bodies	48	2	96.0 (86.3-99.5)
Pure autonomic failure	22	0	100 (84.6-100)
No synucleinopathy	4	116	3.3 (1.3-8.0)

SCIENCE NEWS

A Skin Test Could Detect Parkinson's and Related Diseases

May 02, 2024

New research indicates that a skin biopsy could possibly lead to accurate diagnosis of Parkinson's and other neurodegenerative diseases.

SYN-ONE TEST®

A NEW MILESTONE IN DIAGNOSING PARKINSON'S DISEASE AND RELATED DISORDERS

The Syn-One Test is the first commercially available test of its kind, applying world-class science and proven laboratory techniques to detect and visualize abnormal alpha-synuclein in cutaneous nerves. Delivers greater than 95% sensitivity and specificity as reported in multiple studies.

Limitations of peripheral nervous system biopsy techniques

- May not be reliable in early/pre-symptomatic disease
- May not reliably separate from PD from related conditions (DLB, MSA)
- Doesn’t measure progression, prognosis
- Cost/insurance coverage
- No better than DaTscan?

Spinal Fluid Biomarkers for PD

Why We Exist | Understanding Parkinson's | For Researchers | Take Action

Podcasts

Major Research Breakthrough: A New Biomarker for Parkinson's (Webinar Audio)

April 26, 2023

0:00 / 58:59

Assessment of heterogeneity among participants in the Parkinson's Progression Markers Initiative cohort using α-synuclein seed amplification: a cross-sectional study

Andrew Siderowf, Luis Concha-Marambio*, David-Erick Lafontant, Carly M Farris, Yihua Ma, Paula A Urenia, Hieu Nguyen, Roy N Alcalay, Lana M Chahine, Tatiana Foroud, Douglas Galasko, Karl Kieburtz, Kalpana Merchant, Brit Mollenhauer, Kathleen L Poston, John Seibyl, Tanya Simuni, Caroline M Tanner, Daniel Weintraub, Aleksandar Videnovic, Seung Ho Choi, Ryan Kurth, Chelsea Caspell-Garcia, Christopher S Coffey, Mark Frasier, Luis M A Oliveira, Samantha J Hutten, Todd Sherer, Kenneth Marek, Claudio Soto, on behalf of the Parkinson's Progression Markers Initiative†*

Lancet Neurol 2023; 22: 407–17

- Taken from **PPMI** cohort: 545 PD, 163 HC, 51 prodromal (RBD, anosmia), 310 non-manifesting gene carriers
- Analysis (SAA) done on spinal fluid (required spinal tap)
- α-syn SAA had a sensitivity of 87.7% in PD, 96.3% in HC
- May be able to detect prodromal PD
- Not as accurate in PD with LRRK2 or without anosmia
- Specificity for PD vs Lewy body dementia/other atypical forms of Pdism is unclear but appears not to be associated with MSA
- Testing is technically demanding and not widely available

Paws for thought: dogs sniff out Parkinson's disease with 90% hit rate

Author: Almaz OhenePublished: 27 October 2016

Dogs involved in a groundbreaking pilot study have detected Parkinson's disease on sample clothing with a successful hit rate of up to 90% – no we're not barking mad!

Why are biomarkers useful?

- Diagnosis of disease
- Prediction of disease
  - "Hey doc, should I worry about getting parkinsons?"
- Measuring progression of disease/ detecting response to treatment
- Understanding prognosis

Can we predict who is going to get PD?

- Genetic testing
  - Monogenetic forms only account for small percentage of cases
  - Having a gene mutation doesn't always predict disease
- Prodromal features
  - Anosmia, REM sleep behavior disorder, chronic constipation
- Pre-symptomatic application of blood, CSF, imaging biomarkers?
- Short answer: Not yet.

Why are biomarkers useful?

- Diagnosis of disease
- Prediction of disease
- Measuring progression of disease/ detecting response to treatment
  - "Hey doc, am I getting worse?"
- Understanding prognosis

How can we measure disease progression?

- Very important for understanding success or failure of experimental disease modifying/slowing treatments
- Clinical measures not reliable enough, especially in treated patients (ldopa)
- Imaging measures (DaTscan) haven't always agreed with clinical measures in studies
- Biochemical signs of neurodegeneration might measure progression in near future (NFL)
- Clearly, more work to be done here

Why are biomarkers useful?

- Diagnosis of disease
- Prediction of disease
- Measuring progression of disease/ detecting response to treatment
- Understanding prognosis
  - "Hey doc, am I going to develop dementia?"

Can we predict which patients will develop advanced disease complications and when?

- Dementia
  - Psychosis
- Imbalance/freezing gait
  - Falling
  - Hip fractures
- Loss of independance

- Short answer: No

How about prevention of advance disease complications?

- No disease modifying medications yet
- No dietary supplement proven to slow or prevent disease yet (in humans)
- Exercise has been shown to slow progression in PD and reduce dementia risk in PD and AD!!

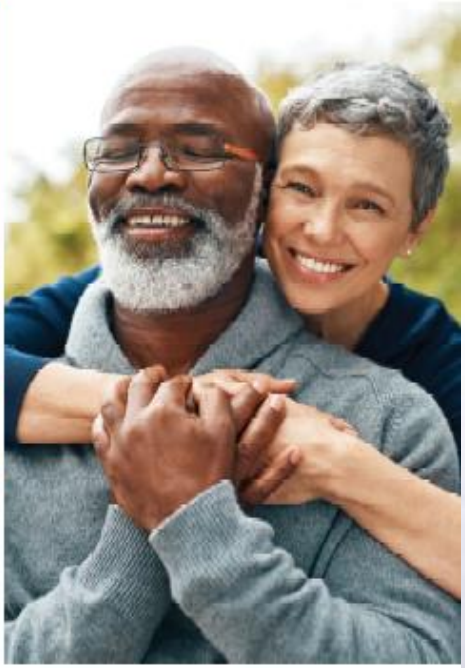
How about preventing hip fractures?

Join a Parkinson's Disease and parkinsonism Study without ever leaving your home

PARTICIPANTS NEEDED

TOPAZ

TRIAL OF PARKINSON'S AND ZOLEDRONIC ACID



Did you know?
People with Parkinson's Disease and parkinsonism have a higher risk of fractures (breaking bones).

Help us find a solution.
The TOPAZ study will test if a medicine called zoledronate can prevent fractures in people with Parkinson's Disease and parkinsonism. A team of doctors who are experts in bone health and Parkinson's Disease are leading the study. The use of zoledronate in this study is investigational.

You can join if you:
- Have Parkinson's Disease or parkinsonism.
- Are 60 years old or older.

This study is done from your home!
- If you are eligible for the study, a nurse will come to your home to give you a short exam.
- You'll receive a one-time dose of the study treatment (either zoledronic acid or a placebo).
- During the study, we will contact you every four months to check if you have had any new fractures.

Earn $100 upon enrollment & $50 per year during the study.

Want to learn more about joining TOPAZ?

Ready to join? Visit **topazstudy.org** and enter invitation code

or call:
1-800-4PD-INFO
(1-800-473-4636)

This study is endorsed by:

Parkinson's Foundation

PSG
PARKINSON STUDY GROUP

Study Assessments

- Online Screening
  - Determine eligibility
- Nurse home visit
  - Premedication with Vit D x 1 month
  - Premedication with acetominphen 1000mg
  - Finger stick for kidney function
  - Mouth exam
  - Infusion over 45 minutes
- Remote follow up
  - Every 4 months via phone, email, mail, online

Biomarkers in PD - Conclusions

- Much progress made
- Much work to be done
- Biomarker development will play a critical role in the effort to cure PD
  - Early identification of PD – prodromal, presymptomatic
  - Accurate measurement of PD progression
  - Successful disease modifying therapies will have to be applied in very early disease and we will need to have an accurate way to show slowed progression

Thank you for your attention!