



Beyond the Diagnosis:

Managing Changing Symptoms

Hosted by the Parkinson's
Foundation Gulf Coast Chapter

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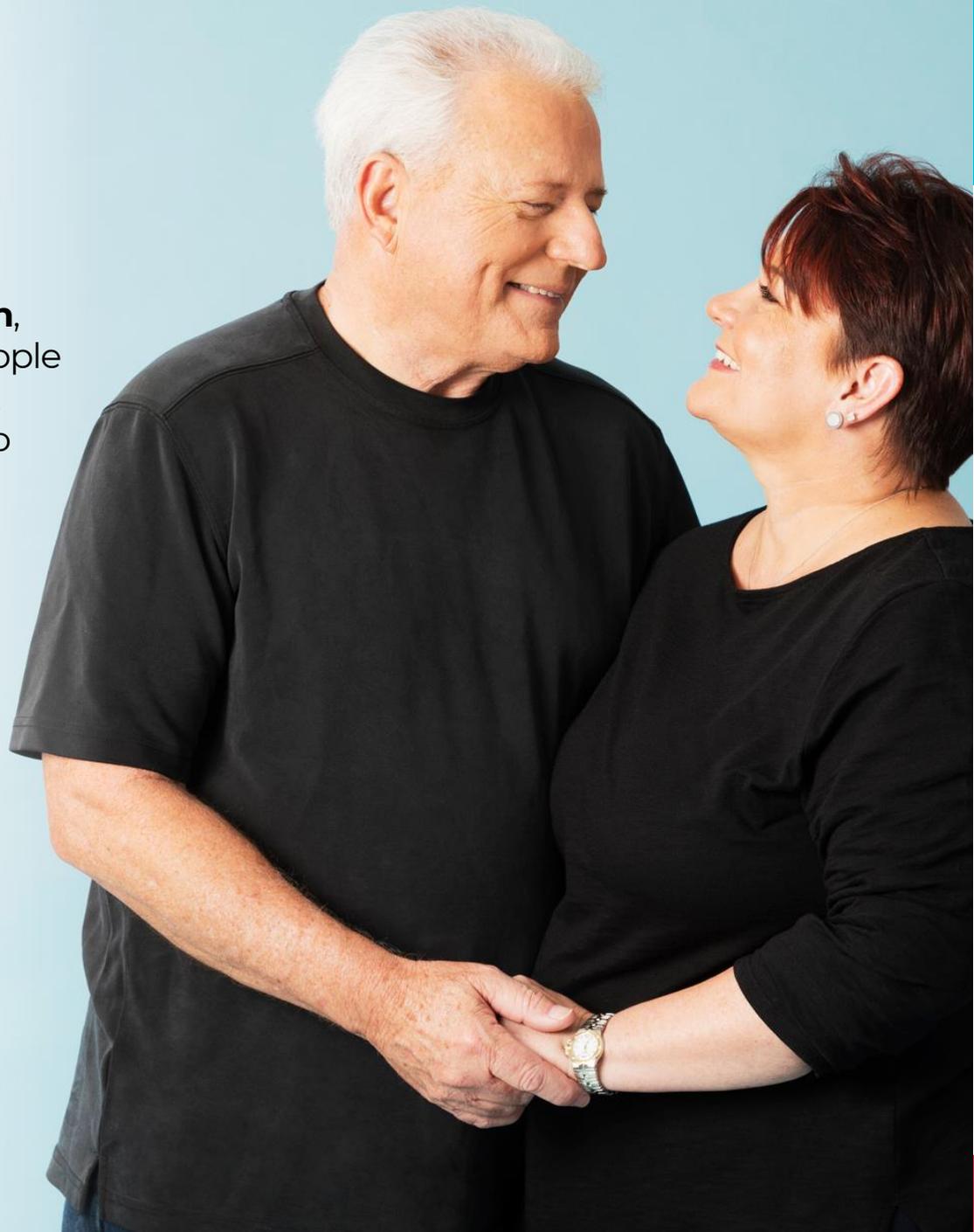


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those who love them and those who
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The one million Americans living
with PD deserve the promise
of a cure and a better life today.

**We have everything you need to
live better with Parkinson's.**



For Today: Learn More To Live Better

We help people live well with PD by providing families with free resources including: educational books, webinars, podcasts, a life-saving hospitalization kit and our toll-free Helpline, staffed by Parkinson's specialists who answer nearly **20,000 calls annually**.



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Please participate in our **PD Health @ Home** events.

- Mindfulness Mondays
- Wellness Wednesdays
- Fitness Fridays



Visit [**parkinson.org/PDhealth**](https://parkinson.org/PDhealth) to learn about upcoming events and to register.

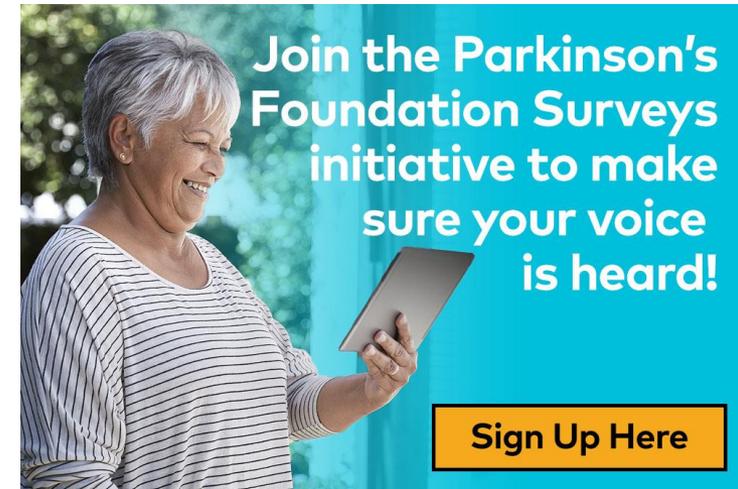
Join Parkinson's Foundation Surveys



People with Parkinson's help design and review each survey. We collaborate with researchers from our Centers of Excellence and pharmaceutical partners to design surveys that meet research and community interests.

Recent Parkinson's Foundation survey findings include:

- COVID-19 and Parkinson's
- Cannabis Use and Parkinson's
- Exercise Professionals



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- **[Facebook.com/PFGulfCoastChapter](https://www.facebook.com/PFGulfCoastChapter)**
- Community Grant Programs
- 2 Moving Day Events
- Educational Programming

Apply for a Community Grant!

- \$1 million in community grant funding
- Community Grants support health, wellness and education programs that address unmet needs in the Parkinson's disease (PD) community
- Applications are due Jan. 28, 2022
- For more information and to apply, please visit: [Parkinson.org/CommunityGrants](https://www.parkinson.org/CommunityGrants)

Upcoming Events in the Gulf Coast

On the Menu: Nutrition in Parkinson's (Baton Rouge, LA)

Friday, March 11, 2022, 10 a.m. – 12 p.m. CT | Paula G. Manship YMCA

Featured Speakers: Gerald J. Calegan, II, MD, The NeuroMedical Center and Sarah Broekhoven, MS, RDN, LDN, YMCA of the Capital Area

Register: [Parkinson.org/BatonRougeEdu](https://www.parkinson.org/BatonRougeEdu)

Beyond the Diagnosis: Next Steps in Treatment (Biloxi, MS)

Saturday, March 12, 2022, 10 a.m. – 12 p.m. CT | South Beach Event Center

Featured Speaker: Daniel D. Dees, MD, USA Health

Register: [Parkinson.org/BiloxiEdu](https://www.parkinson.org/BiloxiEdu)

Veterans with Parkinson's: Building Your Care Team (VIRTUAL – Zoom)

Tuesday, March 15, 2022, 11 a.m. – 1 p.m. CT

Featured Speaker: Danielle S. Shpiner, MD, University of Miami Miller School of Medicine and the Bruce W. Carter VA Medical Center

Register: [Parkinson.org/SEVets](https://www.parkinson.org/SEVets)

Let's Talk About It: Symptoms Beneath the Surface (Jackson, MS)

Friday, April 22, 2022, 10 a.m. – 12:30 p.m. CT | First Baptist Jackson

Featured Speaker: Juebin Huang, MD, University of Mississippi Medical Center

Register: [Parkinson.org/JacksonEdu](https://www.parkinson.org/JacksonEdu)

Moving Day Walks in the Gulf Coast

Moving Day Baton Rouge

Saturday, April 2, 2022

Register today at
MovingDayBatonRouge.org

Moving Day South Alabama

Saturday, April 9, 2022

Register today at
MovingDaySouthAlabama.org



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June 11, 2022 – Birmingham, AL | Greystone YMCA

Parkinson's Revolution is an indoor cycling experience that combines passion, determination and community to generate awareness and advance our mission toward a cure.

Register Today: [Parkinson.org/Revolution](https://www.parkinson.org/Revolution)

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Helpline@Parkinson.org**



Beyond the Diagnosis:

Managing Changing Symptoms

Marissa Dean, MD

Assistant Professor of Neurology

Division of Movement Disorders

University of Alabama at Birmingham

January 21, 2022



None relevant to this lecture.

Research support:

Abbvie, Inc., CHDI Foundation, Inc., Hoffman-La Roche, Retrophin, Inc., Annexon, Inc., Michael J. Fox Foundation for Parkinson's Research, Neurocrine Biosciences, Praxis Precision Medicines, Jazz Pharmaceuticals, Inc., UniQure Biopharma B.V.

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(W81XWH-18-1-0508)

Learning Objectives

- Understand **symptom progression and common mid-stride challenges** such as motor fluctuations, dyskinesias, dystonia and freezing of gait.
- Learn about **more complex medication and multidisciplinary management for changing symptoms**
- Learn when it is **appropriate to expand the Parkinson's care team and seek out rehabilitative therapies or other healthcare services.**

Poll

Are you:

1. A patient with Parkinson's disease?
2. A caregiver for someone with Parkinson's disease?
3. Other?

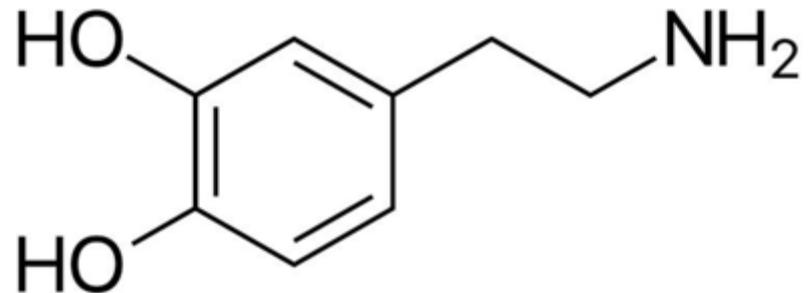
- **Cardinal Features:**
 - Resting tremor
 - Bradykinesia (slowness of movements)
 - Rigidity
 - Postural Instability (imbalance)
- **NOTE:** These features vary between each patient, including severity.

Stages in Parkinson's disease

Stage	Features
Stage 1	Symptoms on only one side of the body
Stage 2	Symptoms on both sides of the body, but no imbalance
Stage 3	Symptoms on both sides of the body, with some imbalance
Stage 4	Requires help with some daily activities, but able to walk or stand independently
Stage 5	Requires assistance to walk

Dopamine deficit in Parkinson's disease

- Injury to cells in brain producing **dopamine**
 - Brain transmitter important in **motor pathways** of brain
 - Other areas require dopamine, including the **gut**



Medications for motor symptom management

- Primarily act on **dopamine pathways** of brain, in 3 ways:
 1. Dopamine **replacement** (carbidopa/levodopa)
 2. **Stimulation** of dopamine receptors (dopamine agonists)
 3. Blocking **dopamine breakdown** or **stimulating release** of dopamine (examples to follow)

Poll

Do you currently take carbidopa/levodopa?

1. Yes
2. No

Medications for motor symptom management

- **Initiation of treatment:**
 - **Individualized** to each patient
- **Patients may or may not notice:**
 - **ON state** (medications working well)
 - **OFF state** (medications not working)
- **Motor symptoms can remain well-controlled without complications for years**

“Mid-stride” Parkinson’s disease

- **As Parkinson’s disease progresses:**
 - Less dopamine produced by body
 - Brain (dopamine receptors) may become more sensitive to changes in dopamine levels
- **Patients may notice corresponding changes in symptoms and medication response.**
 - Can be effectively managed with adjustments to medication and other treatment!

Common issues in “Mid-stride” Parkinson’s disease

■ Motor fluctuations:

- Fluctuation of motor symptoms relative to medication doses
- Main issues:
 - Medications “**wear off**”
 - Excessive, **involuntary movements** related to medications themselves
 - Dyskinesias
 - Dystonia

Poll

Have you experienced:

1. Wearing off?
2. Dyskinesia?
3. Dystonia?

Motor Fluctuations: Wearing off

- **Definition: recurrence of Parkinson's disease symptoms as dopaminergic medications wear off**
 - Motor symptoms: stiffness, slowness, tremor
 - Non-motor symptoms: tingling, restlessness, sweating, fatigue/malaise, anxiety
- Over time, fluctuations may become more frequent or noticeable

■ Management: Avoiding OFF states

- Adjust **timing and/or dose** of dopaminergic medication to address problematic periods of day
 - Keep symptom diary to track timing of symptoms relative to medications
- Add dopamine agonist or carbidopa/levodopa to regimen
- In some cases, adjust timing of medications **relative to meals**
 - Avoid high protein meals (e.g., meat, eggs) 30 minutes prior to levodopa

Motor Fluctuations: Wearing off

■ Management: Avoiding OFF state

- Medications to **increase duration of medication effect** (prevent breakdown of dopamine)

Category	Benefits	Possible downsides
Catechol-O-methyltransferase (COMT) inhibitors: entacapone, opicapone	<ul style="list-style-type: none">■ Extends effect of levodopa	<ul style="list-style-type: none">■ May worsen dyskinesia
Monoamine oxidase B (MAOB) inhibitors: rasagiline, selegiline, safinamide	<ul style="list-style-type: none">■ Extends effect of levodopa	<ul style="list-style-type: none">■ May worsen dyskinesia■ Side effects: insomnia, headache, GI upset■ Cost

Motor Fluctuations: Wearing off

■ Management: Avoiding OFF state

- **Longer-acting** forms of levodopa

Medication	Benefits	Possible downsides
Carbidopa/levodopa Controlled Release formulation	<ul style="list-style-type: none">■ Slower release than immediate release carbidopa/levodopa■ Helps with: Wearing off	<ul style="list-style-type: none">■ May worsen dyskinesia■ Slightly lower effective dose (dose may have to be increased)■ Takes time to 'kick in'
Carbidopa/levodopa Extended Release capsules (Rytary)	<ul style="list-style-type: none">■ Short and long-acting levodopa formulations in one capsule■ Helps with: wearing off	<ul style="list-style-type: none">■ May worsen dyskinesia■ Cost

Motor Fluctuations: Wearing off

- **Management: Avoiding OFF state**
 - **Add-on medication to prevent OFF state**

Medication	Benefits	Possible downsides
Adenosine receptor blocker: Istradefylline (Nourianz)	<ul style="list-style-type: none">■ Decreases daily OFF time	<ul style="list-style-type: none">■ Dyskinesia, hallucinations, impulse control disorders

Motor Fluctuations: Wearing off

■ Management: Treating OFF state (“Rescue” medications)

- Shorter-acting forms of levodopa

Medication	Benefits	Possible downsides
Carbidopa/levodopa immediate release (chewed, taken with ample water)	<ul style="list-style-type: none">■ Ease of use	<ul style="list-style-type: none">■ (*Nausea, low blood pressure, dyskinesias, hallucinations)
Carbidopa/levodopa DISINTEGRATING tablets (sublingual (placed under tongue))	<ul style="list-style-type: none">■ Ease of use■ Faster absorption than immediate release	<ul style="list-style-type: none">■ Nausea, low blood pressure, dyskinesias, hallucinations
Levodopa INHALATION powder	<ul style="list-style-type: none">■ Faster absorption than immediate release	<ul style="list-style-type: none">■ Avoid with lung disease■ Less ease of use

* With all forms of levodopa

Motor Fluctuations: Wearing off

- **Management: Treating OFF state (“Rescue” medications)**
 - Add-on medication to facilitate ON state

Medication	Benefits	Possible downsides
Dopamine agonist: Apomorphine (subcutaneous injection) or sublingual (under tongue) formulations)	<ul style="list-style-type: none">■ Fast onset of action	<ul style="list-style-type: none">■ Risk of low blood pressure (requires monitoring to start)■ Dyskinesia, nausea, hallucinations■ Injection (subcutaneous formulation)

Motor Fluctuations: Other treatment options

- **Management:** What if non-invasive management/medications are not effective?

Medication	Benefits	Possible downsides
Carbidopa/levodopa Intestinal gel (Duopa)	<ul style="list-style-type: none">■ Continuous daytime delivery of carbidopa/levodopa gel by surgical placement of tube into small intestine for delivery of medication	<ul style="list-style-type: none">■ *Surgical procedure■ Risk of low blood pressure (requires monitoring)■ Nausea, dyskinesias

Motor Fluctuations: Other treatment options

- **Deep brain stimulation** surgery may be an option for symptoms not adequately controlled with medication adjustments, **for some patients**
 - Involves surgical procedures to place small wires into specific brain structures and insert battery into chest wall
 - Precise electrical stimulation constantly delivered to specific brain areas
 - Can improve some motor symptoms at least as well as levodopa, without fluctuations
 - Programming is adjusted over time to target changing symptoms

Motor Fluctuations: Other treatment options

- **Focused ultrasound** may be an option for symptoms not adequately controlled with medication adjustments, **for some patients**
 - Non-surgical procedure that used ultrasound beams to create thermal lesions deep in the brain
 - FDA approved for PD symptoms in December 2021
 - Can improve some motor symptoms at least as well as levodopa, without fluctuations
 - May be option for patient's at higher risk for surgery

Motor Fluctuations: Dyskinesias

- **Definition:** Involuntary, repetitive movements which may involve face, trunk or limbs.
 - Consequence of exposure to dopamine medications in patients with Parkinson's disease
 - **Not** harmful and may not bother the patient, but may cause discomfort

■ Management: Avoiding dyskinesias

- May occur in ON or OFF state (or both)
 - Symptom journal
- Adjust dopaminergic medication dosing or timing
- Extend duration of dopaminergic medications (OFF dyskinesias)

Motor Fluctuations: Dyskinesias

- **Management: Treating dyskinesias**
 - Direct treatment of dyskinesias

Medication	Benefits	Possible downsides
Amantadine (long-acting and short-acting formulations)	<ul style="list-style-type: none">■ May reduce dyskinesia severity or frequency	<ul style="list-style-type: none">■ Leg swelling, skin changes■ Hallucinations

Motor Fluctuations: Dystonia

- **Definition:** Involuntary, excessive muscle contraction of specific muscles
 - Can occur in face, trunk, limbs.
 - Examples: Toe curling/cramping, foot turning
 - May be painful

- **Management: Avoiding dystonia**
 - May occur in ON or OFF state
 - symptom journal
 - Adjust dopaminergic medication dosing/timing

- **Management: Treating dystonia**
 - Botulinum toxin injections to affected muscles
 - Benefits: Minimal risk of systemic side effects
 - Downsides:
 - Risk of temporary weakness
 - Not available in all areas (requires special training)
 - Oral medications: trihexyphenidyl, clonazepam
 - Downsides: May be limited by side-effects (sleepiness)

Motor Fluctuations: Freezing of gait

- **Definition:** sudden episodes of inability to move feet forward when attempting to walk
 - “My feet feel like they’re stuck to the floor”
- Significant impact on quality of life
 - Increases fall risk
- Cause is unknown but involves several different brain areas

Motor Fluctuations: Freezing of gait

- **Management:**

- Identify if in ON state or OFF state
 - Symptom journal
- Adjust dopaminergic medications, if freezing occurs in OFF state

- **Management:** In either OFF or ON state freezing:
 - Physical therapy!!
 - Strategies:
 - Shift weight
 - Shift attention to another task/movement
 - Visual cueing (e.g., laser pointer)
 - Auditory cueing: music
 - Avoid triggers:
 - Tight spaces (thresholds, revolving doors)
 - Rushing
 - Take wide turns

- **Regular exercise is critical in Parkinson's disease!**
 - Improves symptoms
 - Slows disease progression
- **Options:**
 - BIG physical therapy
 - PD exercise classes
 - Boxing
 - Dance
 - ****Any form of exercise if effective! Most important to be safe and enjoyable**
 - **Consistent**

■ Care team

- Movement Disorders Neurologist
 - Physical therapy
 - Occupational therapy
 - Speech therapy
-
- Other physicians, if needed: Important for all of your providers to be aware of your diagnosis
 - Psychiatry/psychotherapy
 - Urology
 - Internal medicine (blood pressure)

- Motor fluctuations are a normal part of mid-stride Parkinson's disease
- Multiple medications available to improve **duration of symptom control** or to achieve **faster symptomatic relief**
- Understanding **recurring patterns in timing** of symptoms can help to tailor treatment plan
- A **combination of medications/formulations** in mid-stride disease is often used to tailor symptom control
- Physical therapy and exercise can have significant effects in improving symptoms and slowing disease progression!!

THANK YOU!

Questions?

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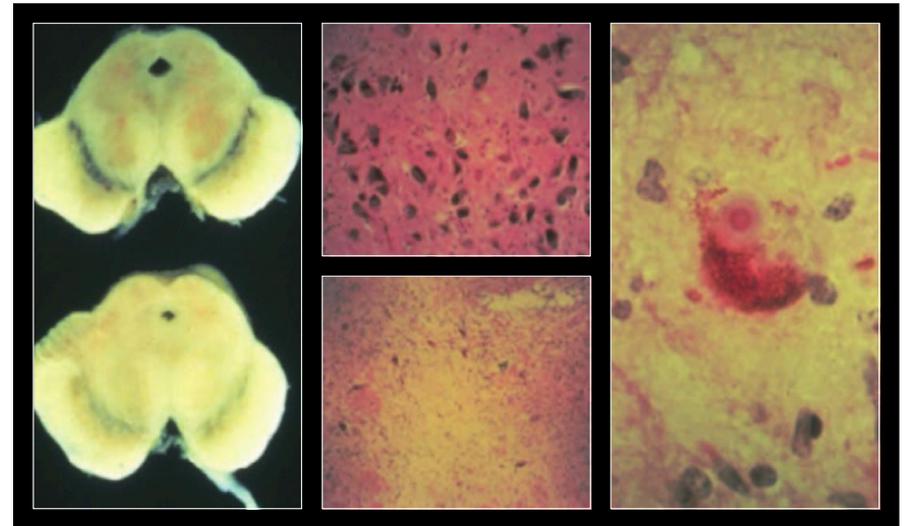
Exercise and Parkinson's Disease

Amy W. Amara, MD, PhD

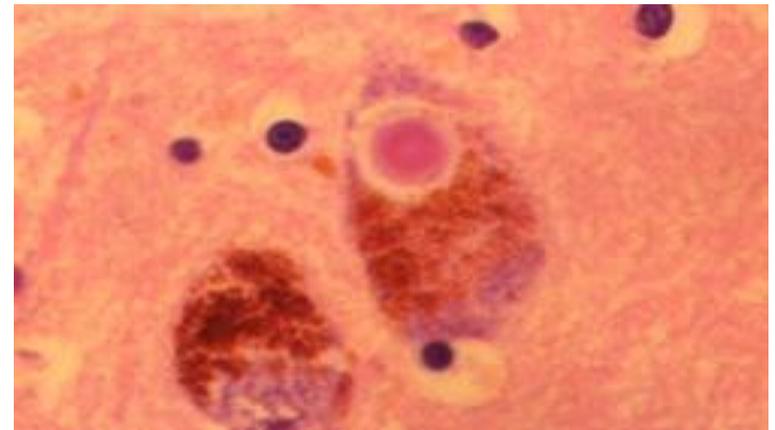
January 21, 2022

Parkinson's Disease

- Motor Symptoms
 - Slowness of Movement
 - Stiffness
 - Rest tremor
 - Postural Instability



Sir William Gowers
PD sketch 1886



Olanow et al. Neurology 72(Suppl 4):S1 2009

Exercise



Different Types of Exercise



Endurance (Aerobic) Exercise



Resistance (Weight training) Exercise



Aquatic Exercise



Tai Chi/Stretching/Dance

Beneficial Effects of Exercise



- Cardiovascular Health



- Reduced stroke risk



- Improved bone health



- Improved physical fitness



- Sleep consolidation and increased alertness



- Improved cognition

Barriers to exercise



- Pain



- Fear of falling



- Impaired fitness



- Low confidence (Self-efficacy)

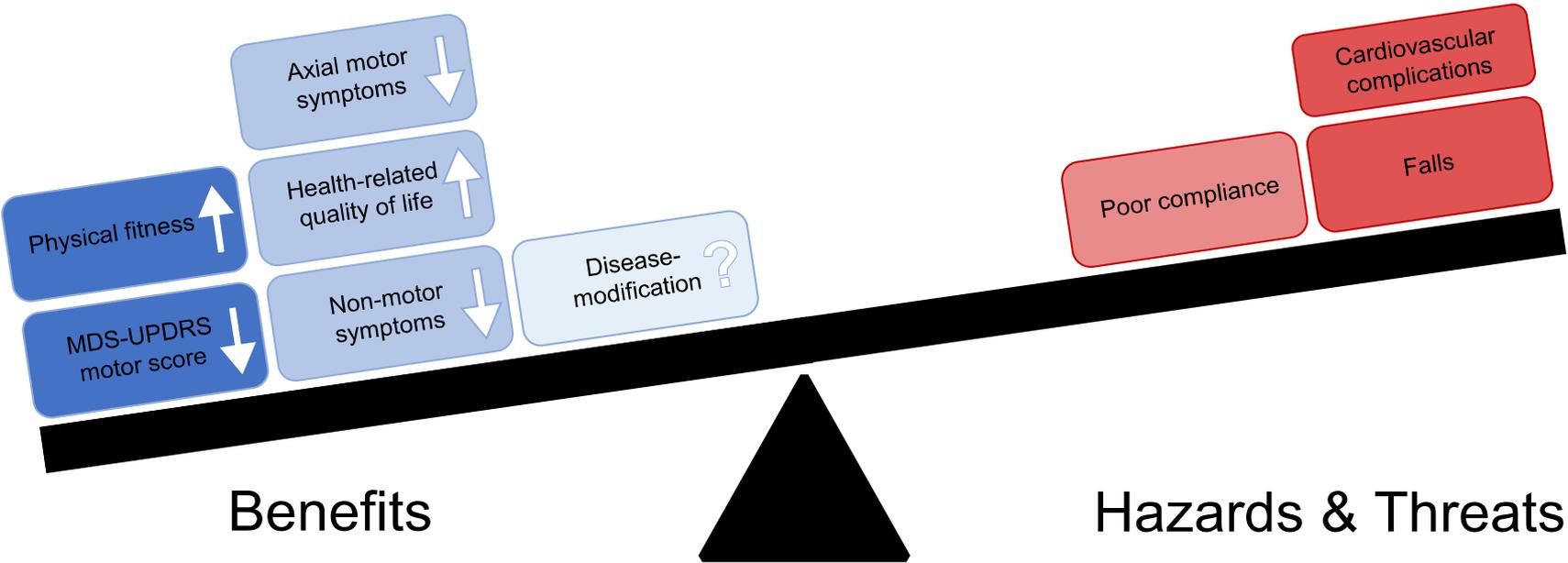


- Other obligations



- Fatigue

Exercise and Parkinson's Disease



Benefits

Hazards & Threats

Schootemeijer et al. Neurotherapeutics 2020. 17:1418

Exercise and Parkinson's Disease

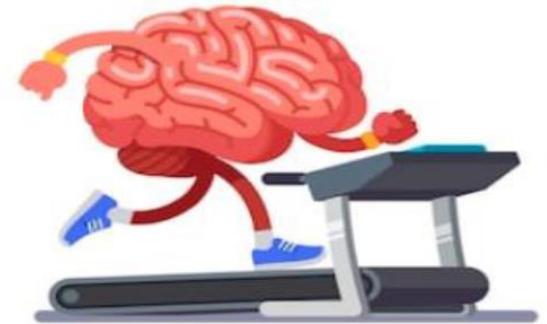
- Large epidemiological studies show that people with more physical activity have lower risk of PD
- Higher activity levels are associated with slower progression of motor symptoms and cognitive impairment over time in PD
- Physical activity levels decrease with disease progression in PD



Saaksjarvi K, et al. Eur J Epidemiol 2014;29:285-292.; Chen H et al. Neurology 2005;64:664-669. Thacker et al. Mov Disord 2008;23:69-74; Oguh et al. Parkinsonism Relat. Disord. 2014. 20: 1221. Xu Q et al. Neurology 2010;75:341-348; Amara et al. Parkinsonism and Rel Disord. 2019. 61:118

Effects of Exercise on Motor Symptoms¹

- Exercise can improve motor symptoms, balance, walking speed in PD
- Study in Parkinson's Disease of Exercise (SPARX)
 - High intensity exercise (treadmill) was safe and showed less worsening of motor symptoms compared to no exercise
- Ongoing: SPARX3 (recruiting newly diagnosed patients with Parkinson's disease who are not yet on medications)



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Exercise and Non-Motor Symptoms

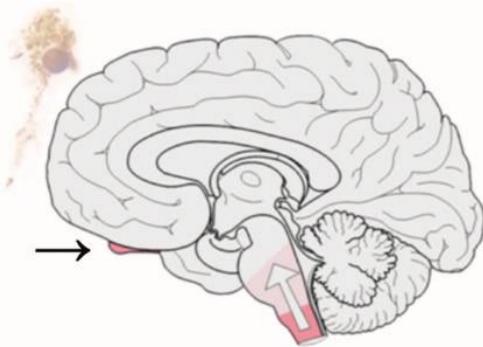
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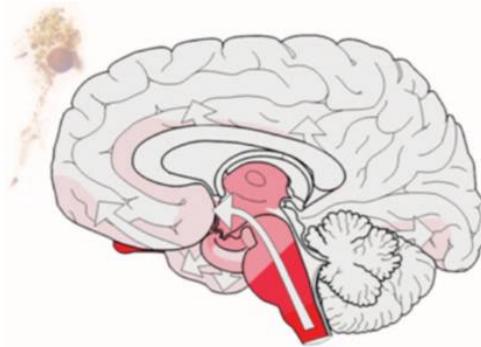
Cognitive Problems in Parkinson's Disease

Cognitive Problems in PD

- PD → Increased risk for cognitive impairment
- Affects quality of life and daily functioning



Braak Parkinson's disease stages 1 & 2
PRECLINICAL



Braak Parkinson's disease stages 3 & 4
CLINICAL PARKINSON'S DISEASE



Braak Parkinson's disease stages 5 & 6
COGNITIVE IMPAIRMENT

This hypothesis suggests that pathologic changes are first noted in the olfactory region and lower brainstem, and only later extend to involve dopamine neurons in the SNc (Courtesy of Heiko Braak).

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How does exercise affect cognition?

Exercise and cognition

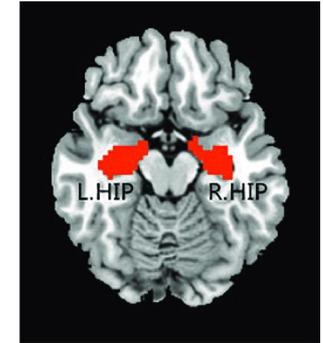
- Exercise in healthy adults improves performance on tests of memory, attention, processing speed, and executive function
- Exercise in mid-life reduces risk of dementia and mild cognitive impairment
- People with dementia who participate in an exercise intervention have better cognitive testing scores compared to sedentary participants



Ahlskog *et al.* Mayo Clinic Proc. 86:876 2011

Exercise and Cognition

- Exercise increases brain volume and enhances connectivity in the brain
- Exercise reduces risk factors associated with dementia (cardio/cerebrovascular disease)
- Exercise increases production of neurotrophic factors in animals and humans



Ahlskog *et al.* *Mayo Clinic Proc.* 86:876 2011
Xue *et al.* *Frontiers in Aging Neuroscience.* 11. 2019

Exercise and Cognition in PD

- Different types and durations of exercise have been studied
- Adapted tango → improved visuospatial function
- Passive cycling → improved executive function
- Aerobic exercise → improved executive function
- Resistance training → improved attention and working memory



McKee and Hackney *J. Mot Behav.* 45:519, 2013
Ridgel *et al. J. Aging Phys Act.* 19:87, 2011
Tanaka *et al. Brain Cogn.* 69:435, 2009
David *et al. Mov. Disord.* 30:1657, 2015

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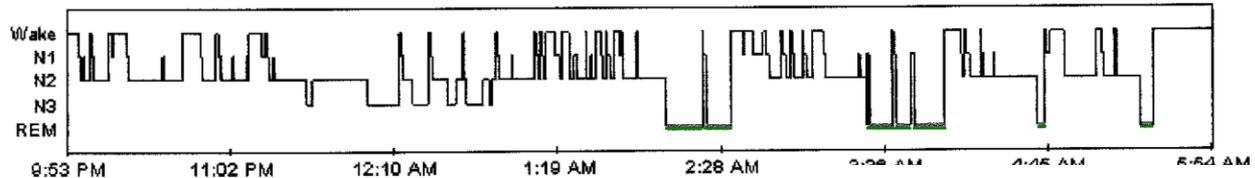
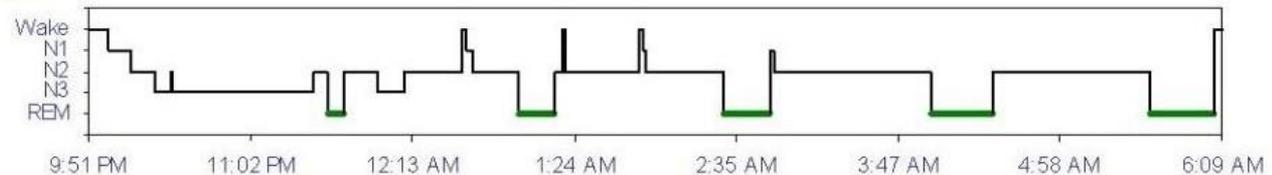
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Sleep in Parkinson's Disease

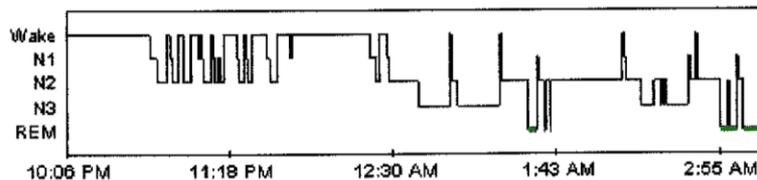
Sleep in Parkinson's Disease

- Sleep problems are common and disabling
- Reduced sleep efficiency and decreased deep sleep
- Sleep fragmentation

Healthy Adult

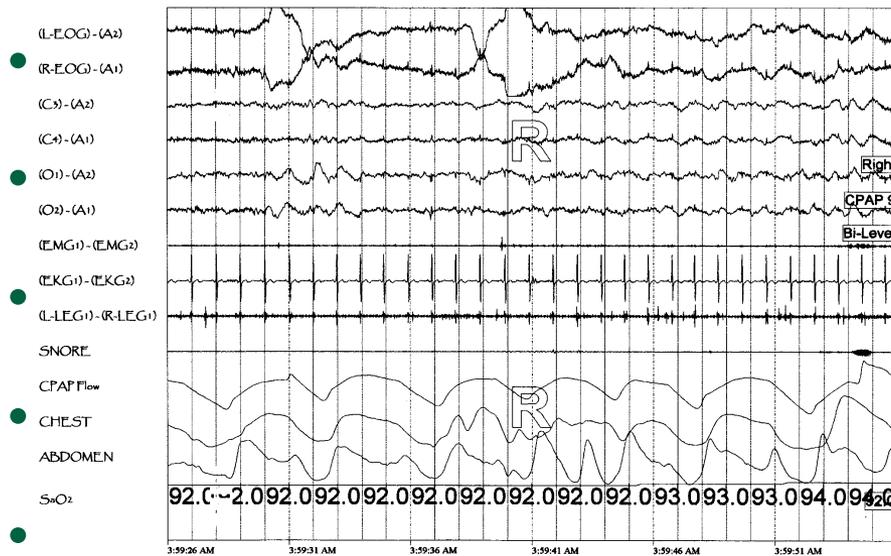


Parkinson's Disease



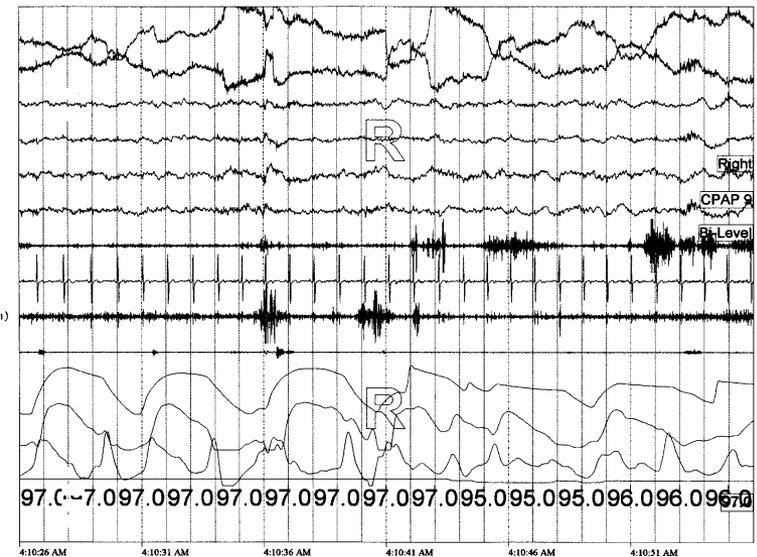
Sleep Problems in Parkinson's Disease

- REM Sleep Behavior Disorder



Normal paralysis (atonia)

- Changes in sleep architecture of dream sleep



Loss of atonia →
Acting out dreams

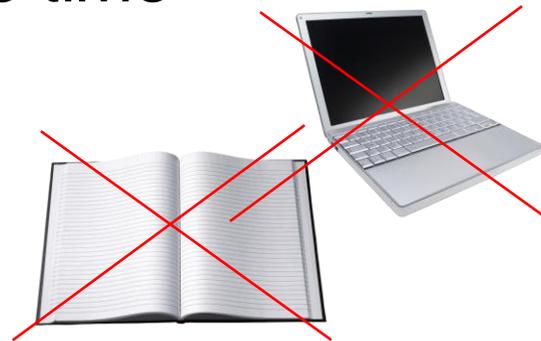
Impact of Sleep Disorders in PD

- Associated with:
 - Depression
 - Fatigue
 - Worse motor symptoms
 - Longer duration of disease
 - Psychosis
 - Cognitive Impairment
 - Worse quality of life

Treatment of Sleep Disorders in PD

Sleep Hygiene

- Maintain a consistent bedtime and wake time
- Avoid TV/reading/electronics in bed
- Don't watch the clock
- Get out of bed if unable to sleep
- Avoid daytime activities at night
- Sleep relaxation
- Minimize alcohol



Treatment of Sleep Disorders in PD

- Evaluate medication timing
- Treat underlying causes: sleep apnea, RLS, RBD, depression, psychosis
- Sleep relaxation techniques (meditation)
- Satiny sheets, bed rails
- Few medications have been studied in PD
- **EXERCISE!!**



Clinicaltrials.gov;
Seppi et al. Movement Disorders. 2011. 26:S42;
Pierantozzi et al. Sleep Med
Ancoli-Israel et al.. Sleep Med 2011. 12:134;
Ondo et al. Arch Neurol. 2008. 65:1337

<http://www.globalhealingcenter.com/natural-health/9-reasons-exercise-best-medicine>

How does exercise impact sleep in Parkinson's disease?

Randomized, Controlled Trial of Exercise on Objective and Subjective Sleep in Parkinson's Disease

Amy W. Amara, MD, PhD,^{1,2*} Kimberly H. Wood, PhD,^{1,2,3} Allen Joop, MS,¹ Raima A. Memon, MD,^{1,4} Jennifer Pilkington,¹ S. Craig Tuggle, MA,^{2,5} John Reams, MA,^{2,5} Matthew J. Barrett, MD,⁶ David A. Edwards, PhD,⁷ Arthur L. Weltman, PhD,⁷ Christopher P. Hurt, PhD,^{2,8} Gary Cutter, PhD,^{2,9} and Marcas M. Bamman, PhD^{1,2,4,10}

- Hypothesis: High intensity exercise training will improve sleep efficiency in PD participants compared to a sleep hygiene control
- Study Design: Randomized, controlled, clinical trial
- Participants with PD were randomized to an Exercise group (N=27) or a Sleep Hygiene control group (N=28)

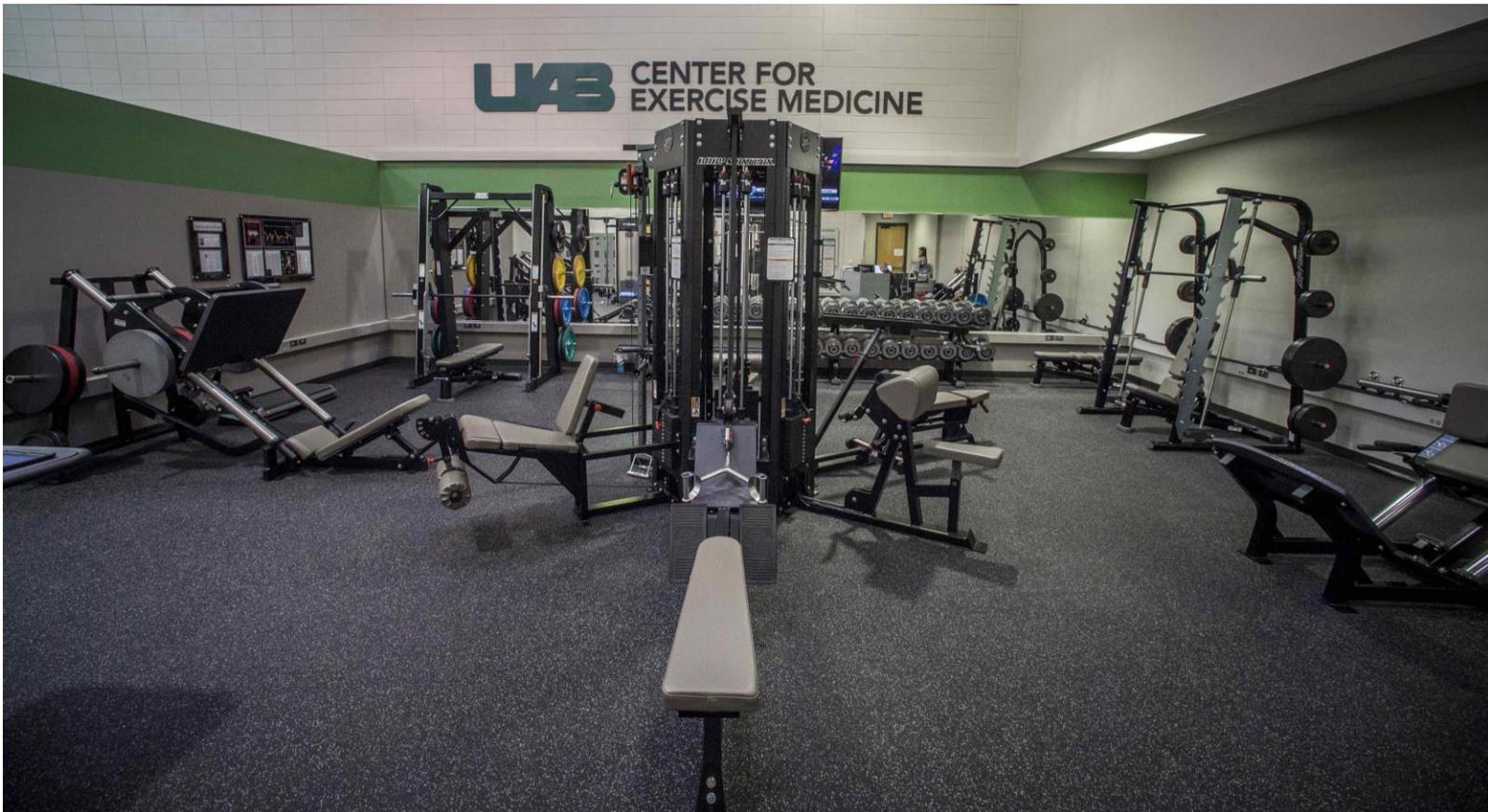
2020 Research Article Award
from *Movement Disorders*

Randomized Controlled Trial of Exercise
on Objective and Subjective Sleep in
Parkinson's Disease

[Read it now >>](#)

Study Methods

- Exercise included supervised, high-intensity resistance training 3 times weekly for 16 weeks



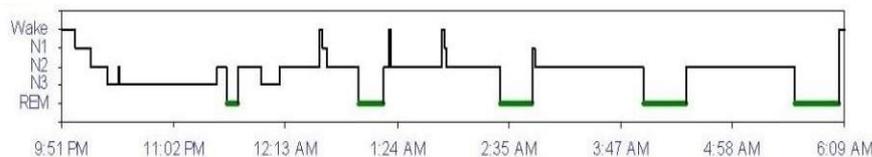
Study Methods

- Sleep hygiene included recommendations for changes in habits to improve sleep
- All participants had a sleep study before and after the intervention
- There were no significant demographic or sleep differences between the groups at baseline

Effects of Exercise on Sleep in PD

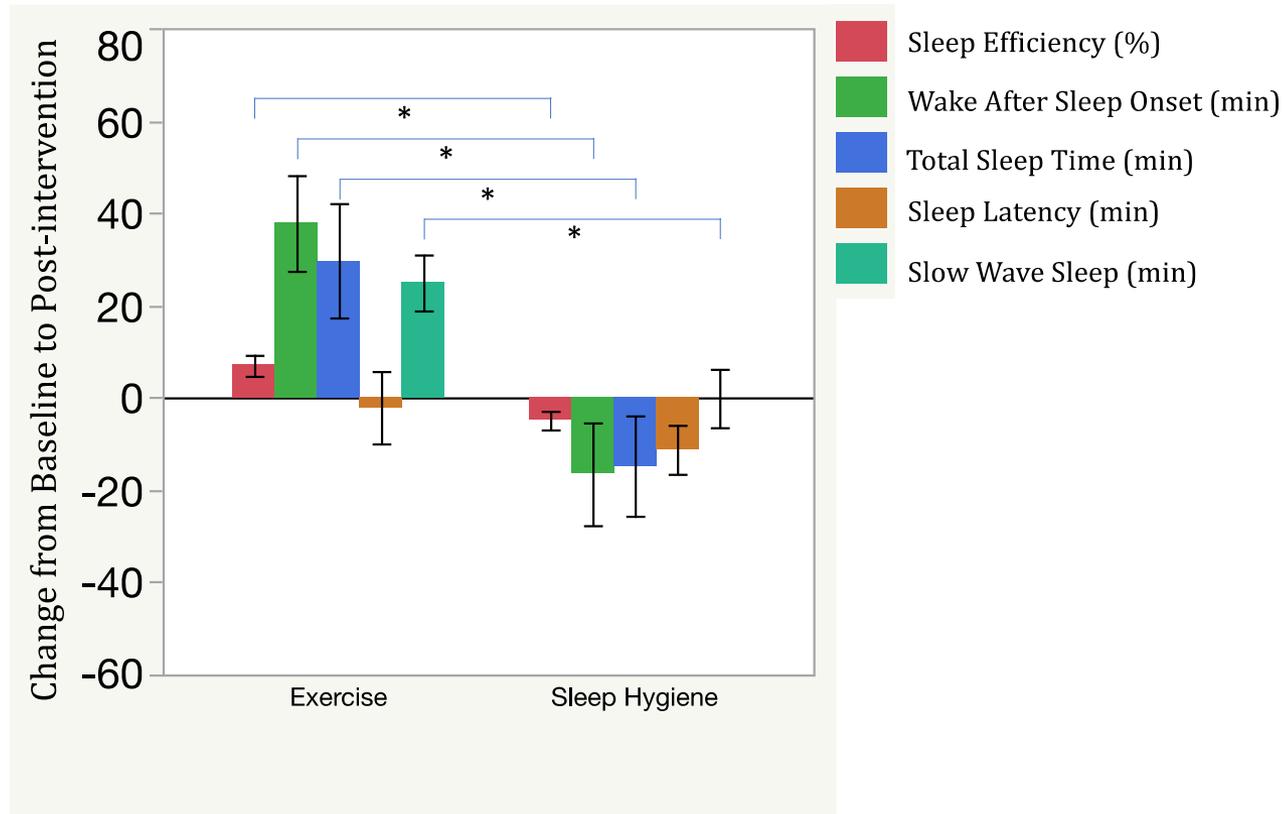
Participants in the exercise group had improved sleep efficiency and increased SWS and total sleep time

Exercise Group (N=27)					No-exercise Group (N=28)				Group x Time Interaction
	Baseline	Post-intervention	F	p	Baseline	Post-intervention	F	p	
SE (%)	76.8 (67.5-86.2)	83.1 (76.9-90.7)	9.3	0.0051	80.0 (73.2-86.7)	75.7 (66.6-82.5)	6.59	0.016	F=16.04 p<0.001
SWS Time (min)	50.5 (27.5-101.5)	88.5 (54.0-130.5)	16.9	0.0003	54.8 (16.8-85.9)	56.8 (17.5-88.0)	0	0.998	F=8.08 p=0.006
TST (min)	388.7 (322.5-414.0)	403.0 (364.5-436.0)	5.7	0.024	371.8 (336.9-415.5)	361.5 (321.3-400.7)	1.84	0.186	F=7.3 p=0.0093



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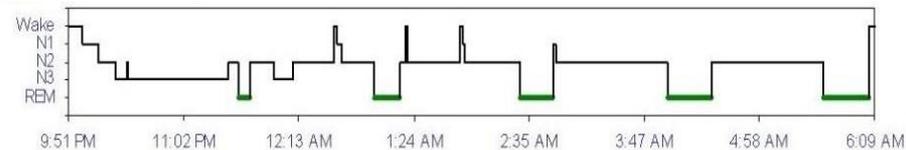
Effects of Exercise on Sleep in PD



Amara et al. Movement Disorders 2020. 35:947

Study Conclusions

- Exercise increases sleep efficiency and total sleep time in PD
- Exercise increases slow wave sleep in PD
- We previously showed that people with PD who have more slow wave sleep also have better cognitive function
- ? Can exercise improve cognition by increasing slow wave sleep?





Exercise-induced Cognitive Improvement Through Enhanced Sleep in Parkinson's Disease

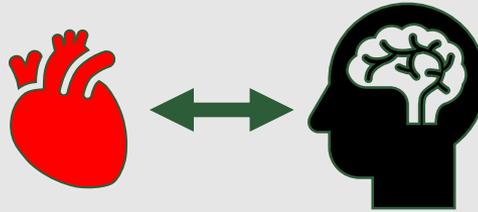
Recruiting PD participants

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The Heart-brain Connection, Neuroinflammation, and Cognitive Dysfunction in Older Adults

Recruiting healthy adults

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Thank you!