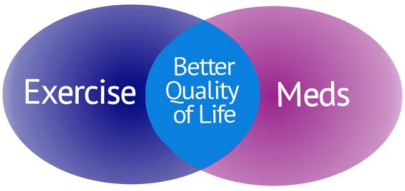
PWR!® Parkinson Wellness Recovery



Understanding the relationship between exercise and medication is essential when managing Parkinson Disease (PD). Research suggests that medication plus exercise is better than meds alone! This synergistic relationship may help you get more out of life and help you do more with less dopamine.

Dopamine medications alone:

- Primarily target the motor symptoms: rigidity (or joint stiffness), bradykinesia (which is slow, small movement) and incoordination (timing interferes with sequencing and automatic tasks).
- Generally do not target non-motor symptoms. These non-motor symptoms might include depression, anxiety, apathy, attention, problem solving, sleep, constipation, or pain.

Exercise alone reduces motor symptoms AND adds additional benefits:

- Reduces non-motor (and motor) symptoms (sleep, mood, constipation, attention, pain)
- Improves everyday habitual movements (function, gait and balance, ADL's)
- Increases brain health and connectivity (of the dopamine system) which helps your brain do more with less dopamine and may decrease the amount of medication you need over time.
- Offers hope for slowing disease progression

Why exercise alone is NOT enough in person with Parkinson disease.

- Medications are needed to help you FEEL like moving and putting in the effort to engage in exercise and daily life with more vigor!
- The optimal medication dosage will allow you to reap the most benefits from your exercise (and overall, greater physical activity)
- Remember, inactivity may be PRO-degenerative! You must counteract inactivity! Once you become sedentary, it is difficult to reverse the deconditioning and loss of flexibility and function.

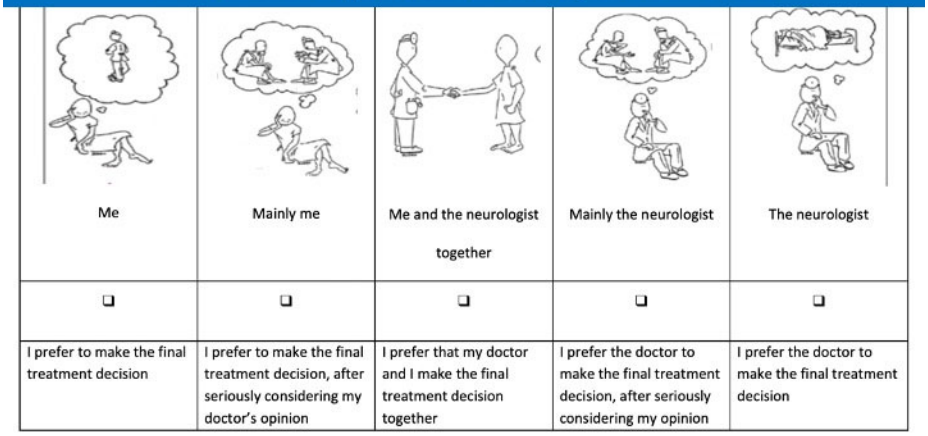
How do you know when medications are not optimized?

- Is your ability to exercise and participate in daily living activities suffering?
- Are you still doing the things you want or enjoy? If not what have you stopped doing and why?
- Worried that you will fall?
- Are you too fatigued to start?
- Unable to fully participate in exercise when you do?
- Are you depressed, unmotivated, don't want to put in the effort?
- Are you unable to sleep?
- Do your meds feel like they quit working early? or you can't predict how long it will take for them to start to work or how long they will last?
- Have you developed muscle cramps or dyskinesias?

Optimizing your exercise and medications takes a partnership – Shared decision making

- Complex, no “one-size fits all.”
  - Find someone that will focus on YOU and YOUR quality of life.
  - Get second opinions till you find someone that is right for YOU.
- Your medication and exercise prescription will change over time.
  - It is an ongoing conversation for life!
    - Symptoms change, health status changes, planned surgeries, unexpected emergencies
    - New meds in pipeline / discoveries everyday
- It is imperative to your quality of life to find a Neurologist that is a Movement Disorder Specialist (MDS) that will work with you to optimize your ability to participate in work, life, and exercise through appropriate medication dosing for YOU.
  - MDS Directory - www.movementdisorders.org
- Let your physician know what role YOU want to play in making decisions about medications.

Imagine you have to make the decision for starting an advanced treatment.
What role would you like when making the decision?
Choose the option that suits you the most.



Me	Mainly me	Me and the neurologist together	Mainly the neurologist	The neurologist
❑	❑	❑	❑	❑
I prefer to make the final treatment decision	I prefer to make the final treatment decision, after seriously considering my doctor's opinion	I prefer that my doctor and I make the final treatment decision together	I prefer the doctor to make the final treatment decision, after seriously considering my opinion	I prefer the doctor to make the final treatment decision

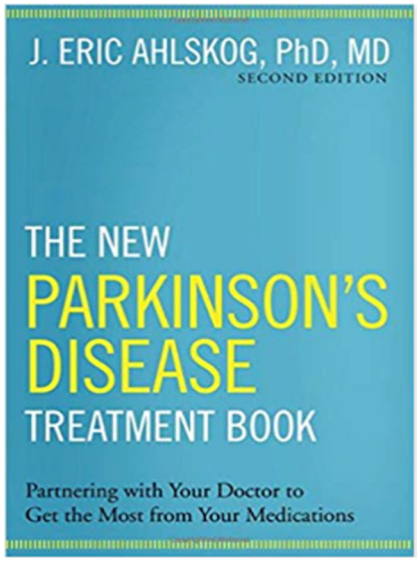
Nijhuis FAP, van den Heuvel L, Bloem BR, Post B, Meinders MJ. The Patient's Perspective on Shared Decision-Making in Advanced Parkinson's Disease: A Cross-Sectional Survey Study. Front Neurol. 2019 Aug 16;10:896. doi: 10.3389/fneur.2019.00896.

- Be consistent with your timing and dosing.
- Track your response to medications to help your physician optimize your medications
  - Davis Phinney Foundation - www.davisphinneyfoundation.org
    - Resources (manual, blog, webinars, and more..) for your wellness goals
    - Every Victory Counts Manual (hard copy or electronic)
      - Worksheets (also electronic from website)
        - Medication Log
        - Symptom Checklist

Optimizing your exercise and medications takes a partnership – Shared decision making

- Don't go with status quo!
  - Ask questions.
    - What are my options? What are the disadvantages and advantages?
    - What symptoms does this medication treat?
    - What is the reason for your preference?
    - How will I know if the medication is working?
    - What are possible side effects that I might experience?
    - How long should I expect to take this medication? What if I want to try something else? Are there consequences of switching?
    - I'd like to think about it and do some research. When is the next time we can talk about my medication regimen?
    - Can you refer me to any good resources?
  - Research your options.
  - Do your homework, talk to peers, check out webinar

- If you don't have a movement disorders Specialist to partner with or want to do some research, check out Dr. Ahlskog's book and find out more about how to his philosophy on how to capture the dose that is "just enough" (when combined with exercise).



"Putting off taking dopaminergic medication may result in lost opportunities to achieve the best level of physical fitness, function, and quality of life that is possible. Levodopa and other forms of dopamine therapy should be used to achieve maximum capability and motivation for patients to maintain fitness."

J. Eric Ahlskog, PhD, MD
Movement Disorders Specialized
Mayo Clinic Rochester, MN

What are your options to achieve an optimal threshold of medication?

- Try intensive rehabilitation first to get started in a personalized research-informed exercise program!!
  - See if you are using your FULL POTENTIAL.
  - Get a baseline on your level of fitness, mobility, and function so you can set goals.

- Find a PD-specialized physical therapist for your exercise prescription.
    - Find a Physical therapist that is PWR!Moves Certified
        - Call the PWR!Gym – 520-591-5346
        - Check out the directory for someone in your area
            - www.pwr4life.org

What are your options to achieve an optimal threshold of medication?

- Become a habitual exerciser first to harness the additive benefits of exercise!
    - Aim for at least 3x/week for a minimum of 180 minutes to decrease PD symptoms and increase the connectivity and efficiency of the dopamine system
- Optimize the use of the gold standard and most potent
    - Use YOUR dopamine most efficiently by adding an MAO inhibitor
    - Replace dopamine with the precursor levodopa (Carbidopa/Levodopa aka Sinemet).
        - Don't "save" it for later.
        - Titrate to the lowest most beneficial dose possible at the beginning. Higher dosing does not translate to better or longer responses.
    - Start with or add oral dopamine agonists (ex. Ropinirole, Pramipexole, Rotigotine patch)
        - Binds directly to dopamine receptors and tricks the brain into thinking it is receiving dopamine
        - Highest tolerable doses are unable to achieve the same robust motor improvement as levodopa
- Get educated. Be prepared with your own questions.
- Ask your physician to share their philosophy and why they recommend what they do and what are the pros/cons that you need to consider.
- When do you start? What are the medications you have to choose from for getting started?
- What are your options when medication side effects begin?

Why does dopamine replacement result in motor fluctuations?

- Agonists are below therapeutic threshold
- Levodopa delivery is pulsatile and unpredictable
    - Slow gastric emptying delays absorption in the small intestine
    - Competes with dietary protein
    - Short half-life and a long way to go
    - As disease progresses, there is less buffering capacity so the levels of levodopa saturate the environment and exceed therapeutic levels
    - Altered dopaminergic signaling and connectivity locally spreads to entire network and other neurotransmitter signaling pathways

PWR!® Parkinson Wellness Recovery

Exercise | Better Quality of Life | Meds

Why does levodopa replacement result in dyskinesias?

- Dyskinesia develop with the same frequency and severity irrespective of whether levodopa was initiated early or late
  - 40% after 4 years but sooner with higher doses or YOPD
  - PwP prefer dyskinesias and optimal function over undermedication
- Therapeutic and dyskinetic thresholds are similar
- High risk groups include:
  - Age of onset, low body weight, female sex, more severe motor disability
- Clinical subtypes:
  - Akinetic-rigid > tremor dominant
- Genetics:
  - YOPD, distinct di-phasic pattern of dyskinesias

What are your options to optimize ON time?

- Increase absorption of levodopa with diet/protein restrictions
- Reduce wearing off
  - Extended release medications (Rytary, Sinemet CR)
  - Help dopamine last longer
    - MAO-B (Rasagiline and Selegiline)
    - COMT (Entacapone and Stalevo)
  - Amantadine for reduced tremors and dyskinesias
- Rescue
  - Apomorphine (short acting agonist not specific to dopamine receptors)
- DBS
  - Gpi > STN target
  - Gpi target reduces dyskinesias despite post-surgical reduction in dosage of dopaminergic therapies
- Duopa
  - Continuous infusion of intestinal gel

NEW options for OLD medications to achieve optimal efficacy

- Goals: decrease dyskinesias, improve symptoms, extend ON time, reduce OFF time, rescue ON time
- Gupta H V, Lyons KE, Pahwa R. Old Drugs, New Delivery Systems in Parkinson's Disease. *Drugs Aging*. 2019;36(9):807-821. doi:10.1007/s40266-019-00682-9

John Goulet's Testimonial and Journey for 4 years as a NeuroDerm (ND), ND0612 Phase 2 clinical trial participant investigating the subcutaneous infusion of Levodopa / Carbidopa using a pump system (much like used for diabetic's)

BeyoND Study – ND0612 Phase 2b Clinical Trial

- 1st study to evaluate the long-term safety of ND0612 – a drug-device combination designed to deliver liquid carbidopa/levodopa by subcutaneous infusion
- Preliminary studies completed and were able to achieve steady state therapeutic levodopa plasma concentrations

BouNDless Study – ND0612 Phase 3 Clinical Trial

- Actively recruiting
- www.clinicaltrials.com
- Search "boundless"

ABBV-951 – Phase 3 Clinical Trial

- Study measures the efficacy, safety, and tolerability of continuous infusion of ABBV-951 versus oral Carbidopa/Levodopa in advanced PwP to achieve reduction in motor fluctuations

Interested in Research?

- Find a study
  - https://www.michaeljfox.org/join-study
  - https://clinicaltrials.gov/
- Your role in research
  - https://www.michaeljfox.org/your-role-research
- Guidebook
  - https://www.michaeljfox.org/sites/default/files/media/document/PDEC_Patient_Guide_Digital_12.11.20_1.pdf
- Talk to other research participants
  - https://www.michaeljfox.org/real-talk-patients
- Ending Parkinson's Disease (a time for hope)
  - https://endingpd.org/resources
  - https://endingpd.org/buy
  - https://davisphinneyfoundation.org/professor-bastiaan-bloem-ending-parkinsons/

Call to Action!

- Find a movement disorders specialist
  - Ask your doctor for all of your options and let them know you want to be involved in the decision making process
  - www.movementdisorders.org
- Get educated, empowered, and live well
  - https://davisphinneyfoundation.org/resources/
- Reliable, up to date information for PwP and care partners
  - https://davisphinneyfoundation.org/resources/every-victory-counts-manual/
  - Track your response to exercise and your daily off periods with worksheets
- Get a consult with a PD-specialized physical therapist to help determine if you are using your full potential!
  - https://www.pwr4life.org/professional-directory/

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