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Session 201: Mood Improved: Exercise Strategies for Parkinson's Disease
Kara Doctor, MS, PT

PARKINSON’S DISEASE - OVERVIEW

Prevalence: Parkinson’s Disease (PD) is the second most common neurodegenerative disease behind Alzheimer’s disease. It currently afflicts over 1.6 million people in the United States, and it is estimated that the prevalence of the disease will grow substantially with the aging population, over the next two decades. 60,000 new patients are diagnosed each year.

While the cause of PD remains unknown, there has been recent progress toward understanding the pathophysiology of the disease. There has been tremendous improvement in the development of treatment strategies and growth of pharmacological agents for PD.

There has been recent advancement and refinement of surgical techniques, as well as recognition of nonmotor manifestations of PD.
EPIDEMIOLOGY

Studies have reported that PD has an overall prevalence in the general population of between 84/100,000 to 775/100,000.1

There is a clear increase in prevalence with age.

A Dutch study reported a prevalence of 1400/100,000 in those aged 55-64 years of age and 4300/100,000 in those aged 85-94 years of age.2

The mean age of onset is in the early 60s, but up to 10% of those with PD have an onset in the early 40s.

The majority of studies report a male predominance, with a roughly 3:2 ratio of males to females.

ECONOMIC IMPACT

The economic burden for the cost of the illness can be measured in direct and indirect costs.

Direct costs = medications and healthcare costs

Indirect costs = lost productivity, cost of providing care and mortality costs.

In the United States, the combined direct and indirect cost of Parkinson’s is estimated to be nearly $25 billion per year.

Almost 50% of the total economic cost of PD is loss of productivity, while just shy of 20% was for both inpatient care and uncompensated care. Prescription drug costs accounted for less than 5% of the total cost.

NEUROANATOMY
NEUROANATOMY IN PD

The cortical areas involved in movement control need “assistance” from other brain circuits in order to smoothly orchestrate motor behaviors. One of these circuits is the basal ganglia. Without the basal ganglia, the cortex is unable to direct motor control properly and the deficits seen in Parkinson’s Disease and related movement disorders become apparent.

A very simple explanation of neuroanatomy can be found at: http://www.neuroanatomy.wisc.edu/coursebook/motor2.pdf

The anatomy of the basal ganglia consists of two important structures, the caudate and putamen.

PD LOSS OF DA NEURONS

PD is a slow and steady loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc). In PD, the activity in direct pathways to the internal globus pallidus increases while activity in indirect pathways to the external globus pallidus increases. This causes excessive inhibition of the thalamus. The increase is inhibitory, and affects the basal ganglia, in effect, “turns down” motor activity from the cortex. This is why PD patients have tremors and trouble performing voluntary movements.
The Four cardinal features of PD are:
1. Tremor
2. Bradykinesia
3. Rigidity
4. Postural Instability

The 3 types of PD are:
1. Tremor Dominant
2. Rigid-Akinetic
3. Mixed: Rigid akinetic/Tremor dominant

Depression is the most common neuropsychiatric manifestation of PD. Mood dysfunction is not simply a reaction to developing PD. Antidepressants work well to manage symptoms. Lithium (OTC elemental) Lithium 5-10 mg BID

Approximately 40% of PD patients have anxiety, which makes it the second most common affective disorder in PD.

Apathy and social withdrawal are more common in PD than in idiopathic depression. Sleep disorders range from 72% to 98% in PD patients.

Constipation is very common in PD. Decreased mobility and decreased swallowing of secretions.
A cut-off of less than five for each PDSS item was chosen.

SLEEP HYGIENE

Keep a diary of sleep habits.

Fix a bedtime and an awakening time.

Avoid napping during the day.

Avoid alcohol 4-6 hours before bed.

Avoid caffeine 4-6 hours before bed.

Avoid heavy, spicy, or sugary food 4-6 hours before bed.

Exercise regularly, but not right before bed. Regular exercise, particularly in the afternoon, can help deepen sleep. Strenuous exercise, if performed within 2 hours before bed, however, can decrease your ability to fall asleep.

Use comfortable bedding.

Block out light and noise as much as possible.

Reserve the bed for sleep and sex. Don’t use the bed as an office, workroom or recreation room.
GETTING READY FOR BED

Try a light snack before bed. Warm milk and foods high in the amino acid tryptophan, such as bananas may help.

Practice relaxation techniques. Deep breathing and relaxation techniques can help relieve anxiety and reduce muscle tension.

Establish a pre-sleep ritual. A warm bath or a few minutes of reading before bed can help with sleep.

Get into a favorite sleeping position. If you don’t fall asleep within 15-30 minutes, get up, go into another room and read until sleepy.

Many people fall asleep with the television on in their room. This can often be a bad idea, because television is a very engaging medium that tends to keep people up. We recommend that the TV not be in the bedroom.

EXERCISE BENEFITS

The potential that exercise has to help both motor and nonmotor symptoms in PD

- The number of publications addressing exercise for PD has more than tripled in the past decade.

- Exercise has the potential to help both motor (balance, gait, strength/endurance) and nonmotor (depression, apathy, fatigue, constipation) aspects of PD, as well as secondary complications of immobility (cardiovascular, osteoporosis).
THE EFFECT OF EXERCISE TRAINING IN IMPROVING MOTOR PERFORMANCE

- In a recent study conducted by Beth Fisher et al., researchers at the University of Southern California found that exercise may have an effect on the brain. On a day-to-day basis, people with PD, who exercised, moved around more normally than those who did not. Based on these findings, they believe that exercise may be helping the brain to maintain old connections, form new ones and restore lost ones. They suggest that, in certain situations, the neuroplasticity created from exercise in patients with PD may actually outweigh the effects of neurodegeneration.

BDNF

Many studies have suggested that physical exercise can have an antidepressant effect by increasing the levels of brain-derived neurotrophic factors (BDNF).

Studies have shown that regular exercise improves sleep quality in normal aging, as well as many aspects of sleep in PD.

EXERCISE INTERVENTIONS FOR PARKINSON’S DISEASE
EXERCISE INTERVENTIONS FOR PD

- PD is associated with a variety of nonmotor symptoms that significantly reduce the quality of life, even at early stages.
- There is an urgent need to develop evidenced-based treatments for these symptoms, which include mood disturbances, cognitive dysfunction, and sleep disruption.
- Our focus here is on EXERCISE INTERVENTIONS, which have been used to improve mood, cognition and sleep in healthy older adults.
- We focus on the benefits of aerobic type exercise and strength training.
- Across the stages of the disease, exercise interventions represent treatment strategy with the unique ability to improve a range of nonmotor symptoms, while also alleviating the classic motor symptoms of the disease.

WHAT KIND OF EXERCISE??

PD Exercise

SUGGESTIONS FOR EXERCISE GUIDELINES IN PD

As the scientific evidence regarding the merits of exercise for PD is growing, all PD patients should be STRONGLY encouraged to increase physical activity and exercise regularly.

Although PD patients suffer from physiological limitations that require specific attention around exercise, recommendations specific to PD patients do not exist.

Guidelines from the American College of Sports Medicine (ACSM) for older adults >50 years with a chronic disability, could serve as a good starting point.

ACSM guidelines recommend incorporating aerobic, strengthening, flexibility, and balance training. Specifically, aerobic training should be done at least 5 x /week, for 30 minutes at moderate intensity or at least 3 x per week for 20 minutes at vigorous intensity.

All PD patients should be encouraged to exercise at their optimal medicated state.
ACSM GUIDELINE SUGGESTIONS

The ACSM recommends at least 2 days of strength training (8-10 exercises involving major muscle groups) and at least 2 sets of 10-15 repetitions. And flexibility exercises for at least 10 minutes.

It has been recommended that for PD patients, a strong focus on strengthening the extensor muscle groups, in order to counteract the flexion of hips and trunk musculature. Focus on flexibility training to flexor, axial and cervical muscles.

Balance training should be initiated early to prevent postural instability and reduce the risk of falls.

VIGOROUS EXERCISE

This may mean something different to each of us, but for these purposes, we are referring to aerobic physical activity that is enough to increase the heart rate and the need for oxygen.

For this to be meaningful, it should be sustained (30-40 minutes) and repeated (3-4 times per week) and ongoing (lifetime).

Physical/Occupational/Speech therapy is routinely utilized in PD treatments, the focus is largely based on ADL’s, gait and balance training, stretching and voice volume.

Our treatment needs to be more directed to physical fitness.

This may be an area that is a neglected opportunity for disease modification in the PD community.

ACTIVITY DEPENDENT NEUROPLASTICITY

Exercises that incorporate goal based training and aerobic activity have the potential to improve both cognitive and automatic components of motor control in individuals with mild to moderate disease through exercise dependent neuroplasticity.

Clinical studies suggest that high intensity (high repetition, velocity, complexity) is a characteristic of exercise that may be important in promoting activity-dependent neuroplasticity in the brain, including the basal ganglia.
PARKINSON’S AND EXERCISE

Exercises that challenge them to change tempo, direction or activity frequently. Activities that involve paying attention and learning, such as dancing, are good forms of exercise to include.

People with PD should aim to exercise four or five times per week for at least 30-40 minutes.

The heart rate should be maintained between 70-80% of its maximum, which is 220 minus the person’s age.

Lifting light weights and performing closed chain exercises can be particularly beneficial.

TAI CHI

• Tai Chi naturally combines slow control of movement, strength, multidirectional movement, and complex sequential action requiring cognitive attention. It has been known to improve balance in the elderly, and has a strong emphasis on maintaining control of one’s center of mass.
Tai Chi

Excellent exercise for balance, flexibility, body awareness and breathing.
Hug the Tree.
Feel the Cliff.

DANCING

Exercise Strategy in PD

Dancing

- Dance has receiving attention as an interesting exercise strategy for PD because it naturally combines cueing, spatial awareness, balance, strength and flexibility, and physical activity (or even aerobic activity if the intensity is sufficient). It is enjoyable and stimulates social engagement and peer support.
- Recent studies show improvement in nonrelated tasks after a 12 month program, dancing 2 x per week for 60 minutes, suggesting a disease modifying effect.
The term **Neuroplasticity** is derived from the root words Neuron and Plastic. A neuron refers to the nerve cells in our brain. Each individual neural cell is made up of an axon, dendrites, and is linked to one another by a small space called the synapses. The word plastic means to mold, sculpt, or modify. Neuroplasticity refers to the potential that the brain has to reorganize by creating new neural pathways to adapt, as it needs.

New neural cells are generated throughout a lifetime, as well as the generation of new neural pathways. The elderly can create measurable changes in the brain organization. These changes are not always easy but can happen through concerted effort.
EARLY INTERVENTION

Exercise is an important part of healthy living for everyone. For people with PD, exercise is more than healthy, it is a vital component to maintaining balance, mobility and the ability to perform activities of daily living.

The Parkinson's Outcomes Project shows that people with PD who exercise a minimum of 2.5 hours per week, experience a slowed decline in quality of life measurements. After 6 months of exercise, scores improved by approximately 30%

Establishing early exercise habits is an essential part of overall disease management.

DOES VIGOROUS EXERCISE HAVE A NEUROPROTECTIVE EFFECT IN PD?

According to the Journal of Neurology, “Parkinsonian animal models reveal exercise-related protection from dopaminergic neurotoxins, apparently mediated by brain neurotrophic factors and neuroplasticity.”

There is increasing evidence suggesting that ongoing vigorous exercise may favorably influence the progression of PD:

“Exercise consistently improves cognition in animals, also linked to enhanced neuroplasticity and increased neurotrophic factor expression. In these animal models, immobilization has the opposite effect.”

“In humans, exercise increases serum brain-derived neurotrophic factors (BDNF), which is known to cross the blood-brain barrier.”

PD risk in humans is significantly reduced by midlife exercise, documented by enlarged prospective studies.

DECREASED COGNITIVE DISORDERS ASSOCIATED WITH EXERCISE IN PD

• Exercise, or physical fitness has not only been associated with better cognitive scores, but midlife exercise significantly reduces the later risk of both dementia and mild cognitive impairment.

• Numerous studies in seniors, with and without dementia, have reported increased gray matter volumes associated with physical fitness or exercise.
PD AND EXERCISE

- A major focus in PD research has been on neuroprotective mechanisms known to slow progression. Medications are most often researched.
- Often overlooked is the potential benefit of sustained vigorous exercise on PD progression.
- Exercise is well known to have benefits on general health, including cardiovascular and cerebrovascular health, reduction of osteoporosis/fracture risk, improvement in psychological health, and perhaps a general anti-inflammatory effect.
- Evidence is accumulating that suggests that ongoing vigorous exercise may have a neuroprotective effect in PD.

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MEDICATIONS IN PD

- Anti-psychotics
- and Supplements
Levodopa is the primary medication used to treat PD. Levodopa is a precursor to Dopamine and is turned into Dopamine in the body. Levodopa can be used alone or in combination with carbidopa. When combined with carbidopa it is less likely to cause gastric upset. The formulation is generally 1:4, carbidopa to levodopa. Generally written in the form 25/100 mg (25 mg of carbidopa, combined with 100 mg of levodopa). Levodopa helps with the symptoms of PD by improving muscle control. There are several different formulations of levodopa, including regular release, which is fast acting and controlled release (CR or ER), which lasts a little longer. There is a new formulation of levodopa, which lasts for 8 hours, called Rytary. Levodopa formulations should be taken either 30 minutes before a meal or 45 minutes after a meal for best absorption. Protein in foods interferes with proper absorption. Levodopa and carbidopa are often referred to by the brand name Sinemet.
CARBIDOPA LEACHES THE BODY OF VITAMIN B6

Recent research suggests that the carbidopa in Sinemet has been shown to leach the body of Vitamin B6, which is instrumental in the production of serotonin, which is vital for mood stabilization. **Vitamin B6- 25-50mg.** To improve bioavailability, secondary to leaching from carbidopa.

LITHIUM OROTATE

Start with 10mg each morning. 1 week later take 10 mg morning and bedtime and continue (Weyland brand makes a 10 mg version).

Lithium Orotate may actually absorb into cells better than prescription brand lithium carbonate, and therefore less is needed to achieve intended effect.

A growing body of evidence suggests that the benefits of lithium extend beyond simply mood stabilization. Lithium treatment has been shown to provide neuroprotection against neurological insults. In particular, lithium treatment is associated with neuroprotection against neurodegenerative conditions such as Parkinson’s, Alzheimer’s and Huntington’s diseases, as well as ALS. Chronic lithium treatment has been shown to significantly increase BDNF expression in the hippocampus of a rat brain.

MEDICAL CANNABIS

Marijuana for Treatment of PD
MARIJUANA IN PD

While the cause of Parkinson’s disease is unknown, genes and environmental triggers likely play a role. Some genetic mutations have been identified and having a close relative with Parkinson’s increases chances of developing the disease. Exposure to certain toxins like herbicides and pesticides could also increase risk. Evidence suggests that cannabis could potentially slow the progression of Parkinson’s by providing neuroprotective effects. The cannabinoids found in cannabis are able to suppress excitotoxicity, glial activation and oxidative injury that cause the degeneration of the dopamine-releasing neurons. In addition, they improve the function of cell mitochondria and activation of cellular debris clearance, further encouraging neuroprotection (Mare & Choi, 2015) (Garcia-Arencibia, Garcia & Fernandez-Ruiz, 2009) (Lastres-Becker & Fernandez-Ruiz, 2006) (Dexter, et al., 2015) (Zeiher, et al., 2013). Researchers have found evidence that one specific cannabinoid found in cannabis, tetrahydrocannabinol (THC), helps in the treatment of Parkinson’s disease by assisting in the prevention of damage caused by free radicals and activating a receptor that encourages the formation of mitochondria (Zeiher, et al., 2013). Another major cannabinoid found in cannabis, cannabidiol (CBD), has also been studied to support the health of neural cells mitochondria, causing the researchers to conclude that CBD should be considered as a potential therapeutic option in neurodegenerative disorders like Parkinson’s because of its neuroprotective properties (da Silva, et al., 2014) (Zuardi, 2008).

MEDICAL MARIJUANA

Researchers began to show enthusiasm to study cannabis in relation to Parkinson’s after people with PD gave anecdotal reports and posted on social media about how cannabis reduced their tremors. Some researchers think that cannabis might be neuroprotective — saving neurons from damage caused by Parkinson’s. Besides reducing tremor, cannabinoids like dronabinol in marijuana have also been used for treatment of other symptoms, like bradykinesia (slowness caused by PD) and dyskinesia (excess movement caused by levodopa). Despite some promising preclinical findings, researchers have not found any meaningful cannabis benefits for people with Parkinson’s due to a lack of evidence.

Researchers issue caution for people with PD who use cannabis because of its effect on thinking. Many people with Parkinson’s experience impairment of the executive function — the ability to make plans and limit risky behaviors. People with a medical condition that impairs executive function should be cautious about using any medication that can compound this effect.

VIGOROUS EXERCISE VS. TRADITIONAL EXERCISE
VIGOROUS

Vigorous intensity aerobic exercise is where you’re breathing hard and fast and your heart rate/energy expenditure has increased significantly.

WHERE TO START

Start with your initial evaluation.
Get a feel for what their endurance is like.
6 Minute Walk Test.
Set realistic and achievable goals for them to progress—add 2 minutes per week until they reach 30 minutes, then increase the intensity.
Interval Training is effective for elevating heart rate and increasing intensity of exercise.
Timed Get-Up-And-Go
Sit to Stand Test (30 Second Best)

DR. HENRY

74 year old male with history of PD x 12 years.
Retired anesthesiologist.
S/P bilateral STN DBS
Unable to walk for 5 minutes on the treadmill 6 months ago.
Performs vigorous exercise x 45 minutes, 3-4 times per week.
FLOOR EXERCISES

- Developmental Positions - Reversed
- Abdominal Exercises
- Diaphragmatic Breathing Exercises
- Closed Chain Exercises
- Stretches

CLOSED CHAIN EXERCISES

Where To Start:
- Squats
- Wall Push Ups
- Floor exercises

START LOW AND INCREASE SLOWLY

Start with 3 minutes, increase by 2 minutes each week.

We started with 3 minutes, after 6 months, he is able to exercise vigorously, 4 times per week.
GOOD CORE STRENGTH!
Start with isometric core exercises
- Diaphragmatic Breathing—
  with book or weight
- Crunches
- Prone-prone on elbows—prone press ups
- Transitions—Turkish Get-Up

HOME EXERCISE PROGRAM
DR. HENRY
MODIFY AS NEEDED. REPEAT AS TOLERATED

Warm up: (15-20 reps each)
- Sit to stand with overhead reach and toe raise.
- Biceps curls with bar.
- Squat with bar over shoulders.
- Trunk twists with bar over shoulders.
- Dead lift with bar (head up, butt out, hang).
- Pushups.

DR. HENRY- HEP (CONT.)

Treadmill: Start at your regular speed for 3 minutes. Then increase your pace or the incline and go as fast as you can for 30 seconds. Go as hard as you can without becoming short of breath. Then resume your regular speed for 2 minutes. Repeat as tolerated throughout your walk. Try walking for 15-20 minutes with heart rate elevated.

If your experience chest pain, become lightheaded or nauseated, STOP immediately and contact your doctor OR call 911.

Progressive Resistance Exercise: Perform exercises slow and with good form. Try to perform 8-12 repetitions. When it becomes easy or you can perform 15-20 reps, increase the weight. Try Circuit Training, 4-6 machines, alternating body parts for 2-3 sets. Don't rest between machines.

If something hurts, modify your movement or stop.

If you are unable to recite your name without shortness of breath, SLOW DOWN.
STRETCHES:
- Long stretch on back
- Hamstring stretch
- Piriformis stretch
- Press ups
- Child’s pose

Exercises:
- Pull single weight up to chin
- Single weight in hand, lean to side and straighten
- Chest Press on bench
- Single arm rows

LOWER LEVEL PATIENTS (SNF, ALF, NF)
- Walking with assistive device
- Upper Extremity Bike
- Balloon Exercises
- Closed Chain Exercises
- Start Low and move SLOW
- Wheelchair push ups
- Wall push ups
- Lower level Exercises: Review 4 Go-To Exercises

REVIEW OF EVIDENCE
- Exercise Research: The Latest on Research into Parkinson’s and Exercise
EXERCISE RESEARCH

At Rhodes University in Memphis, Dr. Gerecke et al. report that exercise can protect mice against toxic exposure. MPTP is a neuro toxin that is used as an animal model for PD, as it selectively kills dopamine neurons in the substantia nigra. Dr. Gerecke showed that 3 months of exercise provided complete protection against MPTP-induced neurotoxicity in mice. Also, if the duration of running was limited to 1 or 2 months or if the amount of daily running was decreased, the protective effects of the exercise were abolished. Thus, daily, sustained exercise was necessary for full protection.

RHODES UNIVERSITY IN MEMPHIS, DR. GERECKE ET. AL.

Dr. Gerecke also found that 3 months of exercise induces changes in proteins related to energy regulation, cellular metabolism, cytoskeleton dynamics, and intracellular signaling events.

This means that exercise must be sustained (30-40 minutes), repeated (4-5 times per week), and ongoing (lifetime) to be meaningful in PD.

DR. ZIGMOND, AT THE UNIVERSITY OF PITTSBURGH

Dr. Zigmond, et al. found that exercise reduces the impairments elicited by dopaminergic neurotoxins as well as loss of DA neurons. This study focused on one of several possible explanations for the beneficial effects of exercise: an exercise-induced increase in the expression of BDNF, specifically GDNF (glial-derived neurotrophic factor). Observations indicate that GDNF can reduce the vulnerability of DA neurons, in part due to the activation of key intracellular cascades.

This raises the possibility that some individuals with PD suffer from a reduction of these neuroprotective mechanisms, and the treatments that boost these mechanisms— including exercise— may provide therapeutic benefit.

Depression is a neuropsychiatric manifestation that is commonly found in PD. Many studies have suggested that physical exercise can have an antidepressant effect by increasing the BDNF (brain-derived neurotrophic factor), and may also prevent neurodegeneration. However, different forms of exercise may promote different changes in the brain. The researchers in this study investigated two types of physical training on depressive-like behavior, and on BDNF. The animal models were subjected to 60 days of exercise, either running on a treadmill or performing strength training. Both types of physical exercise demonstrated increased levels of BDNF and both prevented depressive-like behavior. These results demonstrate that exercise training was effective for neuroprotection in the striatum and hippocampus in an experimental model of PD.

# RESOURCES

- Michael J Fox Foundation: [www.michaeljfox.org](http://www.michaeljfox.org)
- American Parkinson's Disease Association (APDA): [www.apdaparkinson.org](http://www.apdaparkinson.org)
- Davis Phinney Foundation: [www.davisphinneyfoundation.org](http://www.davisphinneyfoundation.org)

Local Support Groups
- APDA City Chapter
- Parkinson’s Action Network (PAN): [www.parkinsonaction.org](http://www.parkinsonaction.org)

Register with Fox Trial Finder to be matched with clinical studies in your area.
- Rock Steady Boxing: info@rocksteadyboxing.org

# SPEAKER: KARA DOCTOR, MS, PT

**SESSION 201: MOOD IMPROVED: EXERCISE STRATEGIES FOR PARKINSON’S DISEASE**


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Thank You For Your Participation!!