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High intensity exercise: the evidence and application in Parkinson's Disease

Mike Studer, PT, MHS, NCS, CEEAA, CWT, CSST

Objectives

- Describe at least two examples of the latest evidence to best individualize a balance program for individuals with Parkinson's and Parkinsonism diseases.
- Identify to examples of evidence for individualize interventions as related to subtypes of PD.
- List at least three principles of the ICF motivational and psychological characteristics in management of patients with PD and Parkinsonisms.

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OUTLINE

Neurophysiology of PD and changes associated with high intensity exercise

Evidence in high intensity exercise for persons with PD

Applying high intensity exercise in PD – individualizing across phenotypes

Case studies in PD – video review

Questions

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PD – statistics and trends

- Incidence
  - 4-6 million affected directly
  - 60,000 newly diagnosed cases/year
  - Frequency of PD will increase 4 fold by 2040
- Prevalence
  - 0.3% in general US population
  - Prevalence increases to 4-5% in those >85 years
  - Average age of onset 60 years

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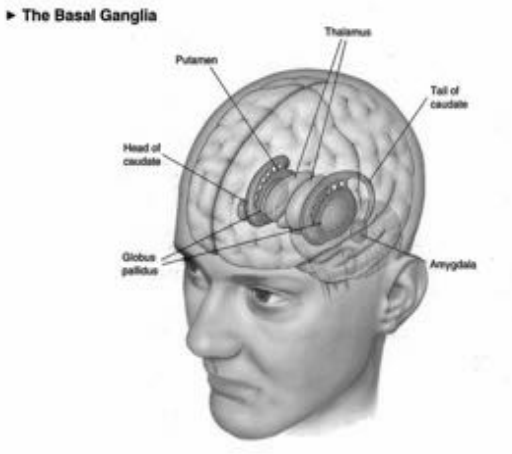
Neurophysiology of PD



Functional correlates:

Motor planning
Procedural memories
Sensory processing
Emotion
Selective + divided attention

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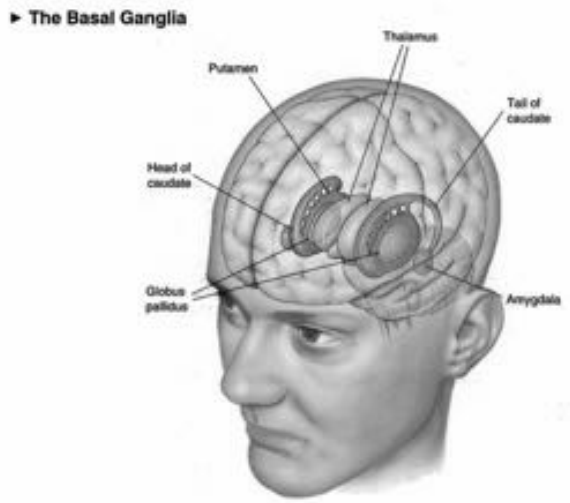
The basal ganglia…



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Pathophysiology of Parkinson's Disease

Structures involved:

Substansia Nigra

Basal Ganglia: Putamen
Globus Pallidus
Striatum

Dorsolateral Prefrontal Cortex

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Pathophysiology of variant subtypes (phenotypes)

1) Primary dyskinesia

2) Primary tremor and rigidity

3) Freezing of gait; posture; and festination

+/- Cognitive changes

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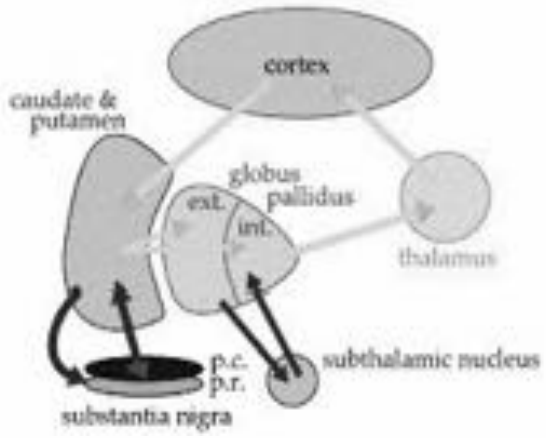
Neurophysiology "the of PDs"



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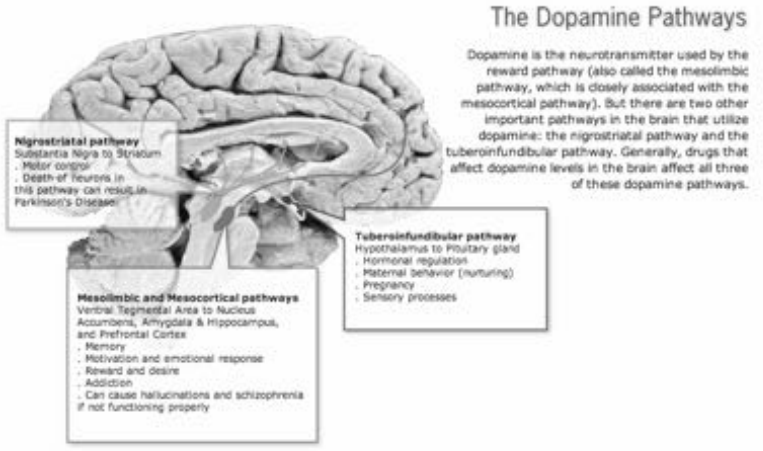

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High Intensity Exercise and PD

CENTRAL

- Endorphins
- Dopamine
- Glial Derived Neurotrophic Factor (GDNF)
- Protecting BG cells (MSNs)
- Cognitive (reaction speed)
- Psychological

PERIPHERAL

- Muscular strength
- Muscular endurance
- Cardiovascular
- Flexibility

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Potential for Neuroprotective benefits in PD

GDNF vs. BDNF

GDNF is more effective than BDNF for correcting the rat model of PD, and that there are no detectable benefits from expressing both of these neurotrophic factors.

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Potential for Neuroprotective benefits in PD

- Glial-derived neural protective factor (GDNF)

"Specific neurotrophic factors, (GDNF) and (BDNF), have been found to attenuate the lesion-induced loss of nigrostriatal dopaminergic neurons in *animal models* of PD. Of note, GDNF and BDNF can interfere with both apoptotic and necrotic forms of cell death."

Sun, et al. Brain Res. 2005

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Potential for Neuroprotective benefits in PD

The survival of the MSN: Medium Spiny Neuron

MSNs of the "direct pathway“ – excitatory

MSNs of the "indirect pathway“ - inhibitory

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Potential for Neuroprotective benefits in PD

The survival of the MSN: Medium Spiny Neuron

DORSAL: Initiating and controlling movements of the body, limbs, and eyes.

VENTRAL: motivation, reward, reinforcement, and aversion.

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Disease Specifics: YOPD

- A slower disease progression (varied)
- An increased rate of dystonia
- A lower rate of dementia
- An increased rate of dyskinesias in response to L-DOPA treatment.
- Genetic tendencies
- DIFFERENTIAL: onset under 50

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Disease Specifics: Late onset PD

- Slower rapid disease progression (varied)
- Three subtypes:
  - Tremor
  - Rigidity
  - Dyskinesia
- Low rate of medication dyskinesias

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Related conditions…NOT PD

- Multiple System Atrophies: MSAs
- Alzheimer's Disease
- Fronto-temporal Dementia (FTD)
- Lewy-Body Disease
- Parkinsonisms due to stroke, toxicity, trauma
- Cortico-Basal Ganglia Degeneration (CBGD)
- Progressive Supranuclear Palsy

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Disease Specifics: Parkinsonism

- Variable presentations given etiology
  Stroke, multiple concussions, encephalitis
- Typically imbalance > tremor and rigidity
- Typically less freezing

* Less responsive to high-intensity exercise

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Disease Specifics: Parkinson*ism*

DIFFERENTIAL: Limited to no responsiveness to dopamine meds in most conditions…

and will exhibit a lower response to exercise…

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Primary dyskinesia

- Structures – Globus pallidus
- Incidence – Young onset, estimated <10%
  Higher incidence with heavy Levodopa use
- Presentation – Whole body, progressive
  Increases with stress, fatigue, distractions

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Primary tremor and rigidity

Structures

- Ventral intermedius n. (VIM) of the thalamus
- Subthalamic n. (STN) between BG and SN

- Incidence 80%

- Presentation: unilateral to B, posture, affect

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Freezing of gait; posture; and festination

- Structures – Putamen (automaticity)

- Incidence

- Presentation: Festination, FoG, cognition

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Individualizing PD programs

- Resources and impairments in the respective phenotypes of PD.
- Diseases are not all the same
- Underlying pathologies are not all the same
- Interventions SHOULD NOT be the same

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Parkinson's Disease POTENTIAL through high intensity exercise

- Central disease-modifying protection
- Central dopaminergic effects
- Psychological

- Muscular strength
- Muscular endurance
- Cardiovascular endurance

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CENTRAL (NEUROPLASTIC) CHANGES IN PD

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Point by point…how you intervene

Sensory neuroplasticity:

- Sensory changes…with PD?
- Remove/alter sensory strengths
- Dual tasking - automaticity
- Vision
- Somatosensation
- Daily +

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Point by point…how you intervene

Motor control neuroplasticity *and* BDNF:

- High intensity
- Task specific
- Repetition-based
- MUST be challenged…and see progress

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Point by point…how you intervene

P S Y C H O L O G I C A L

- Understand that the brain can change
- Understand that I can improve with PD
- SEE that I have improved – USE measurements
- Know that challenge = opportunity to improve
- Knowing, “I will do no harm with this activity”

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Protection through exercise…

Central

Medium Spiny neuron protection

Endorphin release and psychological gains

GDNF + BDNF

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CONDITIONING AND PERIPHERAL CHANGES IN PD

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Point by point…how you intervene

- Muscular strength
- Muscular endurance
- Cardiovascular endurance

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Strength training in PD: Applying the evidence

STRENGTH for function and falls

- Resistance tolerated ONLY 8-12 reps
- 2-3 sets and 3-4 days/week
- Expect soreness*
- Perceived exertion drives intensity
- Eccentric training can be > concentric

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Muscular endurance training in PD: Applying the evidence

Muscular endurance: Symptom management + function*

- Multiple sets
- Resistance 15-20 repetitions
- 3-4 days/week
- The art of cumulative effects
- Consecutive order for sets?
- Perceived exertion drives intensity

*Manage fatigue-based tremor, dyskinesia and falls

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Cardiovascular endurance training in PD: Applying the evidence

Cardiovascular endurance:

- Sustained activity, whole body as able
- 30 minutes
- 10 minutes, 3 +/day acceptable (cumulative)
- 4-7 days/week
- The art of cumulative effects
- Interest, experience, music…what drives *intensity*?

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Protection through exercise…

Peripheral

Fatigue-based tremor

Fatigue-based dyskinesia

Weakness-induced hypokinesia

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Parkinson's Disease – Common outcome measures

- Four square step test
- 2/6 min walk test
- Modified Dynamic Gait Index
- Timed Up & Go
- Gait velocity
- Sit to stands
- Activity-specific Balance Confidence Scale (ABC scale)

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TRANSLATING THE EVIDENCE WITH PRACTICAL INTERVENTION STRATEGIES ACROSS THE SUBTYPES

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Disease Specifics: YOPD

- More rapid disease progression (varied)
- An increased rate of dystonia
- A lower rate of dementia
- Increased rate of medication dyskinesias

- INTERVENTION: maximize flexibility and conditioning, pain in overuse from dyskinesia

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Disease Specifics: Late onset PD

- Slower rapid disease progression (varied)
- Three subtypes:
  - Tremor
  - Rigidity
  - Dyskinesia
- Low rate of medication dyskinesias
- INTERVENTION: Conditioning, power, balance, compensation

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CURRENT EVIDENCE FOR TREATMENT WITHIN EACH IMPAIRMENT AND FUNCTIONAL LIMITATION:

POWER
COORDINATION
DYSKINESIA

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Commonalities in PD

- THE cumulative cycle of INTENSITY leads to good things!!
- Attention
- Strength
- Endurance
- …more intensity!!

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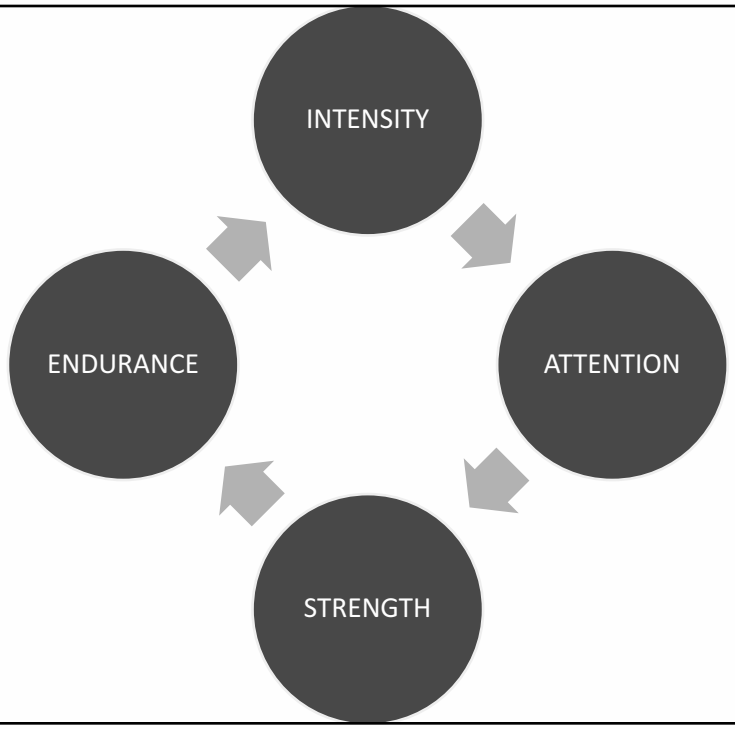

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Task-specific balance training

- Change of direction
- Change of pace
- Change of pathway
- Dual task

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Common balance-related impairments in PD

- Musculoskeletal impairments
  - Posture
  - Muscle flexibility
  - Muscle performance (strength, power, endurance)
  - Tone (hypo- or hypertonicity)
- Voluntary control deficits (e.g., bradykinesia, freezing)
- Poor sensory integration
- Difficulty switching tasks in movement sequences
- Impaired cognitive processing and dual-tasking

King LA, Horak FB . Phys Ther. 2009; 89 (4):384-393.

Barriers to safe balance training in PD

High fall risk in treatment given:

- Rigidity
- Attention
- Anxiety
- Motor control (freezing, bradykinesia)

- BWSTT to the rescue??

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Evidence in aerobic, dual task activities

- Dancing, high speed cycling, higher-intensity aerobic classes can enhance:
  - learning
  - mobility
  - fine motor skills in the UE + agility
  - mood/counter depression

Zesiewica and Evatt, 2009; Hackney, 2010; Kattenstroth et al, 2010; Duncan et al, 2011;Heiberger et al, 2011)

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Body weight support (BWS)

- Functional task
- Many patients have NEVER been on a treadmill
- Ensured safety, reducing anxiety
- Intensity and duration easier to record, replicate
- May induce balance challenges, overload
- Reduces dual task interference

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BWST Training for PD

BWSTT vs. traditional care

- Greater outcomes in QOL, gait speed, balance, endurance
- Responses higher with H/Y patients 1.0 to 3.0

(Herman et al 2007, Miyai et al 2002)

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Future research in PD: Learning Based Exercise Training

- Challenging neural networks/connections with attended learning based activities can improve timing and sequencing across sensory modalities
- Modify the "topographical" and "functional" brain representations of sensation, movement and task performance

  (Jenkins et al, 1984; Merzenich et al, 1985-2011;Byl et al, 1996; Blake et al 2002)

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Evidence in aerobic, dual task activities

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Individualizing PD programs

- Resources and impairments in the respective phenotypes or "Parkinson's ***Diseases***".
- Underlying pathologies are not all the same
- Functional presentations are not the same
- Impairments are not the same

- Interventions SHOULD NOT be the same

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Evidence-Based Practice

Intense Body-weight supported treadmill training

Intense balance challenges: speed, movement, surface and dual-task considerations - the "BIG" movement

Role of VOLUME regulation in all aspects of function

Make them comfortable with the world BEHIND them

Provide PROTECTED practice in changing directions

Postural changes and improving muscular balance

Compensatory efforts with visual, verbal rehearsal cues

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High Intensity Gait training

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Gait speed

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Balance, agility, and coordination

High intensity balance challenges

Eyes closed
Visual aberration
Multidirectional
Forced accuracy

Person-specific with regard to the TYPE of PD

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Multi-directional gait training

- Tremor: Agility and coordination

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Retro-specific gait training

- Level ground retro
- https://youtu.be/ZHGz0UU5Om4

- Festination resisted retro

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Power training

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Perturbation training

- Tremor and rigidity: Perturbation

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Potential for Neuroprotective benefits in PD

- Glial-derived neural protective factor (GDNF)
  - Stimulated or activated through:

- High intensity aerobic activities
- Skill-based speed and coordination activities
- Sport and competition with intensity
- Group programs of dance, balance

- More studies and practical applications…

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Barriers to aerobic exercise in PD

Challenge to achieve sustained heart rate given:

- Imbalance
- Rigidity
- Attention
- Anxiety
- Motor control (freezing, bradykinesia)

- BWSTT to the rescue??

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Body weight support (BWS)

- Functional task
- Many patients have NEVER been on a treadmill
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BWST Training for PD

BWSTT vs. traditional care

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(Herman et al 2007, Miyai et al 2002)

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Commonalities and future trends

- High intensity resistance exercise
- Task specific endurance exercise
- Postural control (reactive and pro-active)
- Feedforward/Feedback (APA and responsive)
- No one has too much strength
- Combine fun with exercise
- Combine personal interest with exercise

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Proven Benefits of Intense Aerobic Exercise

- Increased brain volume (Colcombe et al, 2006)
- Enhanced efficiency of Beta blockers
- Improved BMI
- Improved psychosocial function (Kohut et al, 2010)
- Increased endorphines (Cohen et al, 2003)
- Upregulation of dopamine (Villar-Cheda et al, 2009)
- Increased brain growth factors; Zigmond et al, 2009; Vucckovic et al, 2010)
- Increases walking speed, stride length and endurance (Miyai et al, 2000;2002)
- Improved cardiovascular fitness (Tillerson et al,2003)

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Parkinson's Specific: Forced vs. Voluntary Aerobic Ex

- **BOTH:** VO2 max improved 17% for FE and 11% for for VE

ONLY Forced Ex. improvements

- Improved cardinal motor signs for FE (41% in rigidity)
- Improvement in tremor (38%)
- Improvement in bradykinesia (28%)
- Bimanual motor dexterity (grip coupling) ,grip force and digit placement for maintained for 4 weeks
- UPDRS rating improved by 35% for FE and no improvements for VE ($p<0.002$)

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Is moderate intensity enough in PD?

- General moderate aerobic exercise ***maintains*** mobility and balance in patients with PD
  (Smidt et al, 2005; Goodwin et al, 2008; Suchowersky et al, 2006;Suchowersky et al, 2008; Dibble et al, 2009)
- Reduced fall rates
- Increases dopamine synthesis in available dopaminergic cells (Sutoo, 2003)

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Integrative Dual Task Aerobic PD Exercise Program

- Neurofit activities
- Running and gliding on BWSTT
- Coordination and balance exercises
- Game type activities: basketball, boxing, badminton
- Integrating technology: neuromuscular stimulation

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PD Boxing

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Parkinson's Disease POTENTIAL

- Muscular strength
- Muscular endurance
- Cardiovascular endurance
- Somatosensory neuroplasticity
- Motor control neuroplasticity
- P S Y C H O L O G I C A L

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Lessons in PDs

- Control all variables that you can…
- Consistent and lifelong exercise, activity
- No one ever comes to therapy with too much strength, or…too much endurance
- Balance exercises are a daily routine

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Evidence in exercise and PD

Resistance exercises can increase strength and ↓falls

ROM exercises improve flexibility

Balance exercises improve balance and ↓falls

Aerobic exercises improve cardio-pulmonary, ↓pain, improve cognition and decrease depression.

Auditory, visual, rhythmic and learning based exercises improve sensory processing and cognition

(Keus et al, 2009)

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Frail PD patients: MEASUREMENT

- Objective recordings that can be reproduced to prove real changes within a patient's case

- Bed mobility
- 5x sit to stand
- Unassisted sit to stand height
- 10' w/c propulsion
- Standing endurance

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Frail patient considerations

- Psychology of rehabilitation
- Nutritional considerations
- Evidence and recommendations: ACSM
- Provide body weight support to allow for endurance improvements
- Build RESOURCES, then function

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