Latest evidence: Exercise and activity for Parkinson's disease

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Objectives
- Discuss evidence for improved impairments and overall activity with physical intervention
- Compare and contrast strategies and benefits of exercise and activity interventions.
- Appreciate the importance of vigorous activity and the possible neuroprotective benefits.

Signs and Symptoms
- Cardinal signs
  - Rigidity
  - Tremor
  - Bradykinesia
  - Postural instability
- Other impairments
  - Musculoskeletal
  - Cardiovascular
  - Non motor (e.g., depression, cognition, sleep)

Flexibility
- Reduced early in PD
- Decreased range of motion of trunk related to balance
- Can be improved with exercise

Strength of People with PD
- Strength of extremities / trunk
  - Cano-de-la-Cuerda et al, 2010
  - Kakinuma et al, 1998
  - Bridgewater & Sharpe, 1998
- Abnormal muscle activation patterns & delayed reaction time
  - Corcos et al, 1996
  - Weizbicka et al, 1991
Which people with PD are Weak?

- Comparison of age, gender, BMI matched participants
  - UPDRS Motor and force
    - 30 no difference
    - > 30: 50% reduction in force production (quadriceps)
  - UPDRS Motor and force central activation
    - < 30 no difference
    - > 30 significant and substantial difference

Stevens-Lapsley et al., Neurorehab Neurorepair 2013

VO2 and Speed of Walking

Christiansen C, et al, Mov Disord. 2009

Benefits of Exercise

- Flexibility
- Strength
- Aerobic
- Balance
- Combined
- Tai chi
- Tango

Bottom Line: We don’t yet know which approach is best

- Exercise is important
- Long-term benefits are necessary because of chronic and progressive nature of PD
- Most appropriate exercise prescription is not yet known

Cochrane Collaborative – 2012

- Physiotherapy vs. placebo or no Intervention
- 39 studies in qualitative synthesis; 1518 participants
- 24 studies in quantitative synthesis (meta-analysis)

Conclusions

- Most short-term benefits were small but of a size that patients would consider meaningful.
- Quality of studies improved since last Cochrane review
Types of Studies

- General physical therapy vs. Control
- Exercise vs. Control
- Treadmill vs. Control
- Cueing vs. Control
- Dance vs. Control
- Martial arts vs. Control

Short Term Improvements …

- Gait
  - Velocity, step length, two- and six-minute walk
- Functional reach
- Timed Up and Go
- Berg Balance Scale
- Clinician-rated UPDRS

- Absence of evidence in other outcomes does not necessarily mean lack of benefit

Findings From 5 Additional Recent Studies

- Flexibility
- Aerobic endurance
- Resistive strengthening (2)
- Tai Chi

‘Stay Active with Parkinson’s Disease’

- Flexibility / balance / function vs. Aerobic vs. Control
- Study conducted by Schenkman and her team at University of Colorado
- 121 participants

Schenkman et al.; Phys Ther. 2012; 92:1395-1410

Method

- Design
  - 68 wk RCT comparing AE and FBF to Control
  - Primary end point – 40 wks.
- Outcomes
  - Functional in nature
- Participants
  - Early and mid-stage PD (H&Y 1-3)
  - Successfully completed graded exercise test
  - No other conditions that limit exercise

Outcomes From a 16-month Study

- Randomized controlled trial
  - 121 participants
  - Early to mid-stage PD
- Compared two approaches to exercise to a usual care control group
- Included strategies to enhance development of exercise habits
- Followed participants for 12 months following structured intervention
- Major outcomes were functional in nature

Schenkman et al. Phys Ther, 2012
Interventions
- Flexibility / Function / Balance (FBF)
  - 6 weeks flexibility
  - 8 weeks FBF in group
- Aerobic Endurance
  - 16 weeks supervised conditioning 65%-80% HRmax
- Home Exercise, American PD Booklet: Fitness Counts
  - Group exercise once a month

Outcomes - FBF
- Significantly better on CS-PFP at 4 months than
  - control group
  - AE group
- Not significantly better at 10 months or 16 months
- Significantly better on UPDRS ADL at 16 months (secondary)
- Not significantly better for FR at any time point

Outcomes - AE
- Walking economy improved in the AE group compared with
  - FBF group at 4 months
  - FBF group at 16 months
- Not significantly different at any time point for any other measure

Summary
- Greatest short term benefits
  - Flexibility/balance/function program led to better overall function for household activities at 4 months
- Greatest long term benefits
  - Aerobic endurance training (treadmill, elliptical bikes, etc.) led to better economy of gait over 16 months.
- All participants
  - Overall – almost no change in UPDRS scores over 16 months, which is terrific

Can people with PD continue to exercise?
- Qualitative data from 18 participants from the 16 month exercise study
- Data from about 1 year post graduation
- Attitudes toward exercise following graduation
- Interviewed 18 participants
  - 15 graduates
  - 3 drop outs
- Questions related to motivators, barriers, current activity status

Ene et al., JNPT, 35;34-40, 2011
General findings
- All graduates and some drop outs maintained some activity
- No "one size fits all"

Motivators
- Slow down disease progression
- Feel better
- Encouragement from family

Barriers
- Accessibility – community based

Recommendations
- More encouragement from neurologists

Resistance Exercise for Strength
- Progressive resistance exercise (weight lifting) program vs. General program (Fitness Counts)
- Study conducted by Daniel Corcos and his team at U Illinois, Chicago
- 51 participants


Method
- Design
  - 24 mo. RCT comparing PRE to low intensity balance and stretching
  - Primary end point: 24 mo.

Outcomes
- UPDRS motor

Participants
- Moderate disease severity
- Mean UPDRS Motor: about 21

Exercise Programs
- Exercised 2x/wk
  - Personal trainer 2x/wk for 6 months
  - Personal trainer 1x/wk thereafter

- Programs
  - PRE: 11 strengthening exercises including upper and lower extremities and back extension
  - Control: Modified ‘Fitness Counts’ (Chapters 2 & 3)

Results: Off-Medication UPDRS Motor Score
- Resistance Exercise group improved substantially more on UPDRS motor than Control at 24 months
- Also elbow flexion strength and movement speed

Tai Chi
- Tai chi vs. Resistance vs. Stretching
- Fuzhong Li, Oregon Research Institute, OR
- 195 participants

Method

- Design
  - 6 mo. RCT comparing Tai Chi to resistance or stretching

- Outcomes
  - Primary outcome: Limits of stability (excursion and directional control)
  - Secondary outcomes: gait, strength, FR, TUG, UPDRS motor

- Participants
  - Mild to severe: H&Y 1-4

Exercise Programs

- Exercised 60 min 2X/wk
  - Tai Chi: six forms
  - Resistance training:
    - General strengthening for 10 weeks
    - Added resistance training thereafter
  - Stretching: Low intensity seated and standing exercises

- Supervised exercise for 6 months

Results

- Balance measures: Tai chi better than with strengthening or stretching

- Gait measures: Tai chi better than stretching

- Falls: Tai chi was better than stretching

- UPDRS Motor: Tai chi better than stretching

Results

- Important point:
  Tai Chi was superior to strengthening on balance (primary measure) but not on any other outcome.

Aerobic Condition

- Two intensities of aerobic condition versus stretching and resistance training
- University of Maryland
- 67 participants

Shulman et al., JAMA Neurol. 2013;70(2):183-190

Method

- Design
  - 3 mo. RTC comparing 2 intensities of aerobic condition with stretching and progressive resistance

- Outcomes
  - Primary outcomes: Gait speed, cardiovascular fitness (peak VO2); strength (1 rep. max)

- Participants
  - Mild to moderate disease: H&Y 1-3
Exercise Programs
- **Group 1:** 30 minutes at 70%-80% of heart rate reserve
- **Group 2:** 50 min. at 40%-50% of heart rate reserve
- **Group 3:** stretching and resistance exercises 2 sets of 10 repetitions on each leg on 3 resistance machines

Results
- **Six minute walk:**
  - Low intensity: (12% increase; \(P=.001\))
  - Stretch/resistance: (9% increase; \(P=.02\))
  - High intensity: (6% increase; \(P=.07\))
- **Peak VO2:** Both treadmill groups improved (7%-8% increase; \(P=.05\))
- **Strength:** Only stretching / strengthening improved (16% increase; \(P=.001\))

Bottom Line Message from 4 Studies
- **Flexibility/balance/function**
  - Improves overall ability for household activities; may be hard to continue without a trainer
- **Aerobic conditioning**
  - Improves walking efficiency; improvements sustained long term
- **Resistance exercise**
  - Improves UPDRS Motor; improvements sustained long term
- **Tai Chi**
  - Improves balance; also improves walking, UPDRS Motor, reduces falls

Clinician’s Bottom Line
- Different exercise approaches have different benefits
  - Patient’s greatest problems can help determine best approach
- Short-term benefits are not sufficient
  - With patient, decide how to sustain the benefits
- Program may need to address a combination of issues (strength, flexibility, aerobic exercise, balance)
  - Consider a directed exercise program followed by general activities (e.g., dance, group high intensity exercise)
  - Develop mechanisms for easier community access
- Need studies!

‘Exercise’ vs. ‘Activity’
- Physical therapists tend to think of exercise in terms of specific regimens to improve balance, gait, flexibility etc.
- Overall activity, and particularly vigorous activity, may be just as important as structured ‘exercise regimens’

Physical Activity vs. Exercise vs. Fitness
- **Physical activity** - any bodily movement produced by skeletal muscles that results in expenditure of energy (measured in kilocalories [kcal]).
- **Exercise** is a subcategory – includes activities that are planned, structured, repetitive, purposive; intended to improve one or more components of physical fitness.
- **Physical fitness** - ability to carry out daily tasks with vigor and alertness and without undue fatigue, with ample energy to enjoy leisure pursuits and to meet unforeseen emergencies.

Activity in PD

- People with PD (n=699) are 1/3 less active than older adults generally (n=1,959)
- Activity levels decline with increasing disease severity
- In a longitudinal study: daily steps declined 12% and moderate intensity walking 40% in a year

van Nimwegen et al, J Neurol. 2011;258:2214-21.

Benefits of Increasing Activity

- The ParkFit trial (n = 586)
- 2-year multicentre RCT comparing
  - physical therapy with a specific emphasis on promoting a physically active lifestyle (ParkFit Program)
  - general physical therapy (ParkSafe Program)
- Induce lasting change in exercise behavior through goal setting, overcoming barriers to exercise, recruiting social support, coaching by the physical therapist (PT), and activity monitor with visual feedback for daily activity levels.


Outcomes - ParkFit

- Primary outcome – 7 day recall; not significantly different
- Secondary outcomes:
  - 14 day activity level (Kcal/min) with activity monitor was significantly improved
  - Activity - approximately 90 minutes per week of physical activity increase compared with 30 minutes for ParkSafe.
  - Walking endurance (6 min walk test) significantly greater at 24 mo.

van Nimwegen et al BMJ. 2013;346:f576

Evidence related to vigorous activity

- Prospective evidence – suggests midlife, regular exercise reduces risk of subsequent PD
- Exercise reduces cognitive impairment in general population
  - Prospective and retrospective evidence
  - Studies of older people with / without dementia
- Animal models – physical exercise enhances brain plasticity

J Eric Ahlskog. Neurology 2011;77;288

Clinical Bottom Line

- Encourage regular activity
- For sedentary people – just get up and move
- For more active people – build up to regular, vigorous activity
- Dose???

Is Exercise is Neuroprotective for PD?

- Animal studies (rodents, primates) suggest that exercise might be neuroprotective for PD.
- Studies are needed in humans but are expensive
- Before asking this question, first need to determine:
  - What is the best dose of aerobic exercise?
  - Does exercise provide benefits for people prior to initiation of dopaminergic or other dopamine related therapies?
Forced Tandem Biking

- Comparison of forced pedaling rate vs. self-selected rate during tandem biking
- Ten participants, random assignment
- Forced rate – 30% greater than the individual's voluntary rate
- 3 sessions (1 hr each) for ten weeks

Ridgel et al, Neurorehabil & Neural Repair, 2009

Current Study - Multicenter Trial
Does exercise slow PD symptoms?

Purpose: Define the right intensity of exercise in preparation for a phase III trial of neuroprotection

- Futility trial: Comparison of aerobic exercise at 2 intensities & no exercise
- People recently diagnosed with PD; not on medications for PD
- Expect to complete the study (120 participants) in three years
- Funded by the National Institutes of Health (NIH)

Comparison of 2 intensities of aerobic ex on a treadmill to no ex
- 60-65% HRmax
- 80-85% HRmax
- Wait listed control
- Exercise 4X/wk for 6 mo. with option to exercise for another 6 mo.

Moore et al. Contemporary Clinical Trials 2013;36:90-98

64 participants randomized to date
- 24 completed 6 mo. (primary end point)
- 10 completed 12 mo. end point

We Welcome Referrals!
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Questions?