Exercise Interventions for People with PD: Rational and Recommendations

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Overview

- Exercise as a management tool in PD (Neurophysiological hypothesis)

- The effects of exercise and physical rehabilitation in managing people with PD: available evidence

- Physical rehabilitation in the Middle East countries: barriers and facilitators

- Conclusions/ future directions
Neuro-structural Response to Exercise on a Healthy Brain

Neuron size/ area/speed/ number

Synaptogenesis/ Angiogenesis

Cottman et al, 2006
Molecular and Neurophysiological Response to Exercise on Healthy Brain

- Increases cerebral blood flow
- Suppresses oxidative stress
- Regulates the expression of survival factors including vascular endothelial growth factor (VEGF) and the BDNF factors
- Increases several neurotransmitters, such as serotonin (5-HT), dopamine (D), acetylcholine (ACh) and norepinephrine (NE)

Bottom Line: healthy, efficient brains – have greater recovery, more resistant to stress & toxins and do more with less.

Cottman et al, 2006; Kleim et al, 2003
Can Exercise be Neuroprotective in PD?

- Animal studies
- Epidemiological studies
- Registry data
Research Shows Exercise Can Influence Disease Modification in PD Animal Models

**PD: pre-clinical phase (neuroprotection)**
- Increased overall levels of dopamine
- Increased neurotrphic factor expression
- Reduce oxidative stress

**PD: early phase (neuro-repair)**
- Instead increased localized release of dopamine-shunted
- Downregulation of DA transports- DA stayed in synapse longer
- More D2 receptors

Exercise in PD: Neuroplasticity Mechanisms are Time Dependent

Farley, 2009
Neuroprotective Effect of Physical Activity Against PD: Evidence from Epidemiological Studies

Higher levels of moderate to vigorous activities is associated with lower risk of obtaining PD

Xu et al, 2010
The national Parkinson’s Foundation (NPF) registry data
2252 subjects with PD who had baseline measurements and followed up 1 year later.

Regular exercisers at baseline were associated with
- Better QoL, mobility and functional status one year later.
- Less caregiver burden and less cognitive decline one year later.
- Less progression of disease one year later.
“Take Home” Messages!

- Exercise may have a neuro-protective effect in PD
- Timing matters: earlier is better than latter
- Inactivity is pro-degenerative
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Impact of Physical Therapy in PD: A systematic review

- 2001 Cochrane Systematic review:
- RCT’s= 11
- N=280
- Conclusions: insufficient evidence to support or refute the efficacy of PT in PD
- Variability of outcome measures and interventions
Impact of Physical Therapy in PD: A systematic review

- 2012 Cochrane Systematic review
  - RCT’s= 39; N= 1902
  - Moderate to strong evidence that patients with PD can benefit *in short term* from a wide range of physical therapy interventions in improving:
    - Gait speed
    - Balance
    - Motor sub-score of UPDRS.

Tomlinson et al, 2012
Impact of Physical Therapy in PD: A systematic review

• 2012 Cochrane Systematic review
  ▪ **Wide range of treatment approaches**
  ▪ **Heterogeneity in dose** (*i.e.* intensity, frequency and duration)
  ▪ Most studies have been performed at mid-stage disease; *little is known about very early and late stages*
  ▪ There is evidence on the **short-term benefit of PT for PD**
  ▪ Need more **large, well-designed RCTs**
  ▪ Need to demonstrate **longer-term efficacy**
  ▪ Need to establish a consensus of what “**best-practice**” means.

Tomlinson et al, 2012
European Physiotherapy Guideline for Parkinson’s Disease

- Joint project between Parkinson’s Net and 19 member organizations of the European Region of the WCPT (ER-WCPT).
- Systematic review of literature
- Grading body of evidence
  - High, moderate, low or very low
- Recommendations:
  - Strong (for OR against)
  - Weak (for OR against)

Keus et al, 2014
European Physiotherapy Guideline for Parkinson’s Disease

- 70 CCTs
- Type of interventions (n=9):
  - Conventional physiotherapy
  - Treadmill training
  - Cueing
  - Strategies for complex motor sequences
  - Massage
  - Whole body vibration
  - Martial arts
  - Dance

<table>
<thead>
<tr>
<th>Recommendations FOR</th>
<th>Symptom</th>
<th>Intervention</th>
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<tbody>
<tr>
<td></td>
<td>Functional mobility</td>
<td>strategies for complex motor sequences + with cueing</td>
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<tr>
<td></td>
<td>Balance</td>
<td>Tai Chi or strategies + cueing</td>
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<tr>
<td></td>
<td>Falls</td>
<td>Ti Chi</td>
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<tr>
<td></td>
<td>Gait</td>
<td>Conventional physiotherapy (incl. balance, strength, ROM &amp; gait training), cueing or treadmill training</td>
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<tr>
<td></td>
<td>Muscle strength</td>
<td>Conventional physiotherapy or Tai Chi</td>
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<td></td>
<td>UPDRS III</td>
<td>Conventional physiotherapy, Tai Chi</td>
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</table>
"Exercise research in PD has focused primarily on the motor symptoms and largely failed to consider its potential to improve nonmotor symptoms."

"The known benefits of exercise in healthy older adults may very well translate to this population, driven by potentially overlapping mechanisms."

"Future studies should include a variety of nonmotor outcome measures to systematically examine the effects of exercise on these symptoms."
Cycling for Freezing of Gait

- 53 PD patients interviewed
  - 23 of them experienced freezing of gait
    - Only one of those 23 patients experienced episodes of freezing of gait while cycling

Cycling seems to be less affected than walking when used as a physical rehabilitation method for patients with freezing of gait in PD

Anke and Bloem, N Engl J Med 2010
The Cycling Sign in PD (video section)
Forced vs Voluntary Exercise: Does It Matter?

- **Intervention:**
  - Randomly assigned to forced- or voluntary exercise groups
  - Three 1 hr. sessions/wk for 8 weeks
  - 10 min. warm up, 40 min. main set, 10 min cool down
  - 60-80% ACSM target HR
  - Forced-exercise *group pedaled 30% faster* and produced 42% less work compared to the voluntary exercise group.

Ridgel et al, 2009
Aerobic Exercise Improves Fitness, Only FE Improves Clinical Rating

Rate of exercise appears important for PD symptoms management

Mean Change in UPDRS III Motor Scores Decreased Significantly After 8 weeks of Forced Exercise but Returned Toward Baseline After the Exercise Training Was Completed

Ridgel et al, 2009
Forced Exercise (video section)

Off DBS (4 hours)  (post-exercise)

Jay Albert (Cleaved Clinic), used with permission
Vigorous Exercise and PD

- Ongoing structured progressive training is highly encouraged particularly for de-conditioned patients with PD.

- Levodopa and other forms of dopamine therapy should be used to maximize an individual's participation, and motivation for achieving optimal physical fitness.

Ahlskog, 2011
Effect of Annual Intensive Boats of Exercise on Motor Score and Medication use in PWP

**Group 1 (IRT):**
3 sessions daily of 5 days for 4 weeks.

Frazzita et al, 2012
Barriers to Regular Independent Engagement in Exercise in PWP

- Low self efficacy
- Low outcome expectations
- Fear of falling
- Lack of time
- Level of education
- Lack of support provided by health care professionals and organizations

Overview

- Exercise as a management tool in PD (Neurophysiological hypothesis)

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  - Physical Rehabilitation in the Middle East countries: barriers and facilitators

- Conclusions/ future directions
### Barriers and Facilitators in Physical Rehabilitation for Parkinson's Disease in the Arabian World

Hanan Khalil, PhD, Jawad A. Bajwa, MD, PhD

<table>
<thead>
<tr>
<th>Category</th>
<th>Possible barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Personal</strong></td>
<td>Lack of knowledge</td>
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<td></td>
<td>Lack of informational resources</td>
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<td></td>
<td>Lack of interest and motivation</td>
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<td></td>
<td>Lower base of physical activity and fitness level</td>
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<td><strong>Social/Cultural</strong></td>
<td>Gender discrepancies; social norms may impact on provision of services provided for women</td>
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<tr>
<td><strong>Environmental</strong></td>
<td>Limited access to resources</td>
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<td></td>
<td>Lack of specialist therapists</td>
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<td>Lack of multi-disciplinary rehab centres</td>
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<td></td>
<td>Lack of appropriate public transport system</td>
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<td></td>
<td>Lack of reimbursement</td>
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Khalil H and Bajwa J, 2015
Exploring practices and perceptions toward exercise among PD patients in Jordan

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2. Department of Maternal and Child Health, Faculty of nursing, Jordan University of Science and Technology

Introduction
Exercise has significant positive effects on motor symptoms in PD [1]. Sustained supervised exercise, however, may not be the most feasible for life-long disease management. Engagement in an independent exercise programs is therefore particularly important. However, adherence to such programs represent a wide-base challenge. A number of barriers are known to negatively influence independent exercise participation in people with PD [2]. The available evidence may only apply to a limited culture or ethnicity as all existing studies were conducted in US or Canada. There is a clear need to expand our knowledge of how people with PD from different cultures and ethnicity perceive exercise and what factors would affect their participation.

Aim
To explore attitudes, practices, and perceptions of physical activity and exercise in patients with idiopathic PD in a group of PD from Arab ethnicity in northern Jordan.

Method
Qualitative design was used to elicit these information as such studies offer valuable information on attitudes and barriers that extend beyond the traditional outcomes associated with surveys. Two focus groups were conducted with patients with PD and their carers (n=6 PD patients; n= 3 carers). Conversations were digitally recorded and transcribed verbatim. Transcripts were analysed and coded using thematic analysis and validated via researcher triangulation and verified by peer checking.

Results
Two main themes emerged from the study: exercise barriers and exercise motivators.

Theme 1: Barriers to exercise
It was evident from the focus groups that participants with PD felt that there were significant barriers to engage in exercise (Figure 1).

1. Lack of information and support: Participants reported that they were in dire need for information and education about their disease, management and prognosis especially at the time of the diagnosis. Relying only on medication and not knowing what else to do to improve their quality of life left them in dilemma. Interestingly, none of the participants was previously referred to physiotherapy.

2. Lack of self efficacy: Some participants had tried to initiate exercising at home, however not knowing exactly of how to apply exercises and feeling unsafe limited their participation.

3. Disease-specific physical symptoms: Some participants felt that some of the disease specific symptoms such as stiffness and fatigue may limit their potential participation in future exercise program.

4. Setting-related issues: The location of the exercise was considered an important consideration for the participants to engage in an exercise program. This consideration is related to social and commitment aspects.

Management strategies to overcome these barriers were identified (Figure 1).

Theme 2: Motivators to exercise
Two main factors were reported as being important to participants to initiate and maintain an exercise program (Figure 1).

1. Outcome expectations: most participants reported that they wanted to do things to improve their functional capacity and concomitant sense of independence.

2. Family support: family commitment of support to engage in exercise was very important particularly for female participants, including psychological support and provision of transportation.

Results - continued

Figure 1: Summary of barriers and motivators in exercise and their management strategies

<table>
<thead>
<tr>
<th>Theme 2 and 3: Barriers and facilitators to exercise in PD</th>
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</thead>
<tbody>
<tr>
<td>Barriers</td>
</tr>
<tr>
<td>Lack of information</td>
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<tr>
<td>Lack of self efficacy</td>
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<tr>
<td>Disease-specific physical symptoms</td>
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<td>Setting-related issues</td>
</tr>
<tr>
<td>&quot;Home&quot; if time/lifestyle is an issue</td>
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References

Acknowledgements
The authors would like to acknowledge all of the participants of the study. Further acknowledgement for funding support is to Jordan University of Science and Technology.

Note: *Exploring practices and perceptions toward exercise among PD patients in Jordan 426. " Hanan Khalil: hekhalil@just.edu.jo
Figure: Barriers to exercise in PD

Patients’ perspectives
- Difficulty of diagnosis
- Hope of being misdiagnosed
- Limited information about PD
- No information about exercise in PD

Neurologists’ perspectives
- Inappropriate referral system
- Limited number of neurologists
- Very limited time at clinic
- Limited physician knowledge about PT role in PD
- Limited resources

Lack of informational support

Lack of instrumental support

The need for specialized multidisciplinary clinic
Home Use of Exercise DVD for PWP: A Patient’s Resource in Arabic Language

- Exercise DVD in Arabic (home use; strength & balance plus self directed PA) for people in early-mid stages of PD
- Just completed evaluating its feasibility and acceptability

Khalil et al, 2015b
Home use of Exercise DVD for PwP: A Patient’s Resource in Arabic Language

- **Adherence rate:** 70% of the subjects performed at least 50% of the total prescribed sessions (range 0% to 100%).

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<th>Challenges</th>
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<tr>
<td>Co-morbidities</td>
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<td>Physical symptoms (fatigue)</td>
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<td>Not perceiving importance of exercise</td>
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<td>Stigma</td>
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<td>Culturally exercising is not the norm for old people</td>
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<td>Secrecy of diagnosis</td>
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<td>Gender discrepancy (women when lack family support)</td>
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“Take Home” Messages!

- Exercise is an important management tool that address limitations in this population.
- Early intervention/ early referral.
- Inactivity is prodegenerative/ neurologist advice.
- Forced use/ rate of exercise may be important for PD motor symptoms’ management.
- Meds to maximize participation.
Continuous (threshold) of exercise to sustain.
Barriers exercise engagement to be addressed.
Barriers to exercise engagement needs to be looked at within social and cultural contexts.
Future Directions

- Further research in this area is required to:
  - Determine optimal exercise dose.
  - Comparative studies to determine best approach.
  - Understand underlying mechanisms.
  - Potential benefits on non-motor symptoms.
  - Innovative approaches to empower people and help them to engage in regular exercise.
Acknowledgement

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  - Dr. Elham Alshorman, Dr. Alia Algwiri, Dr. Hikmat Hadoush, Prof. Khalid Elsalem, Prof. Monica Busse, Dr. Lori Quinn, Mr. Hassan Khawaldeh, Ms. Shada Khazaaleh, Ms. Lamees Abualfoul
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