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A Systematic Review on Various Modes of Exercise on People with Parkinson Disease

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ABSTRACT

Purpose: It is important to understand the benefits of exercise for patients with Parkinson's Disease (PD). A systematic review (SR) was conducted in order to report exercise-based interventions on PD. **Methods:** A literature search in MEDLINE, CINAHL, WEB of SCIENCE, and Cochrane database was carried out. In this particular study, we focused on the articles that reflected the effectiveness and efficacy of exercise on PD patients. Randomized Controlled Trials (RCTs) were included for the review to investigate the various modes and effectiveness of exercise being offered to PD patients. **Results:** 10 published RCTs were included in the review, and they were rated as high quality by the PEDro Scale. The RCTs involved 579 patients altogether. The 10 RCTs indicated 5 specific core areas of exercise that include flexibility, muscle strengthening, gait, balance, and physical conditioning. These core areas of exercise appear to support the physical, psychological, and sociological aspects of the life of PD patients. A range of functional and appropriate outcome measures were chosen and the outcomes showed beneficial effects of exercise on PD patients. **Conclusion:** Exercise appears to provide benefits for physical functioning and health-related quality of life of people with PD. Further study needs to be conducted to establish efficacy of exercise (e.g., meta-analytic SR or further trials).

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder that causes movement dysfunction. Symptoms include slowness initiating and difficulty maintaining movement (bradykinesia), rigidity, tremors, and postural instability.¹ Medication is used in the management of PD, but pharmacological treatment alone does not relieve all symptoms.² As PD is a chronic and progressive disease, other management (non-pharmacological) methods, e.g. exercise, is needed to manage PD in complement to pharmacological treatment.

Exercise has been used as one of the management methods to support the pharmacological treatments in order to improve non-dopaminergic symptoms such as lack of balance control and resulting falls. According to Goodwin et al, exercise programs have proved to be an effective strategy to delay and reverse functional decline for people with PD, and a large body of empirical evidence has emerged in recent years regarding the beneficence of exercise on PD patients.³ Exercise serves as an important adjunct to the available pharmacological and neurosurgical treatment regimens, in view of the facts that most pharmacological and surgical treatments are able to reduce, but not eliminate, the neurological deficits of bradykinesia, rigidity, and freezing. Regular physical exercise therapy sessions, supported by qualified allied health professionals, could be useful for most patients with PD, but it remains unclear what level and which type of exercise is most appropriate for people with PD. For example, a number of studies have shown that exercise, in the form of dance, encouraged motivation, social-interaction, and improvement of

axial-impairment of PD patients.⁴⁻¹⁰ A systematic review is needed to determine the effectiveness of various type of exercise in people with PD.

MATERIALS SELECTION AND IDENTIFICATION

Publications between 1970 and July 2010 were searched using various databases (such as MEDLINE, CINAHL, WEB of SCIENCE and Cochrane database of systematic reviews). In addition, cross-references, references recommended by experts, bibliographies of review articles, narrative reviews, and abstracts published in conference proceedings were also searched for relevant publications. Only articles written in English were included for the review. After an extensive literature search by using two key words "Parkinson" and "exercise" in the title of the publication, 156 publications were identified. The various categories were: 78 articles, 60 meeting abstracts, 5 reviews, 5 proceeding papers and 4 letters. The 78 articles were assessed by the researchers for the design. This criteria narrowed the number to 10 RCTs, all of which indicated positive outcomes from exercise for PD patients.¹¹⁻²⁰ Only RCTs were included for the present review, as trials with this design are considered to be the highest level of evidence.²¹ The inclusion criteria for 10 RCTs were the trials of either practical or explanatory design and sample participants aged from 20-85 years of age and suffering from PD. Exercise (alone or multi-modal) is the main intervention method under investigation for the 10 RCTs.

AIM AND QUALITY APPRAISAL

The aim of the review is to explore the therapeutic effectiveness of exercise in order to provide evidence for the enhancement of health status, functional status, and quality of life of people with PD. The Medical Research Council (MRC) guidelines were used as a methodological template by the researcher for this research.²² It is a framework used for the development and evaluation of RCTs for complex interventions to improve health.

The methodological quality of the RCTs was rated using the Pedro scale and results are presented in Table 1. The 10 RCTs were scored by two researchers. Any disagreement between the authors were discussed and agreement was reached using the consensus method. A score of 4 points or higher is classified as "high quality" and studies with 3 points or lower are classified as low quality. All 10 RCTs scored between 5 and 6 out of a maximum of 10 and are therefore considered to be of "high quality."

Because the current median score of all articles in the PEDro database is a "5," the authors want to clarify the method by which the "quality" of an RTC was determined (using the PEDro scale) for this study. It should be noted that:

- i) In general any study considered to be low quality if it scored 3 or lower in the Pedro scale.
- ii) In practice, it is difficult to blind therapists delivering the intervention or participants in rehabilitation-type trials; therefore, the maximal achievable score for a study is likely to be 8 out of 10 in Pedro scale. Hence, any score of 4 or above is considered to be high quality.
- iii) Pedro scores are not used as inclusion/exclusion criteria of any RCTs, but rather as a basis for best-evidence synthesis and to discuss the strengths and weaknesses of studies.

Table 1: Methodological Quality Assessment of the 10 RCTs via Pedro Scale

Author/Year	Random Allocation	Allocation Concealed	Similar Baseline	Blinded Subjects	Blinded Therapists	Blinded Assessor	Follow up	Treatment-in-analysis	Between group control	Point measures	Total
Ashburn et al, 2007 ¹¹	1	0	1	0	0	0	1	1	1	1	6
Hausdorff et al, 2001 ¹²	1	0	1	0	0	0	0	1	1	1	5
Ellis et al, 2005 ¹³	1	0	1	0	0	0	1	1	1	1	6
Kurtis et al, 2008 ¹⁴	1	0	0	0	0	0	1	1	1	1	5
Fischer et al, 2008 ¹⁵	1	0	1	0	0	0	0	1	1	1	5
Zampieri et al, 2009 ¹⁶	1	0	1	0	0	0	1	1	1	1	6
Morris et al, 2008 ¹⁷	1	0	1	0	0	0	1	1	1	1	5
Schmitz-Hübsch et al, 2006 ¹⁸	1	0	1	0	0	0	1	1	1	1	6
Tickle-Degnen et al, 2010 ¹⁹	1	0	1	0	0	0	1	1	1	1	6
Yousefi et al, 2009 ²⁰	1	0	1	0	0	0	0	1	1	1	5

Of all the RCTs scored, the main shortcomings in methodological quality were i) lack of patient blinding, ii) lack of therapist blinding, and iii) lack of assessor blinding. Close attention to data extraction enabled the researchers to deal with the understanding and character description of the body of evidence. The data extraction process was systematic and transparent and followed four stages carried out by the researchers independently. The process included i) Assessment of eligibility, ii) Assessment of quality, iii) Assessment of study characteristics, and iv) Extraction of findings.

RESULTS

Sample participants

The 10 RCTs combined included 579 participants. A majority of sample participants had idiopathic PD (see Table 2). In most trials the sample size was small. The largest and smallest sample size was in the RCT carried out by Ashburn et al, (n=142) and Zampieri et al, (n=20), respectively.^{11,16}

Table 2. Trial Details for 10 Reviewed RCTs

Author, Year	Study Type and Participants (n)	Interventions	Exercise Mode	Outcomes	Follow-up	Conclusion
Ashburn et al, 2007 ¹¹	Idiopathic PD. Exercise group (n=70); and Control group (n=72)..	Intervention group-exercise therapy. Control group-mainly contacts with the local PD Nurse and exercise tips were provided.	6 levels of exercise progression-muscle strengthening range of motion (ROM), balance training and walking.	Berg Balance Scale, Self-rating Anxiety scale (SAS), Quality of life (QoL) Thermometer and Functional Reach test. Study-Scale-It was small and 6 people dropped out of the intervention therapy and 64 people out of 70 had a positive effect via exercise and their QOL rose as well.	After 6 months. In the follow-up QoL of the exercise group was positive and the QoL of the control group was negative...	There was a trend towards a reduction of fall events and injurious falls with a positive effect of exercises on near falls and QoL.
Hausdorff et al, 2001 ¹²	Older adults with gait instability. Exercise group (n=30); and Control group (n=37).	Intervention group-6 months of multi-modal exercise therapy. Control group-6 months of nutrition education.	The exercises were: chair stands, circle turns, plantar flexion, ankle dorsiflexion, knee extension, standing hip extension.	Mini-mental status score, Physical Activity scale for Elderly (PASE), Geriatric depression scale (GDS) and Physical performance test (PPT). Study-Scale -It was small and intervention group (n=30) reported no drop-out. Findings highlight progress in gait instability achievable by physiological adaptation during targeted, multimodal exercise regimens.	Follow-up not described.	Although the aetiology of gait instability in older persons with mild-moderate functional impairment is multi-factorial, interventions designed to reduce gait instability may be effective in bringing about a more consistent and more stable walking pattern.

Author, Year	Study Type and Participants (n)	Interventions	Exercise Mode	Outcomes	Follow-up	Conclusion
Ellis et al, 2005 ¹³	Patients with idiopathic Parkinson's disease (PD). Hoehn and Yahr stage II or III. 68 participants were randomly allocated to group A and group B. Group A (n=37) and Group B (n=31).	Group A received PT and medication therapy (MT) for the first 6 weeks, followed by MT only for the second 6 weeks. Group B received only MT for the first 6 weeks and PT and MT for the second 6 weeks.	Exercise parameters were- cardiovascular warm-up activities, stretching exercises, strengthening exercises in a functional context, functional training, gait training over ground and on a treadmill with external auditory cueing, balance training, recreation games and relaxation exercises.	The main outcome measures were-the Sickness Impact Profile (SIP-68), the mobility portion of the SIP-68, UPDRS and Comfortable Walking Speed (CWS). Study-Scale -It was small and involved 68 subjects at first but 57 subjects attended the whole intervention.	Follow-up was done at 6 week, 12 week and 3 month.	This study showed that gains were observed in functional status and quality of life related to physical mobility but not at the global disability level (SIP Total). QOL issues related to socialization and participation in household and community activities needs further investigation.
Kurtis et al, 2008 ¹⁴	Patients with idiopathic PD Hoehn and Yahr Stage II. 27 participants randomly allocated to intervention group & control group. Intervention group-13 participants and control group-14 participants.	Intervention group attended a training program on a treadmill for 6 weeks and the control group received no exercise therapy. Both groups were instructed in home-mobility exercises.	Flexibility exercises, ROM exercises and gait training on a treadmill.	The main outcome measures were-timed functional lower extremity tasks (walking at a corridor, U turn, standing on one foot and standing from a chair), exercise tests and patient's global assessment. Study-Scale -it was small and 24 patients completed the whole study.	Follow-up after 6 weeks and 11 patients from the exercise group rated their global physical status as better, where as most of the control group subjects rated their status as same.	Even though long-term effects remain unknown and the study sample was small, it was concluded that treadmill training in PD patients led to improvements in lower-extremity tasks, thus improving patients' physical well-being in daily life.

Author, Year	Study Type and Participants (n)	Interventions	Exercise Mode	Outcomes	Follow-up	Conclusion
Fischer et al, 2008 ¹⁵	Patients with PD within 3 years of diagnosis with Hoehn and Yahr stage 1 and 2. 30 participants. The participants were randomly allocated to 3 groups.	High intensity exercise group-used body-weight supported treadmill training. Low-intensity exercise group-used traditional PT. Zero intensity group followed no exercise but 6 education classes.	Exercise parameters were treadmill training, passive ROM and stretching, active ROM, balance activities and gait training.	Unified Parkinson's Disease Rating Scales (UPDRS), biomechanical analysis of self-detected and fast-walking and sit-to-stand tasks; corticomotor excitability measured by cortical silent period (CSP) durations in response to single-pulse TMS. Study-Scale: small. 30 subjects completed study.	There was no follow-up. Data were collected before, and immediately after, the intervention.	A small improvement in total and motor UPDRS was observed in all groups. The findings suggest the dose-dependent benefits of exercise and that high-intensity exercise can normalize corticomotor excitability in early PD.
Zampieri et al, 2009 ¹⁶	Patients with possible/probable Progressive Supranuclear Palsy (PSP) who were ambulatory for short distances and had far visual acuity. 20 participants. The participants were alternately assigned to either a treatment group (balance + eye) or a comparison group (balance only)(n=20).	Balance training complemented with eye movement and visual awareness exercises was compared with balance training alone.	Exercise parameters: Common exercises including tandem stance practice with eyes open and closed, turning 360 degrees while marching in place, and sit-to-stand and stand-to-sit practice on chair. Group specific exercises involved-saccade exercises in which participants had to respond with a key press to visual stimuli presented in random locations on a computer screen.	Main outcome measures were gaze control assessed using a vertical gaze fixation score and a gaze error index. Study-Scale: It was small and 19 participants. One participant dropped out from the comparison group due to Urinary tract infection (UTI).	Follow-up after 2.5 years.	This study findings support the use of balance and eye movement exercises to improve gaze control in PSP. It is not known how the intervention method translates from laboratory to clinic. Further research is necessary to determine the carryover effects of this therapy and to determine its effects on other populations.

Author, Year	Study Type and Participants (n)	Interventions	Exercise Mode	Outcomes	Follow-up	Conclusion
Morris et al, 2009 ¹⁷	Participant-s with idiopathic PD. Their age ranged from 21-80 years of age but medically stable. 28 participants. The participant-s were randomly allocated to group A (strategies) and group B (exercises).	Group A- Movement Strategy Training Group that dealt with cognitive strategies. Group B- Musculoskeletal Exercises.	Exercise parameters: strategy training involved external cues to enhance walking, turning, standing up from a chair & obstacle negotiation. Extended to ADL performances. Musculoskeletal exercises involved strategies to improve strength, range of movement, posture, general fitness and function based on Schenkman protocol.	The primary outcome was disability as measured by the Unified Parkinson's Disease Rating Scale (UPDRS), UPDRS (motor and ADL components). Secondary outcomes were balance, walking speed, endurance, and quality of life. The Study-scale was small. All the 28 participants continued all the interventions.	Follow-up after 2 consecutive weeks. In Group A (n=14) no loss of follow-up. In Group B lost to follow -up (n=2).	For the exercise group, quality of life improved significantly during inpatient hospitalization and this was refined at follow-up. Inpatient rehabilitation produces short term reductions in disability and improvements in quality of life in people with Parkinson's disease.
Schmitz-Hübsch et al, 2006 ¹⁸	Patients with PD at different levels of disease severity. 56 participant-s randomly allocated to intervention group (n=32) and control group (n=24).	Intervention Group-A weekly 60 minute lessons of Qigong by an experienced teacher in 2 courses of 8 weeks with an 8 week pause in between. The control group had no exercise intervention.	The exercise parameters were – Standing exercises, sitting exercises and closing exercises.	The primary outcomes were- UPDRS-III and PDQ-39. Study-Scale was (n=30) for the intervention group and the control group was (n=19).	At 3, 6 & 12 months. Lost to follow up at 6 months: intervention group (n=1) & control group (n=3). Lost to follow-up after 1 yr: intervention group (n=1) & control group (n=2).	The study finding was positive. They found a stabilizing effect of Qigong exercise on motor performance and several non-motor symptoms in this study.

Author, Year	Study Type and Participants (n)	Interventions	Exercise Mode	Outcomes	Follow-up	Conclusion
Tickle-Degnen et al, 2010 ¹⁹	Patients with PD (mild to moderate stages of PD). Participants (n=117). The participants were randomly allocated to one of the three intensity of rehabilitation conditions for 6 weeks intervention.	Intervention involved: 0 hours of rehabilitation, 18 hours of clinic group rehabilitation plus 9 hours of attention control social sessions, and 27 hours of rehabilitation with 18 in clinic group rehabilitation and 9 hours of rehabilitation designed to transfer clinic training into home and community routines.	The exercise parameters were- physical exercises, speech exercises, functional training and discussion about self-management strategies.	The Health related quality of life (HRQOL) Outcome measure was the Parkinson Disease Questionnaire 39(PDQ-39). The Study-Scale was(n=116) and the effect was positive.	The follow-up took place at 2 months and at 6 months. At 2 months follow-up participants present were (n=108) and at 6 months follow-up participants present (n=107).	The study showed beneficial effect of increased rehabilitation hours on HRQOL measured with PDQ-39 Questionnaires. The positive effects were largest in two targeted domains: communication and mobility.
Yousefi et al, 2009 ²⁰	Participants are patients with PD. Study of 24 participants. poised equally in experimental and control group	Intervention group- Participants (n=12) a 10 week exercise therapy regimen on activities of daily living (ADL) and perceived health status in patients with Parkinson's Disease. Control group- Participants (n=12) had only their pharmacological therapy.	The exercise parameters are-walking, moderate stretching, breathing training, postural, stretching and strengthening exercises.	Short Parkinson Evaluation Scale (SPES/SCOPA) and perceived health status was measured by PD quality of life questionnaire (PDQoL). There were significant differences between the two groups for Parkinson's symptoms, social functioning and overall scores of the PDQL (all p values<0.05), and the ADL (P=0.01) indicating that QoL was improved.	Follow-up not described.	The findings for this study showed that exercise therapy was effective in improving activities of daily living and perceived health status in people with Parkinson's disease.

DISCUSSION

The major purpose of the RCTs reviewed here reflects the effectiveness of exercise on PD patients. The goals were to identify the benefits of various aspects and types of exercise on PD patients and to highlight areas that required further research. In the 10 RCTs a wide variety of exercise intervention has clearly demonstrated the effectiveness exercise on PD patients. One study reflected on the effectiveness of exercise interventions in reducing falls.¹⁰ In another three studies, the enhancement of functional status and quality of life of PD patients with the emergence of exercise in their lives are highlighted.^{12,13,17} One study specifically reports on the positive findings that support the use of balance and eye movement exercise to improve gaze control in PD patients.¹⁶ Two studies described the effectiveness of prescribed exercise regimen amongst PD patients in order to improve mobility and communication within their activities of daily living.^{19,20} One study measured the effectiveness of Qigong exercise on motor performance of PD patients.¹⁸ Two studies reported the efficacy of treadmill training amongst PD patients in order to retain balance and improve gait dysfunctions.^{14,15}

Out of 10 RCTs, 6 RCTs involved various balance training strategies and the remaining 4 RCTs involved various muscle-strengthening and flexibility exercises. The various modes of exercise associated with the 10 RCTs were flexibility, resistance, gait, balance, and mobility exercises (details can be found in Table 2). Unified Parkinson Disease Rating Scale (UPDRS) is an appropriate and reliable measure for assessing signs and symptoms of Parkinson's disease.²³ A well designed RCT by Ashburn et al looked at the effects of a home exercise programme which included balance, strengthening, and range of movement exercises.¹¹ A range of functional, and appropriate, outcome measures were chosen, including the Berg balance scale, the UPDRS, and the functional reach test. Use of the treadmill was one of the effective interventions for PD management. The results of both the studies suggested that the treadmill training improves functional lower-extremity tasks as well as physical fitness.^{14, 15} UPDRS was used as another outcome measure in a study by Fischer et al, which appeared to be more functional and clinically relevant. Fischer et al found that treadmill training significantly improved UPDRS score.¹⁵ The results found trends towards fewer falls and statistically significant improvement for functional reach in the exercise group. Two trials involved balance training with cognitive strategies, such as focusing their attention on movement and responding to external cues to enhance walking, turning, standing up from a chair, and obstacle negotiation.^{13, 17} The authors reported that the external (rhythmic) cues facilitated and motivated the PD patients to walk faster, enhanced their efficacy in gait control, and improved their activities of daily living (ADL).

Schmitz-Hubsch et al used Qigong as an intervention.¹⁸ Qigong is the Mandarin Chinese term used to describe various Chinese systems of physical and mental training for health, martial arts, and self-enlightenment.²⁴⁻²⁶ Hausdorff et al used an intervention that demonstrated benefits for PD management in bringing about a more consistent and more stable walking pattern.¹² They used flexibility, muscle strengthening, and gait/balance exercises as an intervention. Moreover, multi-modal exercises is getting popular these days in adjunct to a conventional care regime and aims at functional restoration programmes which enhance positive coping strategies for cancer patients and people with advanced illnesses.²⁷ All exercises involved in the 10 RCTs are multi-modal as every intervention regime of the 10 RCTs dealt with a mixture of exercises to improve various physiologic conditions related to PD. The most common exercise modes used in the trials included aerobic activities (in various standing and sitting forms), range of motion (ROM) exercises, gait training, and flexibility exercises. Hausdorff et al emphasized flexibility exercises for its effectiveness in improving rigidity conditions in PD.¹² Evidence of all the 10 trials supported exercise as being beneficial for people with PD for physical functioning including strength, balance, and gait speed, and benefits for health related quality of life have also been demonstrated. In all the trials, the exercise dose was not specified, and according to ACSM guidelines, exercise quality is considered "unclear" if the dosage is not highlighted.²⁸

The 10 RCTs therefore emphasized the importance of exercise as one of the primary needs of PD patients apart from pharmacological treatment, and all of the 10 articles highlighted the positive outcomes associated with the implementation of exercise amongst PD patients. There are limitations associated with the RCTs as the dose of exercise needed for the various types of PD patients are not mentioned in any of the 10 RCTs, and further research is needed in this area. Most of the studies had a very small number of participants, so the statistical findings may not be reliable. All the reviewed trials reported no exercise-related adverse events during and after the training period, although a few participants dropped out. Fischer et al only stated in his article that all 30 subjects over 24 exercise sessions had no adverse effects from exercise.¹⁵ The study findings of 10 RCTs emphasized the beneficial effects of exercise, which included improved QoL, increased walking speed, and an increased tolerance of exertion in participating ADL by PD patients.

Methodological Flaws of the Trials

In all 10 trials, researchers followed the consort statement for reporting RCT's. Most of the reviewed trials did not specify if the investigators conducting the assessments were blinded to the intervention group of the participants. It is important to know this when critiquing a paper because randomisation and blinding are key features in conducting unbiased trials.²⁹ The duration of the

intervention programmes ranging from 2 weeks to 6 months has been reported in the 10 trials. So the variety in the time frames did affect the improvement in function. All the studies except in two trials the follow-up period was described (Table 2). They all found that the benefits of exercise were still present in the follow-up period, although they did start to decrease after the intervention ended. The researchers found out that short follow-up time is the drawback in all of the trials. As PD is a chronic and progressive disease, it would be useful to investigate the effects of long term exercise. The design of future research may be improved by addressing methodological flaws of the trials mentioned above.

CONCLUSION AND OUTLOOK

In all 10 RCTs, exercise therapy is offered to PD patients as one of the non-pharmacological management strategies for its therapeutic and cost-effectiveness. The findings of the 10 RCTs support that exercise may be effective for some outcomes for the PD management in improving physical functioning and health-related quality of life (HRQoL). The exploration of these trials also suggest that low to moderate impact aerobic exercises, like treadmill, stretching exercises, walking up and down the stairs, and brisk walking would benefit the PD patients, but the evidence is not conclusive because more research is needed on the dose, frequency, and intensity level of the exercises. These activities need to be checked and monitored by a registered physiotherapist in order to be legally prescribed to the PD patients. Future research (e, g. RCTs with sufficient sample size) needs to establish what elements constitute an optimal exercise intervention for people with PD such as dosage, component parts of intervention and the targeted stage of the disease.

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KEY TERMS

Parkinson Disease, Exercise, Randomized Controlled Trials