



# Effect of Exercise on Motor and Non-Motor symptoms in Persons with Parkinson's Disease: A Scoping Review

Ruiping Xia MS, PhD\*; Briana Baxley BS, DPT; Diego Martinez BS, DPT; Joey Mack BS, DPT

Department of Physical Therapy, Franklin Pierce University, Goodyear, Arizona, USA.

## \*Corresponding Author(s): RuiPing Xia, MS, PhD

Department of Physical Therapy, Franklin Pierce University, Goodyear, Arizona, USA.

Tel: 1-623-518-2386; Fax: 1-623-518-2402,

Email: XiaR@franklinpierce.edu

## Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disease, and characterized by both motor and nonmotor symptoms. Although dopaminergic medications can be effective in management of motor symptoms especially in early PD, they usually cause detrimental side effects to patients at an advanced stage. Physical therapy has been shown to improve patient's symptoms, functional capacity, and quality of life. The objective of this scoping review was to examine effects of exercise on managing both motor and non-motor symptoms in PD. Multiple databases were searched according to pre-selected criteria in that studies must have: [1] enrolled subjects with idiopathic PD; [2] administered exercise treatment for PD; [3] compared an exercise intervention with traditional therapy/medication alone; [4] measured motor and non-motor function; and [5] utilized a design of randomized controlled trial. Eight articles were included in this review. Five of the seven trials measuring Unified PD Rating Scale-III showed significant improvements ( $p < 0.05$ ,  $p < 0.01$  or  $p < 0.001$ ) in favor of interventions including aquatic therapy, progressive resistive training, and LSVT BIG, compared to controls. Among the four studies measuring Timed Up and Go test, all trials reported significant improvements in favor of aforementioned interventions ( $p < 0.05$  or  $p < 0.002$ ). Significant between-group differences associated with Parkinson Disease Questionnaire-39 were observed in three of the seven studies with aquatic therapy and resistive training as interventions ( $p < 0.05$  or  $p < 0.001$ ). Exercise interventions are shown to be effective in treatment of motor symptoms while their effects appear to be inconclusive on quality of life in patients with PD. Clinical management of PD that will address both motor and non-motor symptoms is needed to maximize quality of life in individuals living with PD.

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**Keywords:** Parkinson's disease; Exercise intervention; Motor symptoms; Non-motor symptoms; Quality of life.



## Introduction

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease, currently affecting approximately one million Americans [1]. PD is clinically characterized by motor and non-motor symptoms. The former symptoms include rigidity, resting tremor, bradykinesia and postural instability, and the latter comprise cognitive impairments, sleep disorders, and fatigue etc [2,3]. Patients typically experience gradual losses of physical and mental function, leading to poor quality of life. [4,5].

Currently, there is no cure for PD. Mainstream treatment has been an administration of dopaminergic medications (e.g., levodopa and dopamine agonists etc.), which are mainly efficacious in managing motor symptoms [6]. Ample research evidence indicates a more effective treatment of combining exercise/physical therapy with medication than medication alone in regards to reducing motor symptoms and improving functional ability [7,9]. Emerging evidence has shown benefits of exercise intervention for reducing non-motor symptoms such as cognitive impairments, depression, sleep disorders, and fatigue. [10,11] Non-motor symptoms are prevalent in PD, and are widely believed to occur preceding the onset of those motor symptoms [12].

Both motor and non-motor symptoms must be addressed in clinical management of PD. Thus far, very few studies have been conducted to assess if exercise and physical therapy intervention are beneficial for treating both motor and non-motor symptoms. Considering the gap in the literature on this topic, we performed a scoping review that aimed to synthesize all available evidence with respect to exercise intervention targeting both motor and non-motor symptoms in PD and to explore conceptual effect of exercise interventions on improving both motor and non-motor symptoms of PD as compared to traditional physical therapy or medication alone. The knowledge gained from this review is expected to guide future research.

## Methods

Five databases (PubMed, CINAHL, Cochrane Library, Embase, and Physiotherapy Evidence Database - PEDro) were systematically searched up to date. Search terms included: (idiopathic Parkinson's disease OR Parkinson\*) AND ((Physio\* OR Physical Therap\* OR Therap\*) OR (Exercis\* OR Rehab\* OR Intervention)) AND (Motor and non-motor symptoms).

To be eligible for inclusion, the studies must have:

- [1] enrolled participants with PD;
- [2] administered exercise intervention for PD;
- [3] compared exercise intervention with conventional therapy and/or medication alone;
- [4] measured both motor and non-motor symptoms of PD; and
- [5] used a design of randomized controlled trial (RCT). Two authors independently performed selection by screening titles/abstracts and full texts of potential articles, according to eligibility criteria. Disagreements were resolved by an independent third researcher through discussion until reaching an agreement.

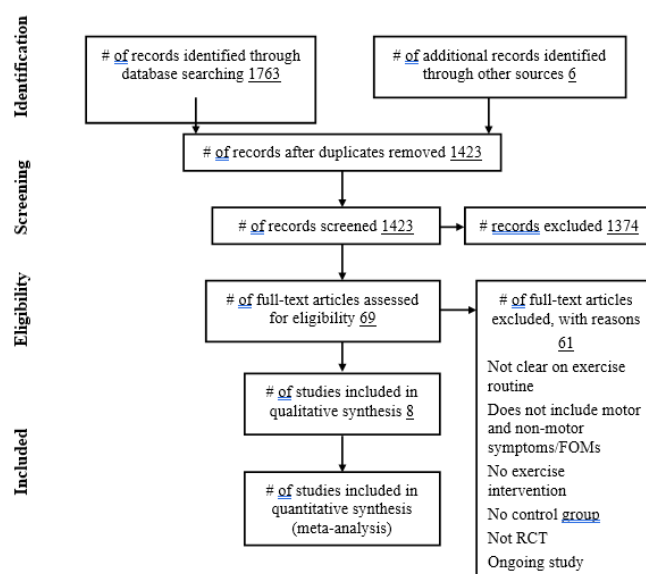
Quality and risk of bias were independently assessed by two reviewers using PEDro scale, which is a valid and reliable assessment tool of methodologic quality of clinical trials [13].

Table 1 lists characteristics and PEDro scale of included studies. Data were synthesized by narrative summary of included studies sharing the same outcome measure regarding the unified Parkinson's disease rating scale – Part III (UPDRS-III), Timed-up and Go (TUG), and Parkinson's Disease Questionnaire-39 (PDQ-39), respectively.

## Results

Figure 1 illustrates the study selection process. Eight articles were included in this review, following removal of duplicate articles and assessment of study titles/abstracts and full texts according to selection criteria. Of the 8 articles selected, intervention programs included LSVT BIG [14,16], aquatic-based therapy [17,19], progressive resistive exercise [20], and Tai Chi. [21]. The outcomes were UPDRS III, TUG, and PDQ-39. The mean PEDro score about risk of bias of the trials was 6.75 out of 10, ranging from 5 to 8 (Table 1).

The UPDRS-III was evaluated in seven articles [14,16,18,21]. All trials reported improvements in favor of intervention, and five showed significant between-group differences ( $p < 0.05$ ,  $p < 0.01$  or  $p < 0.001$ ) [14,16,18-20]. Among the four studies measuring TUG test, all trials reported significant improvements in favor of aforementioned interventions ( $p < 0.05$  or  $p < 0.002$ ) [16-18,20]. The PDQ-39 is a questionnaire that contains components assessing non-motor function. Its overall items are considered having impacts on quality of life [22]. Significant between-group differences were observed in three of the seven studies with aquatic therapy and resistance strength training as interventions ( $p < 0.05$  or  $p < 0.001$ ) [17,19,20].



**Figure 1:** Flow diagram of the study selection.

## Discussion

In this scoping review, we identified 8 eligible trials accounting for a total of 456 participants with PD. To our best knowledge, this is the first scoping review on the topic of exercise and physical therapy regarding both motor and non-motor symptoms in patients with PD. The main findings of this scoping review were that exercise and physical therapy revealed some positive effects on parkinsonian symptoms. It appeared that the motor symptoms and functional outcomes, as measured by UPDRS-III and TUG, were more responsive to non-pharmaceutical intervention than did non-motor features such as quality of life (e.g., PDQ-39).

**Table 1:** Characteristics of included studies.

Study	Study design	Participants with PD (N)	Intervention group	Control group	Outcome measures	PEDro scale
Carroll et al. (2016) <sup>19</sup>	RCT	21	aquatic exercise therapy	“Usual care” conventional physical therapy	UPDRS-III PDQ-39	7/10
Dashtipour et al. (2015) <sup>15</sup>	RCT	11	LSVT BIG	conventional physical therapy	UPDRS-III BDI BAI MFIS	5/10
Ebersbach et al. (2010) <sup>16</sup>	RCT	60	LSVT BIG, WALK	HOME	UPDRS-III TUG PDQ-39	6/10
Kurt et al. (2018) <sup>18</sup>	RCT	40	Ai Chi	conventional physical therapy/ land based	UPDRS-III TUG PDQ 39	7/10
Morris et al. (2015) <sup>20</sup>	RCT	210	Strength/balance	Education control	UPDRS-III TUG PDQ 39	8/10
Pérez-de la Cruz (2018) <sup>17</sup>	RCT	29	aquatic Ai Chi	conventional physical therapy/ land based	TUG PDQ 39	6/10
Schaible et al. (2021) <sup>14</sup>	RCT	44	LSVT BIG and Intensive	conventional physical therapy	UPDRS-III PDQ 39	8/10
Zhu et al. (2020) <sup>21</sup>	RCT	41	Tai Chi	routine exercise	UPDRS-III PDQ 39	7/10

BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; MFIS: Modified Fatigue Impact Scale; PDQ-39: Parkinson’s Disease Questionnaire-39; PEDro scale: Physiotherapy Evidence Database scale; RCT: randomized controlled trial; UPDRS-III: Unified Parkinson Disease Rating Scale Part III; TUG: Timed Up and Go.

Those 8 trials included in this review utilized different exercise approaches in the treatment of motor and non-motor symptoms of PD, including LSVT-BIG, progressive resistive exercise, aquatic therapy/Ai Chi, and Tai Chi. The exercise programs included in this review were largely heterogeneous, making a direct comparison with previous review studies challenging. Several systematic reviews and meta-analysis evaluated specific exercise intervention such as LSVT-BIG on motor function [23], aquatic physiotherapy on motor symptoms, balance, and quality of life for people with PD [24], and Tai Chi and Qigong on motor and non-motor function in PD [25]. Of the systematic reviews listed, significant improvements in motor outcome measures were reported, similar to observation found in current study.

Clinical studies have shown that exercise increases serum BDNF levels that were accompanied by reduced UPDRS scores and improved motor symptoms in patients with PD [26,28]. And exercise has been observed to increase dopamine D2 receptor expression, brain activation and functional connectivity and enhanced neuroplasticity in patients with PD [29,32]. Both pre-clinical and clinical research findings have provided mechanistic underpinning for the positive effect as reported in this study.

The limitations of this review were that only 8 articles met the eligibility criteria. This limited number of articles led to a small number of total participants for a review study. Limitations may also include various intervention types, different study durations, and follow-up evaluations. This review did not compare the results of outcome measures between individual treatment approaches. Since no comparison was made between the treatment approaches in this study, there is no evidence to determine a superior treatment to the motor and non-motor symptoms of PD from this study alone.

This scoping review shows potentials of therapeutic interventions as promising supplementary treatment for both motor and non-motor symptoms in PD. Future studies should be conducted to identify if there are superior treatment approaches to manage this disease and enhance quality of life in patients with PD.

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