Review Article

Role of Physical Activity in Parkinson's Disease

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Abstract

Parkinson's disease (PD) is common, age-dependent neurodegenerative disorder caused by a severe loss of the nigrostriatal dopaminergic neurons. Given the projected increase in the number of people with PD over the coming decades, interventions aimed at minimizing morbidity and improve quality of life are crucial. There is currently no fully proven pharmacological therapy that can modify or slow the disease progression. Physical activity (PA) can complement pharmacological therapy to manage the inherent decline associated with the disease. The evidence indicates that upregulation of neurotrophins and nerve growth factors are potentially critical mediators of the beneficial effects associated with PA. Accumulating evidence suggests that patients with PD might benefit from PA in a number of ways, from general improvements in health to disease-specific effects and potentially, disease-modifying effects. Various forms of PA that have shown beneficial effects in PD include – aerobic exercises, treadmill training, dancing, traditional Chinese exercise, yoga, and resistance training. In this review, we explored available research that addresses the impact of exercise and PA on PD. The original articles with randomized control trials, prospective cohort studies, longitudinal studies, meta-analysis, and relevant review articles from 2005 to 2017 were selected for the present review. Many gaps remain in our understanding of the most effective exercise intervention for PD symptoms, the mechanisms underlying exercise-induced changes and the best way to monitor response to therapy. However, available research suggests that exercise is a promising, cost-effective, and low-risk intervention to improve both motor and nonmotor symptoms in patients with PD. Thus, PA should be prescribed and encouraged in all PD patients.

Keywords: Parkinson's disease, physical activity, review

Introduction

The benefits of regular physical activity (PA) are extensive: PA increases survival and prevents people from chronic diseases such as cardiovascular disease, diabetes, cancer, hypertension, obesity, depression, and osteoporosis. Several biological mechanisms may be responsible for the benefits associated with PA.[1] PA has also been found to influence the brain's neurochemistry and plasticity.[2] The evidence indicates that upregulation of neurotrophins and various nerve growth factors are potentially critical mediators of the beneficial effects associated with PA.[3] In addition, reducing oxidative stress, enhancing energy production, and mitochondrial function also contribute to exercise-induced neuroprotection.[4] The beneficial effects of PA on the central nervous system (CNS) also work through adaptive neuroplasticity.[5] Studies in healthy rodents have shown that regular exercise triggers changes in CNS plasticity which includes synaptogenesis, enhanced glucose utilization, angiogenesis, and neurogenesis.[6] Imaging studies have shown the beneficial effect of exercise in humans. For example, PA-induced increase in the volume of gray and white matter in healthy individuals.[7]

Parkinson's disease (PD) is common, age-dependent neurodegenerative disorder caused by a severe loss of the nigrostriatal dopaminergic neurons.[3] Given the projected increase in the number of people with PD over the coming decades, interventions aimed at minimizing morbidity and improve quality of life are crucial. Although the dopamine replacement therapy is effective for relieving the motor deficits, PD has a progressive course. There is currently no fully proven pharmacological therapy that can modify or slow the disease progression. Thus, finding alternative, nonpharmacotherapies are necessary to delay and slow the dopamine neuron degeneration. PA can complement

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pharmacological therapy to manage the inherent decline associated with the disease.[8] Accumulating evidence suggests that patients with PD might benefit from PA in a number of ways. PA may lead disease-modifying effects in addition to general improvements in health of PD patients.[9] We, therefore, undertook this review to summarize the effects of PA on people living with PD.

Methodology

In order to identify relevant English literature, we searched PubMed using mainly a combination of the following keywords – PD, PA, exercise, physiotherapy, physical therapy, rehabilitation, dance, yoga, traditional Chinese exercise, and aerobics. The original articles with randomized control trials, prospective cohort studies, longitudinal studies, meta-analysis, and relevant review articles from 2005 to 2017 were selected for the present review. Important characteristics and outcomes of these studies were extracted and summarized in the present review.

Definition of Physical Activity

PA is defined as any bodily movement produced by skeletal muscles that result in energy expenditure, which can be measured in kilocalories.[10] The term "exercise" has been used interchangeably with "PA," since the two share many common elements.[11] Exercise is a subcategory of PA involving planned, structured, repetitive, and purposeful body movements to improve or to maintain one or more components of PA.[10]

Physical Activity in Parkinson's Disease: Animal Studies

Various studies have revealed PA-related neuroprotection in animal models of Parkinsonism. Neuroprotection in PD is apparently mediated by brain neurotropic factors and neuroplasticity. The detailed discussion of each of these studies goes beyond the scope of this article. There are excellent reviews available on this aspect. The literature may be summarized as follows. PA in Parkinsonian animal models induces brain neurotrophic factor expression, which may mediate neuroprotective effects.[12] The factors include – brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF).[13] Other exercise effects in PD animal models include – enhanced neural progenitor cell proliferation and migration as well as reversal of age-related decline in substantia nigra vascularization, apparently mediated by vascular endothelial growth factor expression.[13,14] All these changes in CNS apparently lead to the neuroprotective effect caused by PA. Although the evidence from animal studies cannot be directly applied to mechanisms in humans, studies have suggested that PD patients would likely experience a meaningful improvement and disease-modifying effect in response to PA.[13]

Physical Activity in Parkinson's Disease: Epidemiological Studies

A beneficial relationship between PA and PD was first suggested in 1992, when Sasco and colleagues reported that the risk of PD was reduced in men who played sports in college and adult life.[15] This finding has been replicated in nearly all subsequent epidemiologic studies [Table 1]. For example, among 43,368 participants in the Swedish National March cohort, male participants who spent >6 h per week on household and commuting activity had 43% lower risk of PD compared to those with <2 h per week of such activities.[16] Similarly, risk of PD was reduced who engaged in heavy leisure-time PA in Finnish Mobile Clinic Health Examination Survey.[17]

Two studies suggested that PA may influence PD risk differently for men and women.[16,21] In the "health professionals follow-up and nurses health studies," higher levels of exercise reduced the risk of PD for men but not for women.[21] Similarly, in the

Table 1: Epidemiological studies on the role of physical activity in Parkinson's disease

Study characteristics	Study population and duration	Main outcomes
Yang *et al*.[16] - Swedish National March Cohort	43,368 people followed over a mean period of 12.6 years	Reduced PD risk noted in males with medium level of PA compared to low-level PA (95% CI: 0.35-0.87)
Wang *et al*. (2015)[17] - Finnish Mobile Clinic Health Examination Survey	6715 participated followed over a period 22 years	Patients with heavy leisure-time PA had a lower risk of PD than those with no activity (RR 0.27, 95% CI: 0.08-0.9, *P*-0.04)
Xu *et al*.[18] - NIH-AARP Diet and Health Study cohort	213,701 participated in the study	Those with moderate-to-vigorous PA aged 35-39 (95% CI: 0.48-0.81, *P*-0.005) or in the past 10 years (95% CI: 0.51-0.83, *P*-0.0001) had significantly lower risk of PD
Thacker *et al*.[19] - Cancer Prevention Study II Nutrition cohort	143,325 participants followed over 9 years	Participants with moderate-to-vigorous activity had a lower risk of developing PD compared to those with light activity (RR 0.6, 95% CI: 0.4-1.0, *P*-0.02)
Logroscino *et al*.[20] - Harvard Alumni Health Study	10,714 men followed over a period of 10 years	Nonsignificant reduction in PD risk at >3000 kcal/week of PA (RR 0.64; 95% CI: 0.36-1.13, *P*-0.13)
Chen *et al*.[21] - Health Professionals Follow-up Study and Nurses' Health Study Cohort	48,574 males and 77,254 females of followed up for period of 14 and 12 years respectively	Higher levels of PA reduced the risk of PD for men (RR 0.5, 95% CI: 0.3-0.09, *P*-0.007)

CI=Confidence interval, PA=Physical activity, PD=Parkinson's disease, RR=Relative risk

"Swedish National March cohort study," PA was associated with a decreased PD risk for men, but the benefit was less clear for women.[16] Men and women may have different biological responses to PA.[22] The lack of associations between PA and PD risk in females may be explained by (1) methodological issues like low statistical power resulting from smaller number of female PD subjects and/or (2) females may have physiologically different responses to exercise than males, with a less sustained alteration in metabolic rate and lipid metabolism.[23] Although differential effects in men and women are probable, other large studies found PA to similarly benefit both men and women.[18-20] Thus, determining whether PA has different effects in men and women needs further investigation and will be important in developing appropriate interventions.[8] Taken together, these studies provide compelling evidence for an inverse association between PA or exercise and risk of PD.

Physical Activity in Parkinson's Disease: Clinical Studies

Motor symptoms

Individuals with PD invariably experience functional decline in a number of motor domains including posture, balance, gait and transfers. Clinical studies have examined effects of various type of exercise on motor features of PD and reported positive results. We have summarized various review articles and meta-analysis demonstrating the effect of PA and specific type of exercise on motor features of PD in Table 2. We identified 19 systematic reviews and meta-analysis from 2005 to 2017.

The first systematic review on effectiveness of PA in PD was published in 2001.[40] Since then, many subsequent reviews have followed. Most of these reviews supported the effectiveness of PA for people with PD. PA may help to improve mobility, balance, and well-being in patients with PD.[8,24-26]

A systematic review evaluating the effectiveness of aerobic exercise for PD suggested that aerobic exercise significantly improve motor action, balance, and gait including gait velocity, stride/step length, and walking ability in patients with PD.[27,28] The time has come to apply the same standards to exercise as to drugs and to determine the adequate "dose" of aerobic exercise (i.e., frequency, intensity, and duration).

Mehrholz *et al*.'s review concluded that treadmill training was likely to improve gait, hypokinesia, and showed better safety.[29] Herman's systematic review also suggested that treadmill training should play an important role in improving gait and mobility in the management of patients with PD.[30]

Compared with routine PA, dancing might enhance long-term adherence, compliance, and enjoyment in patients with PD.[31] Evidence is emerging that dancing can be a beneficial form of PA for people with mild-to-moderate PD.[31,32] A recent review by Aguiar *et al*. showed that therapeutic dancing could be beneficial for improving mobility and balance in people with PD.[31] Furthermore, Dhami *et al*. hypothesized that rhythmical music used in dancing could activate neurons serving motor control and increase blood flow in regions such as the hippocampus and frontal, temporal, and parietal cortices. This could facilitate neuroplasticity and in turn improve movement, balance, and cognition.[41]

A meta-analysis on the efficacy of Tai Chi in patients with PD suggests that Tai Chi can significantly improve the motor function and balance in patients with PD.[33] A review on the effect of traditional Chinese exercise on PD showed a positive effect of Tai Chi and Qigong exercise in improving motor function and balance in patients with mild-to-moderate PD.[34,35] Thus, there is sufficient evidence from high-quality studies that Tai Chi is safe, feasible, and can improve postural stability in PD. Since long-term longitudinal studies are lacking, the duration of benefit from Tai Chi is unclear.

Yoga is a discipline which dates back to India circa 2000 BC but has only recently gained popularity throughout the Western world. Preliminary results from two reviews suggest that yoga provides modest improvements in functional mobility, balance, upper and lower-limb flexibility and strength. Yoga also helps to reduce the fear of falling. The current evidence suggests that yoga is acceptable, beneficial and safe to PD populations.[25] However, the future trials are needed to determine long-term implications and dosage of yoga therapy (frequency, intensity, and timing) in the PD population.

Progressive resistance training (PRT) is a relatively new intervention for PD. Saltychev *et al*. emphasized the lack of robust data on the effect of PRT in PD.[36] On the other hand, few studies have shown a positive effect of PRT on muscle strength and mobility in patients with PD.[37-39] A combined aerobic and strength exercise intervention was suggested to be even more effective. Thus, to make definite clinical recommendations on the possible use of PRT in PD, further research should focus on larger sample sizes with sufficient follow-up periods. In addition, the safety of PRT in PD population should also be evaluated.

Thus, PA of various types, including aerobics, treadmill training, PRT, dance, Tai Chi and yoga has demonstrated improvement in certain PD motor symptoms. Further studies are warranted to understand which exercise protocol is most beneficial and to determine the adequate "dose" of exercise (i.e., frequency, intensity, and duration) for better gains.

Nonmotor Symptoms

While PD is most commonly associated with motor symptoms, there are numerous nonmotor symptoms associated with the condition such as hyposmia, constipation, cognitive impairment, autonomic dysfunction, sleep disorders, and neuropsychiatric symptoms such as depression, anxiety, and apathy.[42] These nonmotor symptoms adversely affect the quality of life and can be even more disabling than the motor symptoms. Medications are often inadequately effective and can cause intolerable side effects. There is, therefore, an increased interest in the role of nonpharmacologic therapies to

Table 2: Summary of reviews and meta-analysis on the effects of physical activity on motor features in Parkinson's disease

Review	Number of studies included	Inclusion criteria	Outcome/conclusion
Any form of physical activity			
Lauzé *et al*.[8]	106 studies (R or M)	All studies with idiopathic PD patients who participated in PA as a mean of intervention	PA seems most effective in improving physical capacities (57.2% improvement of all reported outcomes) and physical and cognitive functional capacities (55.3% improvement of all reported outcome measures)
Kwakkel *et al*.[24]	23 studies (R or M)	RCTs that assessed physical therapy interventions in patients with PD were eligible for inclusion	Effects of PA in PD patients are task specific 1. Improvement in postural control and balance reported by (9 studies) 2. Improvement in gait and gait-related activities reported by (3 studies) 3. Improvement in physical condition reported by (5 studies) and 4. Improvement in transfer reported by (1 study)
Keus *et al*.[25]	29 studies	All studies with sufficient data on the effectiveness of PA in PD were included	Four specific recommendations 1. Cueing strategies to improve gait 2. Cognitive strategies to improve transfer 3. Exercises to improve balance; and 4. Training of joint mobility and muscle power to improve physical capacity
Crizzle and Newhouse[26]	7 studies	Studies with idiopathic PD patients participated in any form of PA were eligible for the review	Exercise training is beneficial to patients with PD, especially those in the early stages of the disease
Aerobic exercise			
Shu *et al*.[27]	18 studies	Article comparing effect of aerobic exercise intervention with any comparator, including other forms of exercise or PA in patients with PD	Aerobic exercise showed beneficial effects in improving Motor action (SMD-0.57, P=0.003), balance (SMD-2.02 , P=0.01), and gait (SMD-0.33, P<0.0001) in patients with PD
Tambosco *et al*.[28]	36 studies	Literature studying aerobic training and strength training exercise interventions in patients with PD	Aerobic and strength training improve physical abilities of patients suffering from PD
Treadmill training exercise			
Mehrholz *et al*.[29]	18 studies	RCTs comparing treadmill training with no treadmill training in patients with PD	Use of treadmill training in patients with PD may improve clinically relevant gait parameters such as gait speed (95% CI 0.03-0.14; P=0.001) and stride length (95% CI 0.01-0.09; P=0.01), but walking distance and cadence did not improve
Herman *et al*.[30]	14 studies	Studies evaluating the effects of treadmill training on patients with PD	Treadmill training could play an important role in improving gait and mobility in patients with PD
Dance therapy			
Aguiar *et al*.[31]	18 studies	RCTs comparing dance therapy with any other form of PA training in patients with PD	Therapeutic dance can be safe and feasible for people with mild-to-moderately severe PD, with beneficial effects on walking, freezing of gait, and health-related QOL
Shanahan *et al*.[32]	13 studies	Studies evaluating dance interventions for individuals with PD	The evidence evaluated suggests that two 1-h dance classes per week over 10-13 weeks may have beneficial effects on endurance, motor impairment, and balance
Traditional Chinese exercise			
Song *et al*.[33]	21 studies	Studies evaluating the effect of Tai Chi/Qigong for individuals with PD	Fixed-effect models showed that Tai Chi/Qigong was associated with significant improvement in most motor outcomes UPDRS III (P<0.001) Balance (P<0.001) Timed Up and Go (P=0.005) Falls (P=0.004)

Contd...

Table 2: Contd...

Review	Number of studies included	Inclusion criteria	Outcome/conclusion
Yang *et al*. (2014)[34]	15 studies	Studies evaluating the effect of Tai Chi/Qigong (traditional Chinese medical exercise) for individuals with PD	Tai Chi plus medication showed greater improvements in Motor function (SMD-0.57; 95% CI-1.11-−0.04) Berg balance scale (SMD-1.22; 95% CI-1.65-−0.80) However, Tai Chi plus medication did not show better improvements in gait or QOL
Zhou *et al*.[35]	9 studies	RCTs comparing Tai Chi with any comparator without Tai Chi relevant exercises in patients with PD	The aggregated results are in favor of Tai Chi on improving motor function (P=0.002) and balance (P<0.00001) in patients with PD. However, there is no sufficient evidence to support or refute the value of Tai Chi on improving gait velocity, stride length, or QOL
Resistance training exercise			
Saltychev *et al*.[36]	12 studies	Literature studying progressive resistance training versus no treatment, placebo, or other treatment in patients with PD	The effect of progressive resistance training on 1. Comfortable walking speed-(95% CI 0.01-0.05) in favor of intervention but below the minimal detectable change 2. Timed Up and Go test - not significant (95% CI−1.47-0.06) 3. 6-min walk test-(95% CI 7.86-25.48) are in favor of intervention, but below the minimal detectable change There is so far no evidence on the superiority of progressive resistance training compared with other treatments to support the use of this technique in rehabilitation of idiopathic PD
Uhrbrand *et al*.[37]	15 studies	Articles in which the effect of intensive exercise therapy in patients affected by PD was evaluated	There is strong evidence that resistance training can improve muscle strength in PD, which is underlined by the meta-analysis (95% CI 0.22-0.86)
Brienesse and Emerson[38]	5 studies	Studies evaluating resistance exercise programs in PD population	Resistance training was shown to have a positive effect in both muscle strength outcomes as well as functional outcomes related to mobility in PD population
Lima *et al*.[39]	4 studies	Studies evaluating progressive resistance exercise programs in PD population	Progressive resistance exercise increased strength, with an SMD-0.50 (95% CI 0.05-0.95) and had a clinically worthwhile effect on walking capacity, with a mean difference of 96 m (95% CI 40-152) among people with mild-to-moderate PD

CI=Confidence interval, PA=Physical activity, PD=Parkinson's disease, QOL=Quality of life, RCTs=Randomized control trials, SMD=Standardized mean difference, UPDRS: Unified Parkinson's Disease Rating Scale

treat nonmotor symptoms in PD. PA has established efficacy for treating nonmotor symptoms in addition to motor symptoms of PD.[42] We have summarized articles addressing the effects of PA on nonmotor features of PD as the primary outcome in Table 3.

Autonomic dysfunction is common in PD; with the reported prevalence ranging from 14% to 80%.[59] It may include dysregulation of cardiovascular, gastrointestinal, urinary, and thermoregulatory systems.[60] Only one study has been published that addressed the effects of PA on cardiovascular autonomic dysfunction in PD. In this study, PD participants performing exercise had improved cardiac sympathetic modulation, as measured by heart rate variability and blood pressure response.[43] In patients with PD, autonomic impairment of gastrointestinal and urinary tract is also common. No studies to date have investigated the influence of PA on gastrointestinal and bladder dysfunction as the primary outcome.

Sleep dysfunction is another common nonmotor symptom in PD, affecting up to 98% of patients.[61] PA has shown promise for improving sleep in patients with PD as well. Silva-Batista *et al*. found PD group undergoing resistance training had significant improvement in sleep quality.[44] The study used the Pittsburgh Sleep Quality Index to assess sleep quality before and after the intervention. Another study used a Qigong exercise intervention in Patients with PD. After 6 months of Qigong exercise intervention, investigator reported improvement in PD sleep scale score in intervention receiving group.[45] Frazzitta *et al*. and Nascimento *et al*. found improvement in sleep scores in PD group that participated in a multidisciplinary exercise program.[46,47] Taken together, these studies indicate that many different types of PA can improve subjective sleep quality in PD.

Cognitive impairment significantly affects the quality of life in PD. These impairments remain difficult to manage with current clinical therapies, but exercise has been identified as a possible treatment.[42] The clinical studies showed that various types of exercise, including aerobic, resistance, and dance can improve cognitive function, although the optimal type, amount, mechanisms, and duration of exercise are unclear. A study by David *et al*. suggested that resistance exercise may benefit cognition in patients with PD.[48] Uc *et al*. reported improvement in response inhibition test in PD patients who participated in 6-month aerobic exercise program, whereas

Table 3: Role of physical activity in nonmotor features in Parkinson's disease

Study	Intervention	Outcome/conclusion
		Autonomic dysfunction
Kanegusuku *et al*.[43]	Resistance training	Progressive resistance training improved cardiovascular autonomic dysfunction in PD training group 1. Decrease in low-frequency component of heart rate variability after 12 weeks ($P<0.05$) 2. Reduction in systolic blood pressure fall during orthostatic stress after 12 weeks ($P<0.05$)
		Sleep dysfunction
Silva-Batista *et.al*.[44]	Resistance training	After resistance training, patients with PD showed improved sleep scores than the healthy control ($P\leq0.05$). Resistance training is recommended as an adjunct therapeutic method for improving sleep quality of subjects with moderate PD
Wassom *et al*.[45]	Qigong exercise	Improved sleep quality in Qigong exercise group
Frazzitta *et al*.[46]	Multidisciplinary exercise program	On average, in intervention group, sleep scores improved ($P<0.0001$), suggesting multidisciplinary intensive rehabilitation treatment may have a positive impact on many aspects of sleep in PD
Nascimento *et al*.[47]	Multimodal exercise program	Mild-to-moderate intensity of multimodal physical exercises can contribute to attenuating sleep disturbances
		Cognitive impairment
David *et al*.[48]	Resistance exercise	At 24 months, relative to baseline, modified fitness counts improved on the digit span ($P<0.01$) and stroop ($P=0.03$), whereas progressive resistance exercise training improved on the digit span ($P<0.01$), Stroop ($P=0.048$) providing evidence that 24 months of PA may improve attention and working memory in patients with PD
Uc *et al*.[49]	Aerobic exercise	Improved performance on flanker task-response inhibition test ($P<0.05$ to $P<0.001$) after exercise program
Nocera *et al*.[50]	Tai Chi exercise	Large, but nonstatistically significant improvement, was found for the digits backward test ($P=0.08$) suggesting Tai Chi training may help improve executive functioning
McKee and Hackney[51]	Tango dance therapy	Tango participants improved on spatial cognition ($P=0.021$) and executive function ($P=0.012$) compared with education participants. Gains were maintained 10-12 weeks postintervention
Ridgel *et al*.[52]	Passive leg cycling	Improved executive function after passive cycling
Cruise *et al*.[53]	Exercise intervention program	Improvement in frontal lobe-based executive function in exercising group
Tanaka *et al*.[54]	Multimodal physical exercise program	Improvement in executive function in exercising group
		Mood disorders
Dashtipour *et al*.[55]	Combined aerobic and resistance exercise	Sustained improvement in depression (Beck depression inventory postintervention evaluation showed improvement in scores 4-week postintervention ($P=0.001$) 3-month postintervention ($P=0.002$) and 6-month postintervention ($P=0.006$) in combined intervention group
Teixeira-Machado et al.[56]	Exercise program based on the Feldenkrais method	Treated group showed reduction in the level of depression ($P=0.05$)
Park *et al*.[57]	Combined aerobic and resistance exercise	Greater reduction in depression in early-start group (Beck Depression Index mean change from baseline values decreased more in the early-start group, this was statistically significant ($P=0.04$) compared with late-start group
Burini *et al*.[58]	Combined aerobic training and Qigong exercise	No significant improvement in mood (P value not significant) in intervention group

PA=Physical activity, PD=Parkinson's disease

Nocera *et al*. reported improvement in executive function after Tai Chi.[49,50] McKee *et al*. investigated the effects of community-based tango on spatial cognition and disease severity in PD.[51] PD patients with mild-to-moderate disease were assigned to twenty 90-min tango lessons over 12 weeks. Tango participants improved on disease severity, spatial cognition, and executive function compared to control group. Another study examined the effects of passive leg cycling on executive function in PD.[52] Executive function was assessed with trail-making test A and B before and after passive leg cycling. Significant improvements on the trail-making test-B occurred after passive leg cycling. A study by Cruise *et al*. found improvement in frontal lobe-based executive function in PD patients allocated to an exercise intervention program.[53] Tanaka *et al*. analyzed the effects of a multimodal physical exercise program on executive functioning.[54] Participants in the exercise group showed improvement in executive function, as measured by the

Wisconsin Card Sorting Test. Regardless of variations in intensity, mode, and duration of exercise program across these studies; they provide a good evidence for the use of PA to improve cognitive function in PD.

Mood disturbance (anxiety, depression, and apathy) develop in many individuals with PD, even in the early stages of the disease, contributing to poorer quality of life and caregiver burden. There is promising evidence that PA may improve mood among adults with neurologic disorders and healthy older adults.[62] The research on the effects of PA on mood in PD is limited.[56-58] In a sample of 11 participants with PD, 5 participants completed a 4-week general exercise program and 6 participants completed an exercise-based behavioral treatment. The combined group showed improvement in depression and fatigue at all postintervention assessments, suggesting benefits of both exercise approaches.[55] Teixeira-Machado *et al*. showed improvement in depression for the PD group who underwent 50 sessions of an exercise program based on the Feldenkrais method.[56] In randomized control trials, individuals with PD were randomized to either an early or late start group exercise program. Participants in the early-start group reported significantly fewer depressive symptoms after 48 weeks relative to the delayed-start group.[57] In general, these studies provide strong rationale for the targeted use of exercise to improve mood in PD. Large longitudinal clinical trials are needed to examine the sustained benefit of PA on mood disorders in PD population.

Although many gaps remain in our understanding of the most effective exercise intervention for nonmotor symptoms in PD, available research suggests that PA is a promising approach to improve nonmotor symptoms in patients with PD.

Most of the animal, epidemiological, and clinical studies have indicated that PA not only has a significant preventive effect on PD but also has therapeutic value. Hence, PA should be promoted in general population and should be an essential component of the treatment for PD.

Conclusions and Recommendations for Future Research

Epidemiological data indicate that exercise may reduce the risk of developing PD. There is now a convincing body of clinical evidence suggesting that PA is beneficial, cost-effective, and low-risk intervention that improves overall health and provides promise for improving both motor and non-motor symptoms in PD. Furthermore, experimental studies have highlighted the neuroprotective and neurorestorative effects of exercise, but these findings have yet to be translated to the human disease.[9] Thus, exercise should be prescribed and encouraged in all PD patients. When recommending an increase in PA in PD patients, several factors specific to patients with PD should be considered. These factors include motor symptoms, the risk of falls, apathy, fatigue, depression, and cognitive dysfunction. Any of these symptoms can reduce participation in PA and can contribute to a more sedentary lifestyle among patients with PD. Strategies to improve participation include the development of community-based programs and discussing ways to reduce barriers to exercise with the patient and caregiver.[42]

Although most studies suggest that exercise promotes improvements in motor and nonmotor symptoms in PD, many questions remain unanswered. For example, which form of exercise is most effective in reducing PD risk or improving motor and nonmotor symptoms, how frequent exercise should be performed for maximal benefit, and when exercise should start. These and other unanswered questions in combination with the promise of therapeutic efficacy of exercise on the different aspects of motor and nonmotor symptoms in PD make exercise interventions an exciting area of research.

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Conflicts of interest

There are no conflicts of interest.

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