

Aerobic Exercise in Rehabilitation of Patients with Parkinson's Disease

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Abstract

Disability due to Parkinson's disease (PD) is increasing faster than for any other neurodegenerative disorder. A multidisciplinary approach to rehabilitation of patients with PD is recommended including various types of physical training. Because of its general beneficial effect, aerobic endurance training is necessary for all people to maintain their health. Aerobic exercise in PD is also used for rehabilitation of motor and non-motor symptoms. This article justifies the choice of aerobic exercise intensity, shows challenges in selecting intensity based on maximum oxygen consumption due to the influence of clinical and behavioral factors, difficulties in assessing the effectiveness of therapy due to the wide range of training intensity and amount in the studies. The article summarizes types of exercises used in rehabilitation of patients with PD (walking, Nordic walking, training with a bicycle ergometer and treadmill, aquatic exercises) and their benefits for patients with different courses of the disease. For patients with freezing of gait, bicycle ergometer is a piece of equipment of choice for aerobic stationary training, and Nordic walking is a preferred type of outdoor training. The author shows the role of aerobic training in the treatment of non-motor symptoms such as depression, cognitive changes, and sleep disorders. A question about the use of aerobic training in patients with Hoehn-Yahr grade 4–5 of PD remains open. Further studies are needed to evaluate training protocols, assess rehabilitation effectiveness and evaluate physical training in the advanced PD.

Keywords: Parkinson's disease; aerobic exercise; intensity; effectiveness; general beneficial effect; motor and non-motor symptoms

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Аэробная физическая нагрузка в реабилитации пациентов с болезнью Паркинсона

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Аннотация

Болезнь Паркинсона (БП) является заболеванием с самым высоким приростом инвалидности среди нейродегенеративной патологии. Рекомендован мультидисциплинарный подход к реабилитации пациентов с БП, включающий различные типы физических тренировок. Аэробная тренировка на выносливость, вследствие общеукрепляющего действия, необходима для поддержания здоровья всем людям. Аэробную нагрузку при БП применяют также для реабилитации моторных и немоторных симптомов. В статье обоснован выбор интенсивности аэробной нагрузки, показаны трудности в подборе интенсивности при определении максимального потребления кислорода из-за влияния клинических и поведенческих факторов пациентов, сложности оценки эффективности терапии вследствие широкого диапазона представленных в исследованиях показателей интенсивности и объёма нагрузки. В статье обобщены типы спортивно-прикладных упражнений на выносливость, встречающихся при реабилитации пациентов с БП (ходьба, скандинавская ходьба, тренировки на велоэргометре и тредмиле, упражнения в воде), и их преимущества при разном течении болезни. Например, для пациента с застыванием аппаратурой выбора для аэробной стационарной тренировки является велоэргометр, а тренировки на улице предпочтительны в виде скандинавской ходьбы. Автором показано значение аэробной нагрузки для терапии немоторных симптомов: депрессии, когнитивных изменений и нарушения сна. Открытым остаётся вопрос о применении аэробной нагрузки у пациентов с БП 4–5-й стадии по Hoehn-Yahr. Требуются дальнейшие исследования по протоколу нагрузки, оценке эффективности реабилитации и применению нагрузки на развёрнутой стадии БП.

Ключевые слова: болезнь Паркинсона; аэробные упражнения; интенсивность; эффективность; общеукрепляющий эффект; моторные и немоторные симптомы

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Конфликт интересов. Автор заявляет об отсутствии явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Introduction

Parkinson's disease (PD) is a chronic neurodegenerative disease the pathogenesis of which is based on progressive degeneration of dopamine-producing cells in the substantia nigra of the brain. Excessive accumulation of a protein called α -synuclein with the formation of Lewy bodies is the cause of the pathological changes at the cellular level [1, 2]. Familial PD accounts for 5–15% of all cases but genetic studies in these families helped understand the pathogenesis of the disease [3–5].

Clinically, PD is manifested by motor symptoms such as tremor, rigidity, slowness of movements, and postural instability. The resulting motor disturbances make the patient to consult a doctor. Dystonia and dyskinesia are associated with further speech and motor impairment. Patients with advanced PD develop freezing of gait [6]. Apart from motor symptoms, patients may have non-motor dysfunctions, which can bother them long before the onset of the motor symptoms¹. These include depression, orthostatic hypotension, constipation, urinary disorders, weight loss, fatigue, sleep disorders, smell and taste disorders, delirium, hallucinations, pain, etc. [6–8]. The incidence of PD increases with age. PD occurs in 1.6–1.8% of people 65 years of age and older. The average age of onset is 61 years. However, 13% of cases are diagnosed before the age of 50 years [1, 9]. In all countries, disability due to PD is increasing faster than for any other neurodegenerative disorder.

In 2022, World Health Organization (WHO) launched Parkinson's disease technical brief justifying the relevance of increasing PD morbidity and disability and necessary solutions².

¹ The American Parkinson Disease Association. Common Symptoms of Parkinson's Disease [updated 15 Apr 2023].

URL: <https://www.apdaparkinson.org/what-is-parkinsons/symptoms/#nonmotor> (assessed on 11/19/2023).

² WHO. Launch of WHO's Parkinson disease technical brief. 2022 June 14 [updated 02 May 2023]. URL: <https://www.who.int/news/item/14-06-2022-launch-of-who-s-parkinson-disease-technical-brief> (assessed on 11/19/2023).

The technical brief includes respecting the patient's rights to timely diagnosis and treatment and an integrated approach to symptom management. Disease management is considered from a multidisciplinary perspective. Physical rehabilitation is an important part of the treatment. Various techniques are used for rehabilitation such as endurance, strength, balance, and flexibility training, external signal stimulation, dual tasks, etc. The superiority of any method has not been shown. Physical activity is also considered a preventive factor for PD, which reduces the risk of its occurrence, along with the use of tobacco, coffee, or calcium channel blockers [1, 10].

This review **aimed** to assess the effects of aerobic training and different types of aerobic physical exercise on health of PD patients.

Methodology

The search for article titles and abstracts was conducted in two open databases (i. e. PubMed and eLIBRARY.RU) and included available free full-text articles published before 06/07/2023 in English or Russian without restrictions on publication date. Literature search strategy is presented in the table below.

Search in eLIBRARY.RU database gave no articles for these keywords; search in PubMed database with literature references gave 115 articles with subsequent exclusion of non-relevant articles.

Aerobic exercise

The 2020 WHO guidelines for patients with neurodegenerative disease, including PD, define a beneficial minimum amount of physical activity [11]. People with PD, like all other patients and healthy people, need 75 to 150 minutes of vigorous-intensity regular aerobic physical activity per week or 150 to 300 minutes of moderate-intensity regular aerobic physical activity per week. To provide additional

Characteristics of a literature search

Keyword	Parkinson's disease AND aerobic load OR aerobic exercises OR endurance
Databasa	PubMed, eLIBRARY.RU
Language	English, Russian
Document type	Peer-reviewed empirical and theoretical papers
Inclusion criteria	Population: patients with Parkinson's disease; Intervention: aerobic physical activity; Comparison is necessary for empirical papers
Exclusion criteria	Thesis papers, conference materials, articles in other languages

health benefits, moderate-intensity aerobic physical activity may be increased to more than 300 minutes per week or vigorous-intensity aerobic physical activity may be increased to more than 150 minutes per week. This amount of physical activity is necessary to strengthen the cardiopulmonary system, bones and muscles and decrease the risk of non-infectious disease and depression [11]. In this context, aerobic training in patients with PD is considered general beneficial physical activity. Required intensity of aerobic exercise is most often determined by heart rate (HR): 60–75% and 75–90% of the maximum heart rate correspond to medium (moderate) and vigorous intensity of physical activity, respectively. In several studies, intensity was determined by calculating necessary percentage of maximum heart rate [12, 13]. In other studies, heart rate reserve or maximum oxygen consumption ($\text{Vo}_{2\text{max}}$) were used [14]. In some studies, intensity varied during the training course from medium to high, which makes it difficult to assess the effectiveness of therapy [14].

Measuring oxygen consumption during exercise is the gold standard for determining endurance exercise intensity. During physical exercise on a treadmill or bicycle ergometer, oxygen consumption is linearly related to load power until $\text{Vo}_{2\text{max}}$ is reached. Further increase in power is maintained for a short period due to anaerobic metabolism, which is caused by the accumulation of lactate. However, the linear relationship is conditional due to the influence of a person's gender, height, and age on $\text{Vo}_{2\text{max}}$. Several corrections are used for these factors [15]. The influence of common external factors such as lack of training and insufficient muscle mass is obvious; however, they cannot be taken into account by introducing one or another correction into the formula.

Given that patients with PD suffer from motor impairments, often do not have training skills and, like most people today, lead a sedentary lifestyle, determining $\text{Vo}_{2\text{max}}$ to calculate the intensity of aerobic activity in this population is challenging. The “gold criterion” for diagnosing the required intensity of aerobic exercise may be applicable mainly for professional sports. The key benefits of aerobic exercise include cardiovascular fitness, both for primary and secondary prevention of cardiovascular disease. The more time a person engages in moderate-intensity and high-intensity aerobic exercise, the

better their cardiovascular prognosis [16]. Interpretation of results and data on the effectiveness of aerobic exercise therapy for PD are inconsistent, since the studies were performed with different amounts of physical activity (i.e. course duration and frequency of training per week) and a wide range of training intensity (60–80% of maximum heart rate, 50–80% of reserve heart rate or 60–80% of $\text{Vo}_{2\text{max}}$). Exercise with too high intensity, i. e. greater than 11 MET (1200 kgm/min, or 200 W³), is not recommended for people who use exercise solely for health maintenance and disease prevention.

Aerobic training has a general beneficial effect on metabolism. Aerobic exercise was shown to reduce postprandial lipogenesis, muscle insulin resistance, high blood pressure, and metabolic syndrome [17]. The effect of aerobic exercise on metabolism is important for patients with PD because concomitant arterial hypertension and metabolic syndrome can lead to rapid PD progression [17]. Regular aerobic exercise were shown to improve calcium metabolism and bone mineral density. The prevalence of osteoporosis in patients with PD is high. The pathogenesis of osteoporosis is associated with inhibition of osteoclast differentiation, decreased mineralizing ability of osteoblasts with high doses of levodopa, decreased muscle mass due to age-related sarcopenia and insufficient physical activity due to hypokinesia and physical inactivity, as well as low levels of vitamin D due to intestinal dysfunction, decreased sense of smell, taste and appetite [18].

Moderate to high intensity aerobic endurance exercises are used in patients with PD. According to the 2022 Report of American Physical Therapy Association, this intensity has high strength and quality of evidence for aerobic training in patients with PD [19]. In addition to its general effect on the body, training of this intensity has a specific effect. Aerobic physical activity alleviates disease symptoms in patients with PD. This physical activity is associated with improved $\text{Vo}_{2\text{max}}$, motor skills, functional parameters, and quality of life [20]. Studies are being conducted to investigate effects of physical activity on motor and non-motor symptoms of PD and elucidate possible mechanisms underlying these effects. Study results showed improvements in motor symptoms,

³ 1 Watt is equivalent to 6.1 kilogram meters per minute (kgm/min), 1 kgm = 1 J.

mobility, decreased freezing of gait, improved forward and backward walking, and positive effects on cognitive function [19–21].

A study in patients with PD was conducted to evaluate the effectiveness of aerobic exercise with a bicycle ergometer with increasing exercise intensity from medium to high during the course [21]. Intensity was assessed by heart rate reserve. The reference group of patients with PD performed stretching exercise. The authors evaluated the effect of physical activity on the brain using magnetic resonance imaging (MRI) data. During the study, a decrease in brain atrophy rate and an improvement in cognitive function were seen in the main group. Therefore, aerobic exercise was shown to support the stimulation of functional and structural neuroplasticity. MRI, clinical and psychological testing data indicated a slowdown in PD progression.

A similar conclusion was reached in laboratory studies. An experimental study of neurotoxin-induced parkinsonism in animals indicated a specific targeted effect of aerobic exercise on the brain [22]. Physical exercise increased dopamine release, affected synaptogenesis, improved regional cerebral circulation, and increased endogenous levels of neurotrophic substances in the brain (brain and glial neurotrophic factors), which may reduce striatal dopamine loss [21, 23, 24]. Studies of continuous moderate-intensity aerobic exercise were published, indicating an increase in dopaminergic stimulation after a treatment course [25].

Epidemiological and experimental data based on immune markers suggest that aerobic exercise reduces disease progression rate. However, there are still no valid immune biochemical markers for PD progression, so there is no evidence to support the modifying effects of aerobic exercise on the brain of patients with PD. Possible modification effects remain incredibly complex but future studies of aerobic activity are planned to elucidate them and consider aerobic exercise as replacement therapy during the washout period of specific dopaminergic medications or in the delayed treatment initiation setting [26].

Exercises for rehabilitation of motor functions

To perform the required amount of physical activity, different types of exercises can be used. Usually, walking of necessary intensity is used. For the purpose of the studies, physical activity intensity during walking is measured by Vo_2max or heart rate.

In walking training, additional equipment is used such as a treadmill or a modified treadmill with no load to lower body [26]. In addition to improving aerobic capacity, treadmill training improved balance and strength [26, 27]. A modified treadmill with no load to lower body is used for patients with severe pain, which is one of non-motor PD symptoms, and in patients

with mental changes such as excessive fear. This equipment is used at the advanced stage of PD and in patients with orthostatic hypotension [10, 28].

In PD patients, gait impairment has dopaminergic origin, non-dopamine origin, and causes directly related to walking [29]. The latter type of disorders includes freezing of gait, i. e. a disabling phenomenon when the patient is in a state of short-term episodic absence or noticeable decrease in the forward movement of their legs, despite their intention to walk. For patients with freezing of gait, bicycle ergometer is a piece of equipment of choice for aerobic stationary training [30]. In addition, despite postural instability, PD patients demonstrate stability when riding a bicycle or exercising on a bicycle ergometer [29, 30].

At early stage of the disease, aerobic exercise is prescribed regardless of the time when the patient takes drug therapy. As the disease progresses, with many years of levodopa use it becomes impossible to complete the task, and training is carried out in the “on” state [21]. When the effect of high-intensity training on a treadmill and a bicycle ergometer were compared in the general population of patients with PD, no significant differences were found in improvement of aerobic abilities using different equipment [10].

A comparison of physical exercises carried out over a year and aimed at developing various physical parameters showed the superiority of aerobic exercise with a treadmill over dance therapy (tango) and stretching in motor symptoms and walking speed forward and backward, with the results maintaining for 3 months after therapy. Stretching therapy was less effective, although it improved motor function and backward movement speed. No changes in any parameters were reported after tango classes [27]. Another study compared the effectiveness of general and specific aerobic treadmill training, resistance training, and stretching. Only stretching and strength training increased muscle strength. Aerobic capacity assessed by Vo_2max increased only after a course of treadmill training; 6-minute walk test results improved after low- and high-intensity treadmill training, stretching, and strength training [31].

Walking is the most common type of aerobic activity. Walking training in patients with PD has general beneficial and specific effects. Walking is considered an independent rehabilitation method as it reduces the severity of motor symptoms and improves step length, walking speed, mobility, and balance. Modified Scandinavian (Nordic) walking can be a walking option for patients with PD [32]. The exercise power for Nordic walking is 6.6–7.7 MET (700 kgm/min, or 110 W) compared with 3.3–5.0 MET (450 kgm/min, or 75 W) for simple walking. A comparative study that involved stretching, Nordic walking, and simple walking showed the best rehabilitation results with Nordic walking, which was associated with an improvement in motor characteristics such as step length,

speed, gait variability, and postural stability [33]. Another study compared Nordic walking training in healthy people and patients with PD. Gait variability was assessed using a wearable accelerometer-based device placed on the ankle of the patient's most affected lower extremity in 60–120 min after administration of a dopaminergic agent vs. the ankle of the non-dominant leg of a healthy control subject. A course of training was associated with an improvement in spatiotemporal characteristics of walking. Step length and rhythmicity in the main and control groups became almost similar [34].

Freezing of gait impairs patients' mobility, significantly increases the risk of falling, and interferes with daily activities, reducing patients' quality of life. It occurs more often during step initiation and turning [35, 36]. In physical therapy management of PD, specific rehabilitation options such as external signal stimulation (sound, light, tactile) can be used [21]. During Nordic walking, impacts of poles on the ground or floor act as an element of stimulation, thus enhancing aerobic exercise [37]. Use of Nordic walking poles moves the muscles of the upper half of the body, which makes it easier to initiate a step due to better coordination.

Aquatic exercises are another aerobic activity option for patients with PD. M. Avenali et al. compared the effectiveness of deep-water exercises, Nordic walking, and dance therapy (samba) in patients with PD [36]. After a course of deep-water exercises, walking function in the 6-minute walk test and quality of life improved with, however, no effect on motor performances assessed by means of MDS-Unifed Parkinson's Disease Rating Scale, part III (UPDRS-III). Deep-water exercises were effective in most severe patients at the advanced stage of the disease, although in patients with freezing of gait better results were shown with dance and Nordic walking.

Rehabilitation of non-motor functions

Besides motor symptoms, patients are also bothered by non-motor symptoms of PD, which have a negative impact on their quality of life. Unfortunately, not all authors assessed this important aspect of the patient's health when conducting aerobic training. The effects of aerobic training on sleep quality, cognitive level, and depression were evaluated most frequently [37–39]. In addition, non-motor symptoms were not planned as a primary endpoint in the studies [26]. Therefore, patients were not included in the studies based on the severity of their non-motor symptoms. Therefore, it is difficult to compare rehabilitation results for non-motor symptoms in the main and control groups. The motor rehabilitation course may have been not long enough to alleviate some non-motor symptoms, and the study results may have erroneously suggested that physical therapy had no effect on non-motor symptoms.

Depression is a very common symptom in various stages of PD. Its incidence rate is 2–90% [40]. Patients with PD and depres-

sion have worse quality of life. However, they are usually not screened for depression and do not receive treatment [41]. An analysis of depression treatment in patients with PD over the past 10 years showed that exercise is the most popular method of therapy [42]. Results of studies to evaluate aerobic exercises in PD with depression were inconsistent: some studies showed a positive effect of aerobic exercises, while others found no effect [14, 24, 42, 43].

Cognitive impairment in patients with PD is heterogeneous in severity and rate of progression. The symptoms range from cognitive deficits and mild cognitive impairment to dementia. Authors showed improvements in attention, memory, conscious actions, and information processing speed in healthy adults after 4 months of aerobic training with intensity $\text{Vo}_{2\text{max}} = 70\%$ [44]. In patients with PD and mild cognitive impairment, memory and conscious actions improved only after 2 years of aerobic exercise therapy [45]. Other authors found no benefit from aerobic exercise in improving cognitive symptoms in PD [14, 46, 47].

Sleep disorders are another common symptom in patients with PD. This non-motor symptom is seen in 40–80% of patients. Sleep disorders in patients with PD have a complex nature [48–50]. Early PD symptoms such as interrupted sleep and difficulty falling asleep are common in the general elderly population. These disturbances may be related to normal aging processes. PD is characterized by more pronounced sleep fragmentation and daytime sleepiness. Drug treatment for insomnia has limited options in PD. Transcranial magnetic stimulation is not effective [26]. Exercise has a positive effect on sleep; however, it is difficult to evaluate the effectiveness of aerobic exercise therapy [14, 51]. Patients with sleep disturbances are usually administered with mixed physical rehabilitation programs. Therefore, a positive effect (if any) may be related to an improvement of other training qualities but not endurance [51].

Time of initiation is important for physical therapy. Patients often already have Hoehn–Yahr grade 2–3 of PD at first presentation, and, in this case, they are late with starting physical therapy. In early stages of PD (Hoehn–Yahr grade 1–2), physical exercise as a treatment option has a pronounced protective effect with a significant slowdown in neurodegenerative process rate [1]. Individual training programs are an option of choice for all patients. The predictive model for aerobic exercise selection includes patient phenotype and exercise parameters. A common limitation of all studies examining the effects of physical exercise was the exclusion of patients with Hoehn–Yahr stages 4 to 5 [19].

Conclusion

Aerobic training for patients with PD is recommended as a general beneficial activity, used along with other types of physical exercises for rehabilitation of patients with motor

and non-motor symptoms. Further studies on rehabilitation protocols and evaluation are needed. A question about the use of aerobic training in patients with Hoehn–Yahr grade 4–5 of PD remains open; however, aerobic exercise of proven required intensity is unlikely to be performed by this cate-

gory of patients. The amount of aerobic exercise to achieve a modifying effect on motor symptoms remains unclear. It is not known whether high-intensity aerobic training has benefits compared with moderate-intensity training, and there is a lack of studies on the treatment of non-motor symptoms [20].

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