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THE INFLUENCE OF PHYSICAL ACTIVITY ON THE IMPROVEMENT OF MOTOR FUNCTIONING IN PEOPLE WITH PARKINSON'S DISEASE

WPŁYW AKTYWNOŚCI FIZYCZNEJ NA POPRAWĘ FUNKCJONOWANIA MOTORYCZNEGO U OSÓB Z CHOROBĄ PARKINSONA

Anna Marszałek[1(A,B,C,D,E,F)], **Tadeusz Kasperczyk**[2(A,B,C,D,E,F)], **Robert Walaszek**[3(B,C,D,E,F,G)]

[1] Public Elementary School of the Association of Catholic Schools Friends in Hucisko-Pewelka, Poland
[2] Department of Aesthetic Cosmetology, Faculty of Rehabilitation, University of Physical Education in Krakow, Poland
[3] Department of Recreology and Biological Regeneration, University of Physical Education in Krakow, Poland

Authors' contribution
Wkład autorów:
A. Study design/planning
zaplanowanie badań
B. Data collection/entry
zebranie danych
C. Data analysis/statistics
dane – analiza i statystyki
D. Data interpretation
interpretacja danych
E. Preparation of manuscript
przygotowanie artykułu
F. Literature analysis/search
wyszukiwanie i analiza literatury
G. Funds collection
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Summary

Parkinson's disease (PD) is one of the most common chronic neurodegenerative diseases of the central nervous system. Its most common symptoms are motor disorders. So far, no effective forms of treatment have been found, nor have any diagnostic methods been identified that would allow for diagnosis at an early stage. For this reason, clinical trials have been conducted for many years in order to find new methods of therapy which would support pharmacological treatment – and it seems that physical activity comes first here. Studies carried out on humans and animal models of PD have shown that increased physical activity improves the patterns of motor behavior and enhances the process of angiogenesis, synaptogenesis, and neurogenesis in the brain. It also increases the level of neurotrophic factors. The aim of the work was to conduct a literature review and to present the impact of physical activity on improving motor functioning in people with PD. Having people with PD take up physical activity is of preventive importance. It may also be considered an early stage of the rehabilitation process. This paper was based on the work of both Polish and foreign researchers in the following databases: Web of Science, PubMed and Google Scholar.

Keywords: neurotrophic factors, Parkinson's disease, physical activity

Streszczenie

Choroba Parkinsona to jedna z najczęstszych przewlekłych chorób neurodegeneracyjnych ośrodkowego układu nerwowego, której podstawowym objawem są zaburzenia motoryczne. Dotąd nie znaleziono skutecznych form leczenia oraz metod diagnostycznych pozwalających rozpoznać chorobę we wczesnym jej etapie. Z tego względu, od wielu lat prowadzone są badania kliniczne poszukujące nowych metod terapii wspomagających leczenie farmakologiczne – wydaje się, że na pierwsze miejsce wysuwa się aktywność fizyczna. Na podstawie wyników badań przeprowadzonych u ludzi i na zwierzęcych modelach choroby Parkinsona stwierdzono, że wzmożona aktywność fizyczna poprawia wzorce zachowań ruchowych oraz wzmacnia proces angiogenezy, synaptogenezy i neurogenezy w mózgu. Wpływa również na podwyższenie poziomu czynników neurotroficznych. Celem pracy był przegląd literatury oraz przedstawienie wpływu aktywności fizycznej na poprawę funkcjonowania motorycznego u osób z chorobą Parkinsona. Podjęcie aktywności fizycznej przez osoby z chorobą Parkinsona ma znaczenie profilaktyczne, a także może być uznane za wczesny etap procesu rehabilitacji leczniczej. Praca została napisana w oparciu o kwerendę literatury polskiej i zagranicznej pochodzącej z baz danych: Web of Science, PubMed i Google Scholar.

Słowa kluczowe: czynniki neurotroficzne, choroba Parkinsona, aktywność fizyczna

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Address for correspondence / Adres korespondencyjny: Robert Walaszek, Department of Recreology and Biological Regeneration, University of Physical Education in Krakow, al. Jana Pawła II 78, 31-571 Krakow, Poland, e-mail: robertwalaszek63@gmail.com, phone: : +48 605 821 830
ORCID: Anna Marszałek https://orcid.org/0000-0003-0478-3711, Tadeusz Kasperczyk https://orcid.org/0000-0002-6702-5152, Robert Walaszek https://orcid.org/0000-0001-7639-2192

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Introduction

Parkinson's disease (PD) is a chronic neurodegenerative disease of the central nervous system, related to signs of damage to the extrapyramidal system [1]. According to the European Parkinson's Disease Association, there are between 5 and over 35 cases of the disease per 100,000 population per year [2]. This disease is caused by degenerative changes and the gradual death of the pigment-bearing neurons of the compact part of the substantia nigra and the lenticular nucleus of the midbrain [1]. Consequently, this process leads to a drop in the level of dopamine and its metabolites in the striatum and the basal ganglia. Motor disorders, which are the basic symptom of the disease, appear after the destruction of approximately 50%-70% of the dopaminergic neurons of the substantia nigra [2].

Many publications which compared the activity of particular cortical and subcortical areas between healthy and ill people reported differences in the way the subjects dealt with motor tasks, movement planning and the processing of sensory information (mainly tactile). In people affected by PD, reduced activity of the additional motor area was found, with a simultaneous increase in the activity of the premotor cortex, parietal cortex and the cerebellum [3]. According to Wu et al., the emerging greater coherence of cortico-cerebellar connections is probably a form of compensation for disturbances of the connections between the cerebral cortex and the basal ganglia, which allows patients to perform basic motor activities correctly [4]. It should be pointed out, however, that in the research conducted by Helmich et al., changes were observed in the strength of functional connections between particular brain centers during rest and movement, which results in problems performing more complex motor (manipulative) activities [5]. These activities depend on the proper functioning of the dopaminergic pathways, and disturbances in their formation lead to the occurrence of characteristic motor symptoms, such as tremors at rest, muscle stiffness, bradykinesia and postural stability disorders. In PD, there are also non-motor symptoms, such as olfactory, cognitive, or mental disorders, autonomic dysfunctions, sleep problems, pain, and fatigue [6].

As a result of the complexity of the disease, no effective forms of treatment and no diagnostic methods have been found so far that would help detect the disease at an early stage. The treatment consists of relieving symptoms, and it becomes less effective as the disease progresses. For this reason, clinical trials have been conducted for many years to search for new methods of therapy that would support the pharmacological treatment; one such treatment is physical activity. Studies have increasingly emphasized the role of exercise as a factor that effectively reduces the risk of neurodegenerative diseases, including PD [7]. We can distinguish as many as six phases, or developmental stages, in the course of the disease. In the first and second stages, we do not observe any disorders in the motor organ, but they are noticeable by the third stage. Rehabilitation is introduced when there are clear disturbances in physical fitness, walking, body posture, and balance. It includes a wide range of measures in the area of kinesiotherapy, physical therapy, occupational therapy, massage, and psychotherapy. People with PD taking up physical activity should be considered a preventive measure or an early part of the rehabilitation process.

Aim of the work

The aim of the work was to conduct a literature review and to present the effect of various types of physical activity on the quality of motor functioning of patients with PD.

Methods

The work is a narrative review based on the document analysis method with the use of quantitative and qualitative techniques and Polish and foreign scientific literature from the databases: Web of Science, PubMed, and Google Scholar. The article presents the results of studies conducted on patients with PD between 2000 and 2022 containing an assessment of the impact of physical activity on the patients' motor function. It mainly focuses on the international publications and analyzes them in the context of the prophylactic and treatment aspects of appropriately applied regular physical activity, the types of therapeutic treatment, and the documented effects of motion therapy. Seventy-two articles were selected for the analysis, out of which 31 were further scrutinized. Those articles met high methodological standards as well as the following inclusion criteria:

1. They presented the very complex neurophysiological basis of PD.
2. They referred to the effects of regular physical activity in patients with PD.
3. They assessed the progress made by those patients who used various levels of physical activity.

4. They showed the differences in patients with PD in terms of their processing sensor information, their ability to cope with physical exercise, and the planning and execution of the exercise.
5. They contained evidence of how the more advanced physical activity helps improve such processes as angiogenesis, synaptogenesis, and neurogenesis in the brains of people affected by PD.
6. They drew attention to the important role played by brain-derived neurotrophic factor (BDNF) in the neuroprotection induced by physical activity.

Articles unrelated to the subject, meta-analyses, systematic reviews, and case studies were not included in the analysis. The following keywords were used in the search: Parkinson's disease, physical activity, and neurotrophic factors.

The influence of physical activity on the functioning of the central nervous system

It is assumed that physical exertion improves the activity of the musculoskeletal system and the function of the circulatory and respiratory systems. Increasingly, attention has been paid to the fact that physical activity plays a significant role in the development of brain neuroplasticity. According to Petzinger et al., activity-dependent neuroplasticity means a change within the central nervous system, which happens as a consequence of performing targeted physical exercises and which includes the processes of neurogenesis, angiogenesis, and synaptogenesis [8]. According to Moore et al., one of the possible mechanisms of neuroplasticity in PD may be a reduction in cortical-striatal activity by modulating dopaminergic signals [9]. Various studies have shown that dopamine plays the most important role in regulating the motor circuit and motor control, that the proper functioning of the above-mentioned systems depends on the concentration of dopamine in the striatum, and that it also plays an important role in learning motor and executive functions in neuroplasticity when there is damage to the subcortical ganglia [10].

Fisher et al., in an experimental model, assessed how physical exertion can alleviate the symptoms of pharmacologically induced parkinsonism. The researchers used a mouse model of PD in which the animals received 4 intraperitoneal doses of 1-methyl-4-phenyl-1,2,3,6-tetrahydroxypyridine (MPTP). The analysis involved 2 control groups receiving NaCl or NaCl + training and 2 experimental groups receiving MPTP or MPTP + training. The form of physical exertion was an intensive, progressive 30-day treadmill workout, which started 4 days after the injections were completed. The administration of MPTP induced degeneration of dopaminergic neurons in the substantia nigra at the level of 60%-70%. This condition lasted until the 30th day, after the last dose of MPTP was administered. Recovery of motor function and partial improvement of neurochemical parameters took place 2 months after the induction of damage. Both trained groups significantly improved the speed of the run. The authors suggest that intensive training on a treadmill improves motor skills and improves dopaminergic neurotransmission [11].

The molecular mechanism of the influence of exercises on dopaminergic neurotransmission is unknown. The studies point to the participation of trophic factors, such as BDNF, fibroblast growth factor (FGF), and glial cell line-derived neurotrophic factor (GDNF), which are synthesized mainly in the central nervous system but also by peripheral non-neuronal cells, such as T lymphocytes, B lymphocytes, monocytes, and thrombocytes. The most recent study conducted by Castro et al. showed that neurotrophins, by activating the efferent pathways by protein kinases, influence the development of neurons, stimulate dendritic connections and neurogenesis, and inhibit the apoptosis process [12].

In this process, the role of BDNF is especially emphasized, which freely travels through the blood-brain barrier in both directions, while the direction of flow depends on its concentration gradient. Research shows that the level of circulating BDNF in the blood may reflect its level in the brain [13]. It was noted that 70%-80% of the level of BDNF in human serum, both at rest and during physical exercise, originates in the brain [14].

Immunochemical studies by Cunha et al. show that the highest concentration of BDNF is observed in the hippocampus, cerebral cortex, midbrain, thalamus and hypothalamus, striatum, pons, and medulla [15], which – according to Scalzo et al. – affects the development of dopaminergic, serotonergic, noradrenergic, and cholinergic neurons [16]. Moreover, it takes part in the regulation of neuronal plasticity connected with learning and memory processes, influencing the process of long-term potentiation (LTP) and long-term depression (LTD) in the hippocampus. A study conducted by Chung et al. provided evidence that brain neurodegeneration may be partly caused by defects in synaptic plasticity, which is related to an insufficient supply of BDNF to the neurons [17].

The available literature on the subject supports the thesis that BDNF plays an important role in exercise-induced neuroprotection. A study by Żołądź et al. proved that in patients suffering from PD who had a cycle of intensive interval training on a bicycle cycloergometer, the level of BDNF in the blood serum increased, along

with lower levels of proinflammatory cytokines. These effects were associated with an improvement in the general condition of the patient, evaluated according to the Unified Parkinson's Disease Rating Scale (UPDRS) [18]. There is also evidence which shows that BDNF plays a role in the regulation of the metabolism, development, and proper functioning of neurons, with the participation of insulin-like growth factor (IGF-1) [19]. Some authors note that the presence of IGF-1 and BDNF is necessary for the viability and function of neuronal cells. It is known that physical exercise increases IGF-1 secretion and, together with BDNF, may improve memory by changing the number of synapses and neurotransmission in mature neurons [20].

A review of the literature on physical activity's influence on motor fitness in Parkinson's disease

The available literature contains many reports on the role that physical activity plays in preventing the progression of PD. One of the most important scientific studies related to physical activity in people suffering from PD is the work of Fisher et al., in which the authors used the imaging technique of positron emission tomography (PET) to show that an 8-week intensive training cycle on an electric treadmill 3 times a week led to an increase in the number of dopaminergic receptors in the basal ganglia in people in the early stage of the disease. As a result, the patients moved faster, as confirmed by the walk and chair rise tests [21]. According to Luna et al., one theory for presenting the influence of treadmill training on improved gait pattern in people with PD involves the stimulation of somatosensory pathways. Running on a treadmill stimulates the foot receptors, muscle fibers, and the Golgi tendon organs. The head movements that accompany the treadmill exercises stimulate the sensory cells of the vestibular apparatus, and the resulting impulses are transmitted to the neural circuits that modulate posture and motor skills at various levels of the central nervous system [22].

The goal of a study by Ridgel et al. was to assess the effectiveness of aerobic exercise in the rehabilitation of people with PD by using bicycle ergometers. The subjects were split into 2 training groups that used tandem stationary bicycles; their training partners were healthy people. In the experimental group, the patients were forced to pedal at a pace of 80-90 rpm, while in the control group, the subjects pedaled at their preferred pace. All of them were assessed motorically according to the UPDRS scale and were subjected to a dexterity test involving two-handed manipulative movements of the upper limbs. The authors showed that, after an 8-week intensive training cycle, a statistically significant improvement in the motor score on the clinical UPDRS scale was noted in the patients from the study group, including 41% in parkinsonian stiffness, 38% in resting tremors, and 28% in the area of bradykinesia. In addition, the speed of performing a two-handed grasp improved, which testifies to better functioning of the extrapyramidal system. Through dopamine-dependent movement loops, this system is responsible for the smooth performance of movements, especially two-handed ones [23].

Alberts et al. conducted a study using functional magnetic resonance imaging (fMRI) in order to investigate the influence of a single session of intensive physical exertion using a tandem bike on brain function. The results show that in patients affected by PD who are in training, a single training session of intense exercise causes an increase in the metabolic activity of the basal ganglia, which was connected with an improvement in two-handed dexterity and parkinsonian symptoms [24].

Another noteworthy study was done by Reuter et al., who compared the effectiveness of three forms of physical activity in alleviating movement disorders in patients with PD. Groups of patients who practiced Nordic walking, walked, and performed stretching exercises were compared. The exercise program lasted for 6 months and involved performing exercises 3 times a week for 70 minutes a day. Patients from all groups showed a reduction in neck and hip pain and an improvement in body balance and overall physical well-being. The group of walking and Nordic walking patients, in comparison with those who did stretching exercises, showed increased maximum walking speed and stride length, improved body posture and stability, and fewer freezing episodes [25].

According to Docu Axelerad et al., the achievement of a significant improvement in the health of patients with PD is guaranteed by an exercise program including systematic training sessions. From a psychological point of view, the key role is played by the process of motivation. Traditional exercise programs are often insufficiently interesting and encouraging for patients with PD. General body weakening and cognitive decline, as well as being scared of falling over, can have a detrimental effect on the patient's social life and their relationships [26]. One alternative is tai chi, a Chinese form of movement which – according to Ghaffari and Kluger – contains elements of aerobic exertion, stretching, and muscle relaxation [27]. Fuzhong et al. conducted studies comparing the effectiveness of these three forms of physical activity in patients with PD for alleviating motor dysfunctions. In each of the 3 groups, the patients exercised twice a week for 60 minutes a day, for 24 weeks. In the patients who performed tai chi (patients with moderate and moderately advanced disease), the speed and length of the

stride increased, the number of falls decreased, and the mobility according to the subjects' own assessment improved, compared to the group of patients performing resistance and stretching exercises [28].

Apart from aerobic exercises and tai chi, dancing is also worth considering in the motor rehabilitation of people with PD. For most people, dancing is a pleasant form of movement which – in addition to the physical aspect – also has important social values. The music that accompanies dancing and the rhythm imposed by it helps the patients perform smooth movements. Hackney and Earhart studied the effectiveness of dance in an experiment that involved 20 1-hour lessons conducted twice a week for 13 weeks. The research showed better results from the 6-minute walk test, such as increased length of backward steps and a reduced degree of motor dysfunction, as assessed by the Berg Balance Scale, in relation to the control group that did not participate in dance lessons [29]. According to Lim et al., new psychomotor patterns may arise in the mechanism of biological feedback (biofeedback), which changes the activity of regulatory systems. The feedback on changes in the physiological state may modify activities by consciously controlling them. The research showed that the use of auditory stimuli increased the speed of walking and the length of steps in patients with PD and that the improvement was maintained after the signal was removed [30]. According to Ginis et al., auditory and visual perception make it easier for patients to make movements by involving the premotor cortex to a larger extent in movement control than the damaged basal ganglia, which changes the nature of the movement from automatic to controlled [31].

Conclusions

The primary symptom in PD is a progressive decline in motor function. Pharmacological treatment, which relies on the use of dopamine, effectively reduces the intensity of tremors, stiffness, and slowness of movement, but does not affect non-dopaminergic symptoms such as disorders of postural and walking stability, which increase the risk of falls and injuries as much as 10 times over that of healthy people [2].

In the literature on the subject, there are more and more reports about the positive significance of various forms of physical activity which are used to treat PD. The authors demonstrate that both physical rehabilitation and targeted physical activity, which was considered an adjuvant therapy (possibly useful) in the symptomatic treatment of this disease, positively influence neuroplastic changes, neurophysiological mechanisms of the central nervous system, and psychomotor behavior, which positively affects the quality of the patients' lives. The protective effect of increased physical activity is especially visible when various types of exercise are repeated on a long-term basis in patients with PD [7]. According to Opara, it should be remembered that the choice of physical activity depends on the patient's age and current fitness level. The needs and scope of rehabilitation depend on how advanced the disease is and which risk factors are involved. The regularity, perseverance, and motivation of the patients themselves play a major role in conducting rehabilitation. According to the National Institute for Neurological Disorders and Stroke (NINDS), planning and the entire process of rehabilitation should be carried out with the active participation of the patient and their family [1].

In light of these considerations, based on a review of the available literature, the conclusion can be drawn that this knowledge is necessary for physical therapists seeking effective methods of movement therapy based on scientific evidence, indicating the influence of properly dosed effort on the pathomechanism of PD, and also for modifying the health care system concerning these patients. The whole range of physical therapy exercises, including strength building workouts, walking, and coordination and balance training, can definitely improve the quality of life and functioning of patients with PD, and at the same time reduce the workload and pressure on those who care for those patients [32].

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