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Impact of Exercise on the Course of Parkinson's Disease: A Systematic Review

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ABSTRACT

Aim of the study

The aim of this article is to review scientific research on the impact of physical activity on the progression of Parkinson's disease. Specifically, we will discuss the quality of life of patients with Parkinson's disease, various types of physical activity that influence both motor and non-motor symptoms, and the molecular mechanisms through which physical activity affects the human body.

Materials and Methods

The authors conducted an extensive review of articles available in PubMed, Google Scholar, UpToDate. The keywords Parkinson's disease, physical activity, quality of life and exercises were the basis of the review. Studies published between 1992 and 2024 were included in the review.

Conclusions

Physical activity is beneficial for clinical outcomes and quality of life in patients with Parkinson's disease.

Keywords

Parkinson's disease; physical activity; quality of life; exercises.

Introduction

Parkinson's disease (PD) is a progressive and debilitating disorder that is the second most prevalent neurodegenerative condition, affecting an estimated 1–4% of people over the age of 60 worldwide. The onset of the disease varies significantly: early-onset PD occurs before the age of 50, young-onset PD appears between ages 20 and 50, and juvenile PD is diagnosed in individuals younger than 20. Research from 2018 revealed a 50% global increase in the prevalence of PD between 1990 and 2017 [1].

The pathophysiology of PD, like that of its non-motor symptoms, remains complex and imperfectly understood. The currently accepted hypothesis is that the Parkinsons disease is driven by the accumulation of the protein α -synuclein in neurons, forming Lewy bodies and Lewy neurites, which disrupt cellular processes and lead to neuronal death. This primarily affects dopaminergic neurons in the substantia nigra, though other systems, including those involving acetylcholine, serotonin, and noradrenaline, are also impacted. While the specific triggers of α -synuclein accumulation in most cases remain unknown, contributing factors include lysosomal and mitochondrial dysfunction, oxidative stress, and neuroinflammation [2, 3]. Although most PD cases are idiopathic, 5–10% are linked to genetic factors, such as mutations in the GBA gene or variations in HLA genes, which may increase susceptibility. The disease is hypothesized to progress via a prion-like mechanism, with α -synuclein spreading from peripheral areas like the gut and olfactory bulb to the brain through pathways such as the vagus nerve. This may explain the appearance of early non-motor symptoms, such as constipation and olfactory dysfunction, years before motor symptoms develop. Abnormal gut microbiota has also been associated with PD, raising questions about environmental or infectious factors as possible contributors to disease onset [4].

The symptoms of PD usually develop gradually and are mild at first. There are many different symptoms associated with PD. In general, PD symptoms are characterized by motor and non-motor, and these symptoms gradually deteriorate as PD progresses with time [5]. There are four primary motor symptoms of Parkinson's disease: bradykinesia, which is marked by a reduction in both the speed and amplitude of repetitive movements, rigidity, defined as increased resistance to passive joint movement regardless of velocity, tremor, typically presenting as a resting tremor with a frequency of 4–6 Hz, and postural instability [6]. In addition, most individuals with Parkinson's disease experience a range of non-motor symptoms that profoundly affect quality of life and often precede motor symptoms. Gastrointestinal dysfunction is particularly common, with issues such as weight loss, excessive drooling (sialorrhea), swallowing difficulties (dysphagia), delayed gastric emptying (gastroparesis), small intestinal bacterial overgrowth (SIBO), constipation, and defecatory dysfunction. These symptoms can impair nutrition, social functioning, and overall health. Cardiovascular complications are also prevalent, including orthostatic hypotension (OH), postprandial hypotension, nondipping blood pressure patterns at night, and supine hypertension, all of which increase the risks of falls, cognitive impairment, and cardiovascular events. Urogenital dysfunction is another significant concern, with many patients

experiencing urinary symptoms such as frequent urination, nocturia, incontinence, and incomplete bladder emptying. Sexual dysfunction, including reduced libido, erectile dysfunction in men, and lubrication issues in women, is common and has a profound emotional and social impact. Thermoregulatory dysfunction, particularly excessive sweating (hyperhidrosis), is also frequently reported and is associated with worse quality of life, anxiety, and dyskinesia. These non-motor symptoms affect multiple systems and are a significant burden for PD patients. Comprehensive management addressing these symptoms is essential for improving overall patient care and quality of life [7, 8, 9].

Research highlights the need for new approaches, including treatments to manage symptoms (tertiary prevention), slow disease progression (secondary prevention), or prevent its onset (primary prevention). Exercise has emerged as a promising intervention, showing benefits for managing symptoms, slowing disease progression, and potentially reducing the risk of developing PD. These effects are sometimes comparable or even superior to medication. In the last decade, studies on exercise and PD have tripled, evolving from focusing on symptom management to exploring exercise as a potential disease-modifying and preventive strategy. [10].

Materials and methods of research

A comprehensive literature review was undertaken using the PubMed and Google Scholar databases, focusing on studies published between 1992 and 2024. The search strategy aimed to gather an extensive range of research on the role of physical activity on the course of PD. Key search terms included “Parkinson’s disease”, “physical activity”, “exercise” and “quality of life”. To ensure quality, the selected studies were evaluated based on their relevance, methodology, and significance.

Quality of life in patients with PD

The World Health Organization (WHO) defines “quality of life” (QoL) as an individual’s perception of their position in life within the context of their culture, value systems, goals, expectations, standards, and concerns. This definition, enriched with philosophical and cultural nuances, encompasses a broad concept of overall well-being and satisfaction. In contrast, health-related quality of life (HRQoL) takes a narrower focus, defined as the patients’ own perception and evaluation of how a disease and its consequences affect their lives [11]. The assessment of HRQoL includes different aspects: motor and physical skills, mental health, somatic perception, and socioeconomic conditions Cognitive impairment, motor and non-

motor symptoms associated with PD have been found to affect HRQoL significantly. As in all chronic diseases, especially PD patients, the psychological aspect is also very important to the quality of life [12].

The study by Hoseinipalangi et al. aimed to examine the association between patient characteristics like sex, age, duration of illness, or psychological disorders and QoL in people with Parkinson's disease. The QoL was measured by the Parkinson's Disease Questionnaire (PDQ-39), which evaluates the frequency of difficulties patients experience in eight domains: daily activities, emotional well-being, stigmatization, social support, cognition, communication, and bodily discomfort. Age was found to have a significant inverse relationship with QoL, as older patients experienced poorer QoL, likely due to the limitations aging imposes on mobility and daily activities. Although some studies have reported conflicting findings, it seems logical that advancing age negatively impacts QoL. Similarly, disease duration was also inversely related to QoL, with longer durations significantly reducing scores across all PDQ-39 domains. While some previous studies support this finding, others have reported no such relationship. Sex differences were notable, with men at a greater risk of severe PD and experiencing lower overall QoL, particularly in communication and discomfort. Women, however, reported greater difficulties in domains such as mobility, stigma, emotional well-being, daily activities, and cognition. These findings highlight sex-specific differences in how PD affects QoL and underscore the need for tailored approaches to care. Psychological factors, including anxiety and depression, were also found to have a substantial impact on QoL. Anxiety, in particular, had a greater effect than depression, although depression remains a significant determinant of QoL. Previous studies have also emphasized the critical role of these psychological disorders in shaping patients' overall well-being [13].

Bock et al. analyzed the demographic, clinical, and economic factors affecting HRQoL in PD using data from the Fox Insight cohort. The findings demonstrated that both motor and nonmotor symptoms are significant contributors to HRQoL, with depression, motor severity, and cognitive decline having the strongest negative correlations. Nonmotor symptoms such as apathy, anxiety, sad mood, reduced concentration, and falls were prevalent and strongly associated with poorer HRQoL. Motor symptoms like freezing, gait and balance impairment, and nocturnal akinesia were identified as particularly bothersome, with notable differences in their effects across demographic and clinical subgroups, such as sex, education level, and income. The study also highlighted that depression interacts with motor symptoms to amplify their negative impact on HRQoL, suggesting a need for more targeted clinical interventions.

Sleep-related and gastrointestinal symptoms were also prevalent among participants, while falls were identified as a critical predictor of poor QoL due to their effect on mobility and independence. Furthermore, the results reveal disparities in HRQoL based on sex, education level, and income, suggesting that these factors influence symptom perception, treatment access, and outcomes [14].

Physical exercises as a prevention and treatment of Parkinson's Disease

Physical activity has been shown to help prevent and manage PD. The link between physical activity and a reduced risk of developing PD was initially identified in the Nurses' Health Study and the Health Professionals Follow-Up Study (HPFS). This association was later confirmed in five additional longitudinal studies, including the Harvard Alumni Health Study, CPS-II Nutrition Cohort, NIH-AARP Diet and Health Study, Finnish Mobile Clinic Study, and the Swedish National March Cohort Study [15]. The World Health Organization recommends that older adults (65+ years) engage in at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous exercise per week. However, most healthy older adults do not meet these guidelines, and physical activity levels decline significantly following a PD diagnosis, dropping below those of healthy individuals of the same age. Physical activity, which includes any movement increasing energy expenditure (e.g., gardening or household chores), differs from exercise, which is a structured, repetitive form of physical activity aimed at improving fitness. Both play a vital role in enhancing quality of life and managing PD [16].

The study of Still et al. examined the relationship between physical activities performed under free-living conditions and non-motor symptoms in individuals with PD. The findings suggest that engaging in daily, unsupervised activities, such as walking, gardening, or performing household chores, is associated with improvements in cognitive function, mood, and emotional well-being. Specifically, free-living physical activity was linked to reductions in anxiety, depression, and apathy—non-motor symptoms that significantly impact the quality of life in individuals with PD. The study highlights that free-living physical activity offers a practical and sustainable approach for managing non-motor symptoms compared to structured exercise programs, which may be difficult for some individuals to access or maintain. Additionally, regular engagement in everyday movements provides consistent stimulation that may contribute to neuroprotective effects, improved emotional regulation, and enhanced overall mental health [17].

Song et al. examined the effects of Tai Chi and Qigong (TCQ), traditional mind-body exercises, on individuals with PD, focusing on motor and non-motor symptoms as well as quality of life. Based on 15 randomized controlled trials involving 755 participants, the findings highlight the significant therapeutic potential of TCQ as a complementary intervention for PD management. In terms of motor symptoms, TCQ showed notable improvements in balance, gait, and overall motor performance. Participants demonstrated better postural stability and higher scores on motor assessment scales like the Unified Parkinson's Disease Rating Scale (UPDRS-III). These enhancements are crucial for reducing disability and mitigating the risk of falls, which are common challenges for individuals with PD. Specifically, Tai Chi was particularly effective in decreasing fall rates and boosting balance confidence, contributing to greater physical safety and independence for patients. The study also found moderate benefits for non-motor symptoms, particularly in alleviating depression and improving emotional well-being. While there was limited evidence of cognitive enhancements, the mindfulness and stress-reduction components of TCQ appeared to positively influence mood and mental health. However, the authors note that further research is needed to confirm these non-motor benefits and better understand the mechanisms involved. Quality of life measures showed significant improvements among participants engaging in TCQ. These exercises contributed to better mobility, reduced emotional distress, and an increased sense of control over symptoms, as reflected in improved scores on tools like the PDQ-39 [18].

In another meta-analysis Lötze et al. researched the impact of Argentine Tango (AT) on PD, providing compelling evidence that AT is a beneficial therapeutic intervention that addresses both motor and non-motor symptoms. AT showed substantial benefits in motor symptom management, with significant improvements in motor severity scores as measured by tools like the UPDRS. These benefits extend to enhanced balance, as evidenced by higher scores on the Mini-BESTest and improved performance on balance-related tasks. The focus on structured, precise movements in tango, along with its reliance on external cues provided by music, may explain these improvements. Tango also incorporates weight shifts, controlled turns, and coordinated step sequences, which directly address the balance and postural stability challenges commonly faced by people with PD. Gait was another domain positively affected by AT, with studies reporting moderate improvements in gait speed, stride length, and overall walking efficiency. However, gait improvements were not consistently observed across all studies, suggesting that individual variability, disease progression, or differences in

intervention protocols may influence outcomes. Moreover critical benefit of AT is its potential to reduce fall risks in PD patients. By improving balance confidence and dynamic postural control, tango can mitigate one of the most debilitating aspects of PD - frequent falls. This improvement is particularly valuable for maintaining independence and reducing injury risks in daily life. While the primary focus of AT interventions is often on motor symptoms, there is emerging evidence of its positive impact on non-motor aspects of PD. Participants reported increased social engagement, improved self-esteem, and greater emotional well-being. The social and interactive nature of Argentine Tango fosters a sense of connection, reduces isolation, and enhances motivation to participate regularly. The aesthetic and musical elements of tango also contribute to stress reduction and mood enhancement, which are crucial for managing PD's psychological burden [19].

The study of Gomes Neto et al. provides evidence on the impact of water-based exercise on individuals with PD, demonstrating its potential as an effective rehabilitation intervention for improving motor function, balance, mobility, and quality of life. Based on the findings from 15 randomized controlled trials, water-based exercise was found to outperform both land-based exercise and usual care in several areas. The buoyancy and reduced impact of the aquatic environment allowed individuals with PD to perform exercises with greater ease and less strain, improving motor function and confidence. Participants engaging in water-based programs demonstrated better balance and mobility, particularly in tasks like walking and transitioning movements, compared to those in land-based or usual care programs. In addition to physical improvements, water-based exercise enhanced participants' quality of life by reducing stiffness, promoting relaxation, and providing a supportive and enjoyable environment for rehabilitation. While land-based exercises were slightly more effective in addressing the fear of falling, aquatic therapy proved especially beneficial for those with advanced symptoms or difficulty performing weight-bearing activities [20].

Nordic walking (NW), a low-impact aerobic activity involving walking with handheld poles also demonstrates potential benefits for individuals with PD. Study of Salse-Batán et al. revealed that NW positively influences motor and non-motor symptoms, including gait, balance, and functional mobility. Significant improvements were observed in walking ability and quality of life compared to baseline, although the degree of clinical relevance in some outcomes remains uncertain. NW has shown superiority over other rehabilitation exercises in improving gait parameters, with enhancements in walking speed and distance covered. Meta-

analyses confirm statistically significant advancements in functional mobility, balance, and global motor impairment. Beyond motor symptoms, NW also addressed non-motor issues such as fatigue, depression, and anxiety, contributing to better emotional well-being and cognitive function. Physical fitness improvements, such as enhanced cardiorespiratory performance and anthropometric measures, have also been reported [21].

The systematic review and meta-analysis conducted by Suárez-Iglesias et al. evaluated the effects of Pilates on individuals with mild-to-moderate PD, focusing on its impact on motor function, balance, lower limb strength, and functional mobility. The findings demonstrate that Pilates provides significant improvements in physical fitness and motor performance, particularly in enhancing balance, postural control, and lower limb functionality. These outcomes are critical for reducing fall risk and improving gait stability, which are common challenges in PD management. Compared to conventional exercise programs, Pilates offered superior benefits in areas such as lower-body strength and functional autonomy. Participants engaging in Pilates exercises also reported enhanced confidence in performing daily activities, suggesting broader functional improvements. However, the effects of Pilates on non-motor symptoms, such as depression, anxiety, and cognitive decline, remain underexplored and inconclusive due to limited available data [22].

Molecular Mechanisms of Physical Exercise Relieving Parkinson's Disease

Physical activity (PA) has proven to be a significant non-pharmacological approach to managing PD, positively affecting various neurophysiological processes that support brain health and overall well-being. The benefits of PA for individuals with PD stem from multiple mechanisms, including the regulation of neuroendocrine functions, modulation of neurotransmitters, enhancement of insulin signaling, and stimulation of neurotrophic factor activity. Additionally, it helps reduce inflammation and oxidative stress, promotes autophagy, and neural survival. Together, these effects address both the motor and nonmotor symptoms associated with PD, providing promising opportunities for long-term neuroprotection.

Physical exercise (PE) acts as a stressor that activates the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system. This activation leads to the release of hormones like cortisol, vasopressin, and β -endorphins, which help regulate metabolic substrates and maintain homeostasis. Chronic exercise induces adaptations in the neuroendocrine system, such as a reduced hormonal stress response to submaximal exercise, creating a more efficient system over time. The response varies depending on exercise type (e.g., aerobic vs. strength

training), intensity, duration, and individual factors like gender and fitness level. These adaptations may improve the body's resilience to stress and enhance overall physiological stability, which is often impaired in PD [23, 24].

Exercise directly impacts the regulation and synthesis of key neurotransmitters, particularly dopamine (DA), serotonin (5-HT), and norepinephrine (NE), all of which are critical for motor function, mood, and cognitive processes. PA increases dopamine synthesis in the brain by upregulating tyrosine hydroxylase, an enzyme essential for dopamine production. It also enhances dopamine receptor binding affinity, improving the efficiency of dopamine signaling. These effects help alleviate motor symptoms in PD [25, 26]. The effect of exercise on serotonin depends on intensity and duration. For example, moderate exercise can decrease hippocampal serotonin levels, while high-intensity exercise increases them, supporting mood regulation and cognitive enhancement [27, 28]. Chronic exercise also elevates norepinephrine levels in regions like the spinal cord and pons-medulla. Norepinephrine contributes to anxiety reduction, memory consolidation, and retrieval, offering additional benefits for PD patients struggling with nonmotor symptoms. This neurotransmitter modulation not only addresses motor symptoms but also improves cognitive function, emotional well-being, and resilience to stress, all of which are crucial for managing PD [29,30].

Another key mechanism is enhanced insulin signaling, critical for neuronal survival, plasticity, and cognition. In PD, impaired insulin signaling is linked to neurodegeneration and learning deficits. Exercise enhances insulin sensitivity in both peripheral and central nervous systems, reducing inflammation and restoring insulin-dependent processes in the hippocampus, a brain region essential for memory. By improving neural insulin signaling, PA may slow cognitive decline and offer neuroprotective effects in PD [31, 32]. In addition exercise significantly boosts level of brain-derived neurotrophic factor (BDNF), a neurotrophin crucial for synaptic plasticity, neuronal survival and learning [33]. Elevated BDNF levels in regions such as the hippocampus and amygdala promote dendritic growth, synaptic strength, and stress resistance, while also modulates neuronal dopamine content and its release [34]. These effects help delay neurodegeneration and improve both motor and cognitive symptoms.

PA further facilitates neuroprotection through the production of irisin, a myokine released during exercise [35]. Irisin activates neuroprotective pathways like Akt and ERK1/2, reducing inflammation and oxidative stress while enhancing synaptic health [36]. Its interaction with BDNF amplifies its role in alleviating PD symptoms and slowing disease progression.

Exercise also reduces oxidative damage and neuroinflammation, which are central to PD pathology. By increasing the activity of antioxidant enzymes such as superoxide dismutase (SOD) and inducing heat shock proteins (HSPs), PE protects neurons from oxidative damage and supports tissue repair. HSP70, produced during exercise, protects motor neurons from protein denaturation and oxidative stress, which are linked to PD pathology [37, 38]. Exercise also promotes anti-inflammatory cytokines like IL-4 while suppressing pro-inflammatory markers such as TNF- α and IL-1 β , reducing neural apoptosis and delaying neurodegeneration. These mechanisms collectively preserve neural function, delay the onset of PD symptoms, and enhance overall brain health [39].

Another critical process influenced by PA in maintaining neuronal health is autophagy. Autophagy breaks down damaged cellular components and recycles them into building blocks for biosynthesis and energy production. This process is vital for cellular stress adaptation, especially in neurodegenerative diseases like Parkinson's disease. Defects in autophagy can lead to neurodegeneration, impaired neuromuscular function, and sensitivity to stressors such as oxidative damage and starvation [40]. Adaptive stress responses, such as those triggered by physical activity and intermittent dietary energy restriction, can enhance autophagy and other neuroprotective mechanisms. These interventions activate pathways involving calcium, CREB, NF κ B, and PGC-1 α , stimulating mitochondrial biogenesis and cellular repair [41]. Studies have shown that a lack of physical activity and an overabundance of food can suppress these adaptive responses, increasing the risk of conditions like PD, Alzheimer's disease (AD), depression, and stroke [39]. These findings suggest that enhancing autophagy through lifestyle interventions like exercise and dietary regulation could serve as a potential strategy to slow neurodegenerative progression and improve brain health in PD and related disorders.

Exercise also promotes neural survival and plasticity by enhancing neurogenesis, synaptic plasticity, and the expression of survival proteins. Studies conducted on rats have shown that exercise stimulates the hippocampus, through the proliferation of neural progenitor cells, strengthens synaptic connections and creates a "neuronal reserve," which may delay PD progression. Early-life exercise has been shown to induce long-lasting changes in brain morphology, supporting cognitive and emotional resilience later in life [42].

Conclusions

Physical activity (PA) emerges as a critical non-pharmacological intervention in managing Parkinson's disease, offering benefits that address both motor and non-motor symptoms.

Evidence suggests that regular PA, including aerobic exercise, resistance training, and free-living activities such as walking and gardening, contributes to enhanced neurophysiological processes. These include improved neurotransmitter regulation, increased neuroplasticity, and enhanced neurotrophic factor signaling, particularly brain-derived neurotrophic factor (BDNF). Moreover, PA is linked to reduced inflammation, oxidative stress, and improved mitochondrial function, all of which play a role in slowing the neurodegenerative progression of PD. The article highlights the preventive potential of PA, with epidemiological studies showing that regular exercise is associated with a reduced risk of developing PD. For individuals already diagnosed with PD, structured exercise programs, such as Tai Chi, Pilates, and Nordic walking, are particularly effective in improving balance, gait, and motor control. Non-motor symptoms like depression, anxiety, and cognitive impairment also respond positively to these interventions. However, it's important to note that some studies have shown limited or inconsistent effects of exercise on clinical outcomes and quality of life, indicating a need for further research to fully understand the impact of physical activity on this population. Despite these discrepancies, the overall evidence supports the role of physical activity into parkinsons disease as a key strategy for optimizing health and well-being.

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