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Does aerobic exercise help improve brain function and structure in patients suffering from Parkinson's disease?

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Abstract

Background: Parkinson's disease presents as a complicated neurodegenerative pathology characterized by a combination of motor and non-motor symptoms. Noteworthy, there is presently no curative intervention available, imposing a focus on symptomatic intervention. Symptomatic intervention is a broad-based approach consisting of five key elements: rehabilitation, therapy, maintenance, surgical interventions, and restorative strategies, the latter of which notably incorporates aerobic exercise. This study thoroughly examines the impact of aerobic exercise on brain structure and function in individuals with Parkinson's disease.

Methods: Relevant articles published on PubMed, ResearchGate, and Google Scholar dated between 2013-2022 were comprehensively analyzed. The criteria for inclusion incorporated articles that either made comparisons between aerobic exercise and alternative treatments for Parkinson's disease or provided insights into the specific effects of aerobic exercise in managing PD. Articles discussing aerobic exercise for non-PD conditions were excluded, as were those exploring unrelated subtopics to align with the research objective.

Result: The research findings demonstrate that regular aerobic exercise offers neuroprotective benefits, promoting stability in brain function, optimizing neurotransmitter activity, and enhancing overall neural activity. Furthermore, increased connectivity was observed within key brain networks, including the frontoparietal network

Conclusion: Adherence to aerobic exercise regimens has shown promise in alleviating Parkinson's disease symptoms, equivalent to some pharmaceutical interventions, particularly in the mild or early stages of the condition. Patients participating in aerobic exercise control groups exhibited fewer motor symptoms during post-assessment evaluations, and neuroimaging revealed reduced levels of brain atrophy. Guidelines for exercise in Parkinson's disease suggest that having aerobic training for 3-5 days per week, with sessions that last about 20- 60 minutes at moderate intensity, along with 2-3 days of resistance training involving 1-3 sets of 8-12 repetitions at 40-50% of one's maximum capacity. However, challenges arise in patient adherence to these exercise regimens, and there remains a lack of conclusive evidence regarding the impact that aerobic exercise has on non-motor symptoms of the pathology, such as mood disorders and apathy.

INTRODUCTION

Parkinson's disease (PD) is commonly perceived as a movement-related condition, marked by prominent symptoms such as resting tremor, muscle stiffness, slow movement (bradykinesia), and difficulties with balance and posture. Pathologically, PD is characterized by the degeneration of dopaminergic neurons in the nigrostriatal pathway and the aggregation of unusual protein aggregates called Lewy bodies, which primarily are made of misfolded α synuclein, within the neurons that remain. Beyond its characteristic motor manifestations associated with disturbances in dopamine levels, PD is now understood as a complex disorder affecting various neurotransmitter systems, including those involving serotonin, noradrenaline, and acetylcholine.¹

Multiple cross-sectional studies have consistently revealed that physically active individuals tend to manifest superior neurocognitive function in comparison to their sedentary counterparts.¹ Notably, individuals afflicted by Parkinson's disease often experience heightened cognitive engagement when acquiring and rehearsing movements and skills that were once autonomous and subconscious. Aerobic exercise, a form of physical activity primarily reliant on oxygen to sustain rhythmic and uninterrupted muscular contractions, has garnered substantial recognition as a valuable tool. It not only augments blood flow but also fosters neuroplasticity, particularly in the context of elderly individuals.²

Given the current absence of a curative intervention for Parkinson's disease, which is primarily managed through symptomatic approaches, various pharmaceutical interventions and therapeutic modalities are deployed to mitigate its progression. In this context, our study endeavors to delve into the potential ramifications of aerobic exercise on both the functional and structural dimensions of the brain in individuals grappling with a diagnosis of Parkinson's disease. Through rigorous inquiry and empirical examination, we aspire to elucidate a non-pharmacological avenue that holds promise for enhancing the overall well-being and quality of life of those confronting this formidable ailment.

Parkinson's disease (PD) is a neurodegenerative condition characterized by the progressive loss of dopaminergic neurons in the substantia nigra, leading to a deficiency of dopamine in the basal ganglia and the emergence of classical parkinsonian motor symptoms (MS) (³, ¹⁴). These motor symptoms, including :

- 1- Bradykinesia
- 2- Rest tremor
- 3- Rigidity
- 4- Postural and gait changes

Despite its classification as a movement disorder, PD is accompanied by a spectrum of non-motor symptoms (NMS) that affect nearly all patients. These symptoms include , but are not limited to:

- Reduced sense of smell (hyposmia)
- Difficulty with bowel movements (constipation)
- Problems with bladder control (urinary dysfunction)
- Decreased blood pressure upon standing (orthostatic hypotension)
- Impaired memory function
- Feelings of sadness or low mood (depression)
- Physical discomfort (pain)
- Disrupted sleep patterns (sleep disturbances)

The diagnosis of PD is fraught with challenges, even for specialized movement disorder neurologists, with initial diagnostic accuracy often falling below 100%

In clinical practice, a growing trend involves genetic testing, particularly for mendelian forms of Parkinson's disease. This approach is particularly relevant in cases of early disease onset (before age 40), familial history, and high-risk populations where specific monogenic forms of the disease are more prevalent.¹⁴

Treatment options for PD can be broadly categorized into five approaches: rehabilitative, therapeutic, restorative, maintenance, and surgical. Rehabilitation is initiated promptly after diagnosis and involves consultations with physical, occupational, and speech therapists.

Therapeutic intervention typically entails daily administration of levodopa (with carbidopa) or dopamine agonists, aiming to maintain dopamine levels and address both motor and non-motor symptoms. Maintenance therapies explore complementary and alternative medicine to support the brain's microenvironment. Lastly, surgical options , such as deep brain stimulation (DBS), is considered when other treatments fail to yield positive results. Unfortunately, there is currently no cure for PD.¹⁵

This article specifically delves into the potential benefits of aerobic exercise for individuals with Parkinson's disease. Recent studies have unveiled a strong connection between aerobic fitness and cognitive improvements. Neuroimaging studies across diverse populations have consistently highlighted the positive correlation between aerobic fitness and brain function and volume in regions like the prefrontal cortex and the hippocampus, known for their roles in working memory.⁵

Animal studies have further elucidated the relationship between physical activity and behavior, revealing alteration in neurogenesis, make up of neurotransmitter, neuronal spine density, synaptic plasticity, and the expression of neurotrophin genes and proteins, notably brain-derived neurotrophic factor (BDNF). Human studies have put together and confirmed these findings, showing that the cognitive positive impact of aerobic fitness are associated with alterations in blood flow of the cerebrum, neural connectivity, volume of gray matter, and white matter integrity in the central nervous system, as well as changes in peripheral factors like BDNF levels, arterial compliance, and inflammatory markers (e.g., C-reactive protein; CRP).⁵

According to a recent meta-analysis utilizing the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS), aerobic exercise appears to result in reduced motor symptoms among patients with PD, particularly during the off state, in comparison to non-aerobic control groups.⁷ The collective evidence underscores the potential of regular exercise in enhancing motor function, addressing issues such as bradykinesia, and improving gait and turning abilities. Furthermore, it may offer relief from nonmotor symptoms, including cognitive deficits, sleep disturbances, and sensory abnormalities.⁸

PD remains a complex neurological disorder that is not yet fully understood. Research continues to uncover its intricacies. The disease manifests itself as a combination of motor and non-motor features, making it crucial to investigate the various changes it causes. Key motor symptoms (MS) include:

- Shaking or trembling (tremors)
- Stiffness or inflexibility of muscles (rigidity)
- Slowness of movement (bradykinesia)
- Difficulty maintaining balance or posture (postural instability)

Non-motor symptoms (NMS) encompass:

- Cognitive impairment
- Psychological disorders
- Autonomic dysfunction
- Sleep disturbances

Understanding these changes, especially in the early stages of Parkinson's, requires a deep knowledge of the disease's pathophysiology.⁹

PD causes changes in the basal ganglia, cerebellum, brain volume, thalamus, limbic system, hypothalamus, locus coeruleus and glial cells. Basal ganglia play a crucial role in cognitive function and helps in the execution of voluntary movements. This region of the brain is the most affected in the disease and based on the way it is affected it can give rise to two variations in the disease, one which is tremor dominant and the second which is postural instability/gait difficulty dominant. Depending on the stage of the disease, basal ganglion undergoes atrophy. The changes in the substantia nigra and loss of neuronal activity and development of Lewy bodies being the hall mark of the disease has led to further degeneration in the neurological condition of the patients with PD. Cerebellum like basal ganglion has cognitive and motor functions and changes in this region are caused due to the degeneration of dopaminergic neurons.⁹ In a recent study, it was discovered that network degeneration seems to spread beyond the nigrostriatal dopaminergic projections into cortical regions linked to the sensorimotor network. These areas encompass the bilateral precentral gyrus, supplementary motor area, and the IPC, which plays an important part in integrating sensory and motor information.

The distinctive multimodal approach utilized in this study effectively identified cerebral pathologies, ranging from the decline of midbrain nuclei to putaminal dopamine depletion and dysfunction in the striato-cortical motor circuit. These findings align with the level of motor disability observed in the analyzed patients.⁴ Brain volume is also decreased in the cortical and subcortical regions giving rise to degenerative motor and non-motor functions. Both white and grey matter loss is observed. Thalamus is known to be responsible for cognitive functions such as memory, language, and attention. Lesions are observed in this region and loss of thalamus activity can severely affect the patient's ability to think and function. Impairment of hypothalamic function due to neural degeneration in all hypothalamic nuclei. Due to the degeneration of brain tissue, we can notice a decrease in dopamine, serotonin, melanin, hypocretin and acetylcholine in PD patients. A decrease in various neurotransmitters can give rise to other associated health conditions. Changes in the limbic system are often associated with dementia, creativity and emotional dysfunction.

Changes in the locus coeruleus such as noradrenergic neuronal loss and Lewy body formation caused resting tremors, depression, and metabolic dysfunction in other parts of the brain. Defects in the glial cells cause less synaptic communication affecting a lot of the cognitive capability to decrease in PD patients.⁹ When PD is detected early, the progression of the disease is tried to be controlled by reducing the mentioned changes in the brain. Different interventions were considered at the beginning of the disease, which also included aerobic exercise as a part of it.

Generally, exercise is good for health but in the case of PD it might as well just become a very important part of its management. Aerobic exercise which primarily includes walking, jogging, or running, aerobics, swimming, cycling etc, which in layman terms is known as “cardio” has shown to improve PD symptoms to a varying degree. A recent study stated that aerobic exercise and adherence to it has been shown to improve PD symptoms and act like many of the pharmaceutical options for PD in its mild or early stages.¹³ A randomized controlled trial was conducted to check for the effectiveness of aerobic exercise in PD patients and observe their brain changes over the span of 6 months. The study included about 130 PD patients, and they were subjected to aerobic exercise and stretching. The study concluded that aerobic exercise stabilizes disease progression and improves cognitive function.¹⁰

Another review article stated that aerobic exercise has been shown to improve not only cognitive function but also motor function. It also shows that it promotes long term neuronal connections and prevents degeneration of brain tissue. It has also been recorded that it reduces depression and enhances dopamine regulation. Aerobic exercise has neuroprotective effects and facilitates other neurotransmitters function properly and enhance their activity.¹¹ A study undertook a rapid review in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement, following its guidelines meticulously and ensuring comprehensive reporting. Systematic review methodologies were employed to identify, assess, synthesize, and compile resources outlining exercise recommendations tailored for multiple sclerosis (MS), stroke, and Parkinson's disease (PD) individually. Specifically for Parkinson's disease, the exercise guidelines advocate engaging in aerobic training 3-5 days weekly, with sessions lasting 20-60 minutes at moderate intensity. Furthermore, resistance training is recommended on 2-3 days weekly, comprising 1-3 sets of 8-12 repetitions at 40% to 50% of the one-repetition maximum (1RM).⁶

Several studies have been done to understand the effects of aerobic exercise and medical interventions to prevent disease progression. Medication is usually given to patients with PD only after a certain amount of degeneration in their normal lifestyle has been noticed and diagnosed. The main aim of the treatment is to correct the dopamine deficiency. Drugs such as levodopa, carbidopa, entacapone and dopamine receptor agonists such as bromocriptine, ropinirole, pramipexole and apomorphine are used in practice. But the issue of worry with these medications is dependency and their adverse effects. These drugs are usually given in a combination to help prevent the progression of the disease and help patients have more time to feel normal.¹²

Both management interventions come with their own pros and cons. Aerobic respiration, even though is helpful and can prevent disease progression up to a huge degree's, the patient's adherence to an exercise regimen has always been questionable. Medication on the other hand, even though they are much less work compared to aerobic exercise, their dependency and side effects start to affect a patient's day-to-day lifestyle after a certain amount of time. Even then, several studies have stated that diagnosing PD in its early stages and committing to aerobic exercise has far better outcomes than medicine consumption. The benefits of aerobic exercise weigh far heavier than their side effects.¹³

METHODOLOGY

A comprehensive systemic review was conducted by two researchers to analyze the effects of aerobic exercise on patients suffering from PD. A thorough comprehension of the articles that were reviewed was done and the articles specific to the topics were selected. Only articles from 2013- 2023 were considered. Articles that had different results compared to the aim of this article were not considered. The articles were thoroughly researched in research engines such as PubMed, Research gate and Google Scholar. Both published and unpublished studies were searched based on the keywords. A wide range of keywords were used to obtain several articles to be able to consider their accuracy for the research. No ethical evaluation was given consideration to ensure the information in the article is based on existing data and various articles. Limitations of articles were taken into special consideration to evaluate the inclusion and exclusion criteria of the article. All the articles were thoroughly read, and information was collectively selected and mentioned for the support of the article. Any disagreement issue amongst the author was resolved with mutual agreement and understanding.

This comprehensive literature review focuses on evaluating the effects of aerobic exercise in the treatment of PD. The review was conducted by extensively searching databases such as PubMed, Google Scholar, and Science Gate for relevant research articles published from 2014 onwards. The selection criteria were meticulously designed to ensure the inclusion of original research articles, clinical trials, systematic reviews, and meta- analyses that specifically addressed the effects of these procedures on depression.

Inclusion and Exclusion Criteria

To guarantee the precision of our review, we established strict inclusion and exclusion criteria. Articles included in the review were required to pertain directly to the topic of aerobic exercise in context to PD. This entailed the inclusion of articles that either compared aerobic exercise with any other treatment modality used for PD or presented findings on their individual effects in treating PD. Any articles discussing the use of aerobic exercise for conditions other than PD were excluded. Additionally, articles that delved into subtopics unrelated to PD were also excluded to maintain the focus on our research objective.

The research was a collaborative effort involving two researchers who worked diligently through the entire process. Initially, both researchers independently assessed the titles and abstracts of identified articles to determine their relevance. Any discrepancies in their assessments were resolved through discussion and consensus. This rigorous screening process aimed to ensure that only studies directly related to our research question were considered for further review. To enhance the comprehensiveness of our literature search, we manually scrutinized the reference lists of selected articles. This additional step helped us identify any potentially relevant studies that might not have surfaced during our initial database search.

Selected articles underwent rigorous evaluation for both quality and relevance. We systematically collected data on various aspects of each study, including study characteristics, patient demographics, sample size, study design, intervention details, outcome measures, and reported findings. The initial data extraction was conducted by one researcher, and then another researcher cross-verified the extracted data to ensure accuracy and reliability.

The findings from the selected studies were synthesized and analyzed to provide a comprehensive overview of the effectiveness of aerobic exercise in the treatment of PD. Careful consideration was given to the strengths and limitations of each included study. Any discrepancies or conflicting results among the selected studies were addressed and discussed within the review to offer readers a balanced perspective.

Importantly, our review recognizes the inherent biases or limitations associated with using previously published studies. While these studies provide valuable insights, they may carry their own biases, and our review takes this into account. Acknowledging the potential limitations in the data is crucial for maintaining transparency and rigor in our analysis.

It is worth noting that ethical considerations were deemed not applicable in this review. Since our review is based on existing published data and does not involve direct human subjects, ethical concerns related to issues such as informed consent, data privacy, and human research ethics are not relevant in this context.

In conclusion, this literature review demonstrates a systematic and thorough approach to evaluating the effectiveness of aerobic exercise in the treatment of Parkinson's. Through meticulous inclusion and exclusion criteria, collaborative researcher efforts, and a comprehensive data synthesis process, we aim to provide readers with a comprehensive understanding of the current state of research in this field. Furthermore, by acknowledging the limitations inherent in the included studies, we maintain the integrity and transparency of our review, ultimately contributing to the body of knowledge surrounding the use of neurostimulation techniques in depression treatment.

RESULTS

Parkinson's disease is a complex neurodegenerative disorder whose diagnosis can be very challenging, often requiring a comprehensive evaluation due to its complex and varied clinical presentation. There is no curative intervention for Parkinson's. However, there have been recent advancements in its management, one of which is the introduction of aerobic exercise that can be neuroprotective.

A randomized control study conducted in 2022 showed that Aerobic exercise led to increased functional connectivity of the anterior putamen with the sensorimotor cortex relative to the posterior putamen. Behaviorally, aerobic exercise also improved cognitive control. Furthermore, aerobic exercise increased functional connectivity in the right frontoparietal network, proportionally to fitness improvements, and it reduced global brain atrophy.

Moreover, a rigorously conducted randomized controlled trial involving 130 PD patients demonstrated that aerobic exercise, in contrast to stretching exercises, results in disease stabilization and improvements in cognitive function over six months. This study sheds light on the potential neuroprotective effects of aerobic exercise, which extend beyond cognitive benefits, encompassing the promotion of enduring neuronal connections and the prevention of brain tissue degeneration.¹⁰

Furthermore, an additional meta-analysis using (MDS)-UPDRS data revealed that individuals with Parkinson's disease who engaged in aerobic exercise displayed a reduction in motor symptoms during post-assessment, as compared to a non-aerobic control group. Conversely, regarding non-motor symptoms, the data highlights the significant potential of aerobic exercise as an effective intervention for mitigating the progression of motor symptoms in PD.

Additionally, nine separate studies examined the influence of aerobic exercise on mood disorders, with three of them incorporating apathy as an outcome measure.

1. Two studies reported a positive impact of aerobic exercise on alleviating depressive symptoms.
2. However, these findings were not consistently supported by other trials.
3. In the case of apathy, only one study demonstrated a favorable effect.

Therefore, we conclude that there is insufficient evidence for a beneficial effect of aerobic exercise on mood disorders and apathy.⁷

PA critical literature review has concluded that aerobic exercise (AE) and a balanced diet are currently recognized as complementary strategies to drug treatments for mitigating both motor and non-motor symptoms in patients with Parkinson's disease (PD). Here, some researchers have delved into investigating the impact of AE on cognitive and motor skills among PD patients. The study's findings revealed that AE has demonstrated the ability to enhance specific executive functions, specifically spatial working memory and verbal fluency, encompassing both semantic and category-based tasks.

These enhancements were observed in comparison to cognitive tasks primarily mediated by the temporal lobe, such as spatial recognition memory and pattern recognition memory. It was also documented that the integration of cognitive and motor training, such as treadmill exercises conducted thrice weekly over a span of two months, has been shown to yield substantial benefits in terms of overall cognitive function and particular aspects of the attention system and executive functioning among patients who have been diagnosed with Parkinson's disease for six years.¹¹

DISCUSSION

This rapid review synchronized and amalgamated current resources available on research engines such as PubMed, ResearchGate, and Google Scholar to evaluate the effect of aerobic exercise on brain function and structure in individuals with Parkinson's disease.

Key points:

1. The objective was to assess the impact of aerobic exercise on both brain function and structure in individuals diagnosed with Parkinson's disease.
2. The findings supported the hypothesis that aerobic exercise possesses potential neuroprotective properties in the context of Parkinson's disease.
3. It is essential to acknowledge that maintaining a consistent exercise regimen may pose challenges for specific Parkinson's disease patients.
4. Nevertheless, the cumulative evidence underscores that the benefits derived from aerobic exercise far outweigh the challenges associated with adherence.

CONCLUSION

In summary, Parkinson's disease (PD) is predominantly identified by motor symptoms such as resting tremors, rigidity, bradykinesia, and postural instability. However, it is increasingly acknowledged as a complex disorder affecting multiple neurotransmitter systems, leading to a broad spectrum of both motor and non-motor symptoms. While a definitive cure for PD remains elusive, its management involves a combination of pharmaceutical treatments, therapeutic approaches, and lifestyle adjustments.

A particularly promising avenue in PD management that has garnered substantial attention in recent years is the incorporation of aerobic exercise. Aerobic activities such as walking, jogging, swimming, and cycling have demonstrated impressive potential in enhancing both the functional and structural aspects of the brain in individuals living with PD. Emerging research indicates that aerobic exercise can exert a favorable influence on the cognitive function of PD patients, potentially alleviating symptoms like cognitive deficits, mood disturbances, and sleep disorders. The advantages of integrating aerobic exercise into PD management extend beyond motor symptoms. Research has indicated that aerobic exercise has the capacity to diminish depression, enhance dopamine regulation, and facilitate the proper functioning of various neurotransmitter systems. Additionally, aerobic exercise fosters neuroplasticity, a crucial factor for brain health and cognitive function. It also exerts positive influences on variables such as cerebral blood flow, neural connectivity, gray matter volume, and white matter integrity.

Compared to pharmaceutical interventions, which often come with dependency and undesirable side effects, aerobic exercise presents an enticing alternative for PD management, particularly in its early stages. While medications remain pivotal components of PD treatment, aerobic exercise can complement them and potentially delay the necessity for medication by conferring neuroprotective benefits and enhancing overall well-being.

In conclusion, while a definitive cure for Parkinson's remains elusive, the integration of aerobic exercise into the management of PD presents substantial promise in terms of improving cognitive function, stabilizing disease progression, and enhancing overall quality of life for individuals grappling with this condition. As research continues to unravel the multifaceted benefits of aerobic exercise, it becomes increasingly apparent that exercise plays an indispensable role in the holistic approach to managing Parkinson's disease. As our understanding of the disease's underlying pathophysiology deepens, alongside recognizing the full potential of exercise as a neuroprotective intervention, there is genuine hope for improved outcomes and an enhanced quality of life for those navigating the challenges posed by Parkinson's disease.

DECLARATION

Ethical Statement

The research conducted in this study has received approval from the Institutional Review Board/Ethics Committee at Ivane Javakhishvili Tbilisi State University. All procedures performed in this study involving human participants were in accordance with the ethical standards of Ivane Javakhishvili Tbilisi State University and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards.

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Conflicts of Interest

The authors maintain that there are no conflicts of interest related to this research. Neither financial nor non-financial competing interests are present.

Data Availability

The data supporting the findings of this study are comprehensively presented within the article and its supplementary materials. For any additional data, interested parties may request access, and such requests will be considered.

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