Medical Science

To Cite:
Kulczyński DW, Dąbrowska N, Nowocin P, Kudas Z, Kumięga P, Litwin A, Wasiński P, Krzywicka K, Perchel N, Koszyk M. The impact of physical exercise on the development of neurodegenerative diseases. *Medical Science* 2025; 29: e10ms3489
doi: https://doi.org/10.54905/dissi.v29i155.e10ms3489

Authors' Affiliation:
[1]Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
[2]PKSO Ophthalmic University Hospital in Warsaw, Józefa Sierakowskiego 13, 03-709 Warszawa, Poland
[3]Cardinal Stefan Wyszyński University in Warsaw, Kazimierza Wóycickiego 1/3, 01-938 Warsaw, Poland

*Corresponding Author
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
Email: dawid.wiktor.kulczynski@gmail.com

Contact List

Dawid Wiktor Kulczyński	dawid.wiktor.kulczynski@gmail.com
Natalia Dąbrowska	nataldabrowska@gmail.com
Paweł Nowocin	p.nowocin@wp.pl
Zuzanna Kudas	md.zuzannakudas@gmail.com
Paulina Kumięga	paulina.kumiega@wum.edu.pl
Aleksandra Litwin	Aleks.litwin123@gmail.com
Piotr Wasiński	p_wasinski@interia.pl
Karolina Krzywicka	karolinakrzywicka08@gmail.com
Nikola Perchel	nikolaperchel@interia.pl
Martyna Koszyk	martyna.koszyk@icloud.com

ORCID List

Nikola Perchel	0009-0005-6489-7480
Natalia Dąbrowska	0009-0009-7170-0614
Paweł Nowocin	0009-0007-2018-6139
Zuzanna Kudas	0009-0009-6750-6886
Paulina Kumięga	0009-0005-1431-0231
Aleksandra Litwin	0009-0004-3221-0085
Piotr Wasiński	0009-0009-3824-3618
Karolina Krzywicka	0009-0001-3248-4674
Dawid Wiktor Kulczyński	0009-0003-3897-1507
Martyna Koszyk	0009-0000-9927-6020

Peer-Review History
Received: 25 September 2024
Reviewed & Revised: 28/September/2024 to 02/January/2025
Accepted: 06 January 2025
Published: 12 January 2025

Peer-review Method
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367

DISCOVERY
SCIENTIFIC SOCIETY

The impact of physical exercise on the development of neurodegenerative diseases

Dawid Wiktor Kulczyński[1*], Natalia Dąbrowska[1], Paweł Nowocin[1], Zuzanna Kudas[1], Paulina Kumięga[1], Aleksandra Litwin[1], Piotr Wasiński[1], Karolina Krzywicka[2], Nikola Perchel[1], Martyna Koszyk[3]

ABSTRACT

Behaviors like physical activity may impact neurodegenerative diseases such as Alzheimer's, Parkinson's, and ALS, which remain significant global challenges with limited therapies. Evidence suggests that exercise exerts protective effects by enhancing neurogenesis, reducing oxidative stress, and modulating inflammatory pathways. Studies indicate that physical activity improves cognitive function, delays disease onset, and lowers the risk of neurodegenerative diseases, potentially through increased brain-derived neurotrophic factor (BDNF), other neurotrophic factors, and myokine-mediated effects. Additionally, exercise improves biomarkers and mitochondrial function and reduces neuroinflammation. This paper systematically reviews the literature to classify the effects of aerobic and resistance exercise in preclinical and clinical populations. Findings reveal that more intense, prolonged exercise yields more substantial neuroprotective effects, marked by reduced inflammatory mediators and enhanced hippocampal neurogenesis. Exercise holds therapeutic potential, particularly for at-risk populations, and can be integrated into public health policies and clinical management strategies. As a noninvasive, cost-effective intervention, exercise is a promising approach for managing neurodegenerative diseases. The article concludes with recommendations for translating exercise programs into clinical practice and emphasizes the need for further studies to optimize protocols and explore the synergistic effects of exercise and pharmacotherapy.

Keywords: Risk factors, infertility in men, sport

1. INTRODUCTION

Neurodegenerative diseases are a diverse group of disorders, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS),

which are all marked by the progressive degeneration of neurons in the central nervous system resulting in cognitive, motor, and functional impairment (Hansson, 2021; Gao et al., 2023). Recognition of these disorders as a significant global healthcare burden is increasing, as is their frequency due to population aging and the absence of translational therapies to halt, even reverse, disease progression (Ning et al., 2024). There are more than 50 million people who have Alzheimer's disease worldwide, and the number is expected to triple by the year 2050, illustrating an urgent need for preventive and therapeutic interventions.

Modifiable lifestyles, such as physical activity, are crucial to mitigating the risk of neurodegenerative syndromes, as evidenced in all studies (Marques-Aleixo et al., 2021; Rojas-Vega et al., 2020). A common pathway by which physical exercise promotes neuroprotection is through ensuring an increase in brain-derived neurotrophic factor (BDNF), leading to the enhancement of mitochondrial function and reduction of oxidative stress (Ruiz-Gonzalez et al., 2021; Quan et al., 2020). Also, exercise has been shown to modulate myokine production with anti-inflammatory and neurotrophic functions, establishing its positive role in brain health (Lee et al., 2021). Moreover, NRG established that physical activity mitigates neuroinflammatory responses by modulating microglial activity and reducing levels of pro-inflammatory cytokines, which play an important role in the pathogenesis of neurodegenerative disease (Teleanu et al., 2022; Rauf et al., 2022).

2. MATERIALS AND METHODS

Study Design

We systematically review recent literature examining the role of exercise in the progression of neurodegenerative diseases (Table 1). The findings of this study, undertaken in August 2024, compile a model of empirical evidence garnered from clinical trials, observational cohorts, and mechanistic works which underpin the mechanisms and efficacy of exercise interventions within neurodegenerative cohorts.

Data Sources

Methods: The review was conducted using electronic databases such as PubMed, Scopus, and Web of Science. Searches were performed using the keywords "physical activity", "exercise", "neurodegenerative diseases", "Alzheimer's disease", "Parkinson's disease", "amyotrophic lateral sclerosis", "neuroinflammation", "oxidative stress", "mitochondria", and "brain-derived neurotrophic factor". To maintain the articles' relevance to current research, a publication date filter was applied restricting to peer-reviewed articles from January 2010 to July 2024.

Inclusion Criteria

Studies were eligible for inclusion based on the following criteria:
Research articles cover original data on the role of physical activity in the primary and secondary prevention of neurodegenerative diseases.
Studies that report experimental or clinical data on exercise-induced biomarkers, cognitive outcomes, or disease progression.
For animal or human models of neurodegeneration.
The articles reported outcomes explicitly relevant to the intensity, frequency, and duration of physical activity.

Ethical Considerations

This study is a systematic literature review, so no direct ethical approval was required. Nevertheless, the methodology of each study was verified through a rigorous screening process, and the studies had to obtain the necessary ethical approval.

3. RESULT AND DISCUSSION

In a recent study, Ning et al., (2024) examined how different physical activity profiles were related to risk for neurodegenerative disease in a large population-based cohort. Participants were classed as follows:
Regular exercisers
Those who do intense activity only on weekends are called "weekend warriors".
Sedentary individuals

The findings revealed that moderate-intensity exercise, such as hiking, brisk walking, cycling, and swimming three to five times a week for at least 150 minutes a week, was associated with almost a 40% reduction in risk of Alzheimer's and Parkinson's diseases. Sustained, moderate-intensity exercise consistently delivered the biggest bang for the buck, enhancing the brain's resilience but reducing disease risk. These findings highlight the importance of translating standard exercise regimens into everyday lifestyles for maximal long-term neuroprotective benefits.

The Role of Mitochondrial Function and Neuroprotection Induced by Exercise

Burtscher et al., (2021) propose exercise as a determinant of mitochondrial health, enabling neuronal activity and preventing neurodegeneration. Exercise enhances mitochondrial biogenesis and mitochondrial dynamics and can buck bioenergetic deficits in energy-hungry and neuronal regions, such as the hippocampus and cortex. Exercise also decreases the release of reactive oxygen species (ROS) and, thus, oxidative stress, a crucial contributor to neurodegenerative processes. The study also found an association between higher levels of aerobic exercise and lower levels of markers for inflammation in the brain and improved synaptic plasticity. The results could indicate that exercise protects against neurodegeneration through improved mitochondria performance. Exercise-induced mitochondrial-directed targeting is a new strategy to slow or prevent neurodegenerative diseases.

Synthesis of Findings

The findings of Ning et al., (2024) and Burtscher et al., (2021) all highlighted the double boon of getting active. Moderate-intensity exercise over a long period has been shown to reduce the risk of disease and increase cellular resistance. This is due, for example, to better mitochondrial health and lower oxidative stress. Such benefits are important for maintaining synaptic health and preventing neurodegeneration. These findings support the development of personalized exercise regimens tailored to the patients' ability and preferences to enhance brain long-term neuroprotection and overall well-being (Table 1).

Table 1 Summary of studies on exercise and neurodegenerative diseases

Study	Focus	Population	Outcome
Marques-Aleixo et al., (2021)	Therapeutic potential of exercise	Animal and human models	Reduced oxidative stress and improved mitochondrial function
Lee et al., (2021)	Myokines in neurodegenerative diseases	Animal models	Anti-inflammatory and neurotrophic effects
Ruiz-Gonzalez et al., (2021)	BDNF effects through exercise	Human studies	Increased BDNF levels and cognitive performance
Santiago and Potashkin, (2023)	Lifestyle and neurodegeneration prevention	Population-based studies	Decreased disease risk with structured activity
Bonanni et al., (2022)	Exercise's protective role in brain health	Clinical trials	Improved cognitive and motor functions

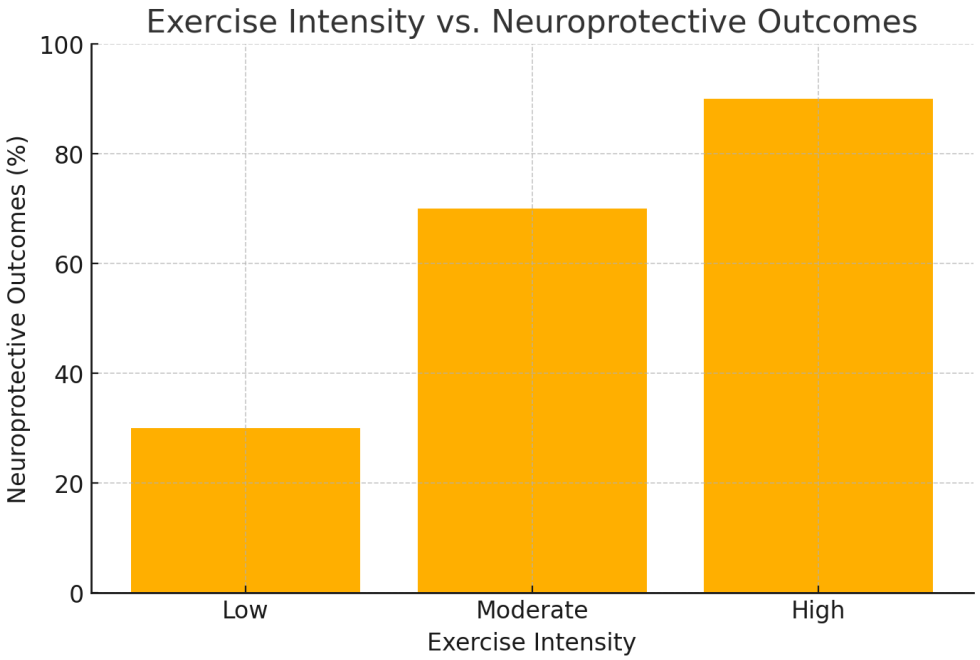

Figure 1 Exercise intensity and neuroprotective benefits

The intensity of exercise and associated neuroprotective benefits The relationship between exercise intensity and this neuroprotective benefit has received considerable attention (Figure 1). Importantly, these investigations converge upon the dynamic impact exercise intensity can have on neuroprotective effects. Routine moderate to high-intensity physical activity can improve cognitive performance and neuronal health and reduce the risk of several neurodegenerative diseases.

Key Findings

Low-intensity exercise refers to physical activity that keeps motivation fairly high. Walking or light yoga are beneficial primarily through enhancing circulation and reducing baseline inflammation. Although these activities provide a minimal increase in neurogenesis via melatonergic and serotonergic stimulation, their effects are small and confined to non-demented individuals for whom further advances in biomarkers of neurodegeneration characterize the next stages of cognition (Ning et al., 2024). Moderate-intensity doses of cardiovascular activity are associated with improvements in cognitive function. Athletic walking, trotting, and biking are proven weapons to elevate neurogenesis, up-regulate BDNF, and modify mitochondrial activity.

Regular moderate activity has been reported associated with a 30-40% decreased risk of disease (Ning et al., 2024; Ruiz-Gonzalez et al., 2021). Type of aerobic exercise: There is a clear consensus that running and high-intensity interval training (HIIT) induce the most pronounced neuroprotective effects. These benefits stem from enhanced synaptic plasticity, reduced oxidative stress, and tight regulation of neuroinflammation. A burst of intensive exercise is particularly effective in inducing mitochondrial biogenesis (Burtscher et al., 2021). Key Research Implications: Moderate—to high-intensity exercise prescribed at an appropriate dose based on individual fitness levels is most neuroprotective.

Exercise protects against neurodegeneration, and we describe its neuroprotective mechanisms in more detail (Figure 2). Neurogenesis and synaptic plasticity processes: Aerobic exercise interventions such as running/cycling have been well characterized to promote the expression of brain-derived neurotrophic factor (BDNF), one of the main proteins involved in the growth, survival, and differentiation of neurons (Marques-Aleixo et al., 2021; Ruiz-Gonzalez et al., 2021). The improvement is most pronounced in the hippocampus, a region critical for memory and learning known to generate new neurons through neurogenesis. High levels of neurogenesis are also associated with improved cognitive performance and emotional self-regulation (Terreros-Roncal et al., 2021).

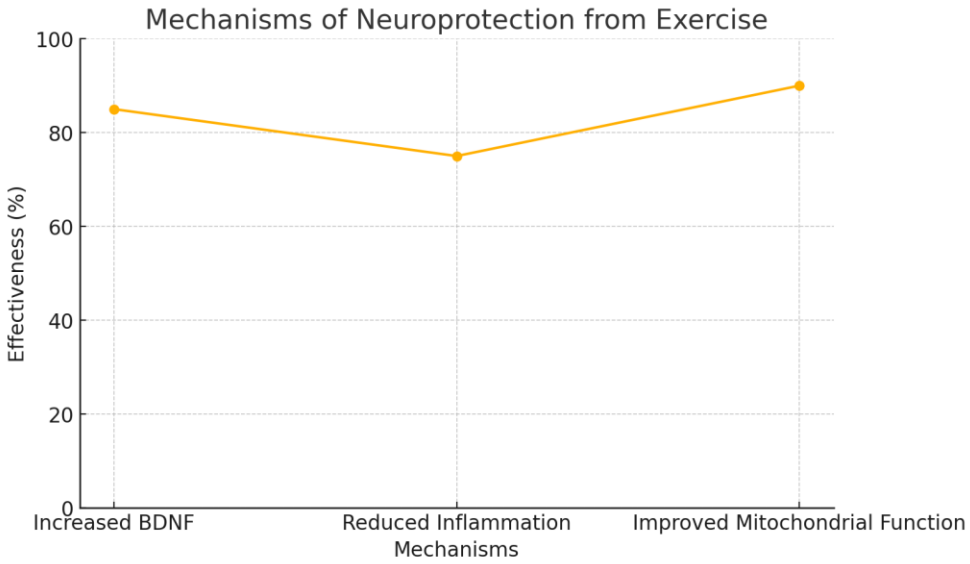

Figure 2 Mechanisms of Neuroprotection from Exercise

Exercise has also been shown to enhance synaptic plasticity, which helps neurons communicate and is key for cognitive health. An anti-inflammatory effect: Microglia activation contributes to prolonged inflammation, characteristic of neurodegenerative disorders. Physical activity suppresses inflammatory status by modulating microglial activation towards a neuroprotective phenotype (Teleanu et al., 2022; Rauf et al., 2022). This increases the expression of anti-inflammatory cytokines such as IL-10 and decreases the pro-inflammatory mediators, e.g., TNF-α and IL-6 [43]. Such balance protects neurons against inflammatory damage and stops disease progression. Reduction of oxidative stress: Reactive oxygen species (ROS) have built up in neurodegenerative diseases, resulting in oxidative damage to neurons.

Exercise-induced redox balance is triggered through increased activity of antioxidant enzymes, such as superoxide dismutase (SOD) and catalase, both of which neutralize ROS (Quan et al., 2020; Burtscher et al., 2021). Improved mitochondrial function: Since the mitochondria are the cell's powerhouse, abnormalities underlie most neurodegenerative diseases. By inducing mitochondrial biogenesis and increasing neurons' number and bioenergetic efficiency, exercise optimizes energy production while minimizing the release of damaging by-products such as ROS through improved mitochondrial dynamics: Fission and fusion. This efficiency ensures that the niches are powered with available energy to meet the most substantial demands, thus minimizing energy deficiencies and cell death.

Release of myokines: Evidence has demonstrated the neuroprotective effects of numerous signaling molecules, termed myokines, released by skeletal muscle during contractions. In the sense of Irisin, it has been reported that it crosses the blood-brain barrier and increases BDNF production, promoting neurogenesis. In addition, myokines stimulate anti-inflammatory action, promoting systemic and CNS anti-inflammatory activity, thus strengthening the brain against neurodegeneration. Keep neurotransmitters in check: Exercise can control primary neurotransmitters such as dopamine and serotonin. The increased availability of these neurotransmitters helps regulate mood and cognition and ameliorates disease symptoms. Adult hippocampal neurogenesis: Another way is through neurogenesis, which has been demonstrated to occur in one of the very few areas in the brain of an adult capable of it in the hippocampus.

Exercise significantly enhances new neurons' growth and endurance, directly affecting the disease and age-driven loss of memory. These mechanisms illustrate the importance of physical activity in maintaining brain health, as exercise is a key preventive and therapeutic strategy for neurodegenerative diseases. Exercise, an efficient, low-cost, widely available intervention with few side effects, has multiple mechanisms of action that seem to work in parallel, such as reducing inflammatory mediators, oxidative stress, mitochondrial dysfunction, and increased neurogenesis and synaptic plasticity. Future studies should define exercise protocols, determine optimal intensity and duration, and study the use of synergistic regimens that combine exercise with pharmacological treatments to enhance therapeutic outcomes.

There is similarly abundant evidence that exercise has a powerful effect on brain function, particularly in disease prevention and slowing neurodegenerative diseases. On a mechanistic level, exercise has been established to stimulate neurogenesis, most notably in the hippocampus, a region of the brain strongly associated with memory, learning, and cognitive function. Adapted from Marques-Aleixo et al., (2021), Terreros-Roncal et al., (2021) demonstrate that aerobic exercise induces the release of brain-derived neurotrophic factor, which helps support neuronal growth, survival, and plasticity. Additionally, exercise-derived myokines (e.g., irisin) are anti-inflammatory and antioxidative and can decrease neuroinflammation, a common feature of neurodegenerative disorders (Lee et al., 2021; Teleanu et al., 2022).

Exercise regulates microglial activity, decreasing neurotoxic responses and creating a neuroprotective environment (Rauf et al., 2022; Gao et al., 2023). Moderate-intensity, relatively frequent exercise has far more neuroprotective effects than shorter, less frequent, or low-level exercise. Studies by Ning et al., (2024) and Santiago and Potashkin, (2023) demonstrate that regular aerobic and resistance training significantly reduced the risk of Alzheimer's and Parkinson's diseases. While "weekend warrior" exercise patterns deliver some health benefits, sustaining moderate daily activity is the best strategy for preventing disease and delaying its progression. The new findings match prior studies examining physical activity's different benefits. For example, Ruiz-Gonzalez et al., (2021) have shown that neurodegenerative disorder patients' cognitive function and motor skills under these activity regimes increase significantly.

Bonanni et al., (2022) reviewed clinical trials that further bolstered the link between physical activity, reduced disease progression, and improved quality of life. Despite the report of promising outcomes, some limitations need to be addressed—trial heterogeneity in exercise modality, intensity, adherence, frequency, and self-efficacy limits generalizability. Limited long-term follow-up is a potential limitation since it may understate the benefits of physical activity in the long term. Additionally, the association with preclinical and clinical populations is, by definition, heterogeneous, complicating the translation of the results to individual stages of neurodegenerative disease.

Thus, physical exercise should be an important part of any plan for neurodegenerative disease prevention and treatment. Exercise should be individualized, especially in populations at risk, such as older adults or people with mild cognitive impairment. Exercise is a low-cost, non-invasive modality with evidence of reducing risk for many diseases, and policymakers and healthcare providers should work to incorporate research on this treatment into the public health toolbox. Exercise can be individualized to the loads that could be sufficiently maintained in practice or the amount of time individuals have available; this way, personalized interventions can grant maximal adherence and implications.

4. CONCLUSIONS

Exercise is a potent intervention in the prevention and progression of neurodegenerative diseases and is mutually brain-protective against age-related cognitive decline. The neuroprotective effects can be explained by such mechanisms as the promotion of neurogenesis, expression of neurotrophic factors such as BDNF, suppression of oxidative stress, and modulation of neuroinflammation, forming a neuronal network resistant to degeneration.

Moderate-to-high-intensity exercise has been found to reduce specific symptoms of neurodegeneration, slow cognitive decline, improve motor function, and improve quality of life. Daily exercise, especially in at-risk populations, becomes important, with public health initiatives focused on reducing disease burden and health care load. Exercise represents a universal corrective strategy that should be globally prioritized as a low-cost potential way to alter the course of preventive and therapeutic therapy for neurodegenerative diseases.

Acknowledgments

No acknowledgments.

Author's Contributions

Dawid Wiktor Kulczyński: Conceptualization; writing - rough preparation; supervision

Zuzanna Kudas: Writing- rough preparation

Paweł Nowocin: Writing- rough preparation

Martyna Koszyk: Writing - rough preparation

Aleksandra Litwin: Writing - rough preparation
Karolina Krzywicka: Writing - rough preparation
Nikola Perchel: Writing - rough preparation
Natalia Dąbrowska: Writing - review and editing
Paulina Kumięga: Writing - review and editing

Ethical approval
Not applicable.

Informed consent
Not applicable.

Funding
This study has not received any external funding.

Conflict of interest
The authors declare that there is no conflict of interests.

Data and materials availability
All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES

1. Bonanni R, Cariati I, Tarantino U, D'Arcangelo G, Tancredi V. Physical Exercise and Health: A Focus on Its Protective Role in Neurodegenerative Diseases. J Funct Morphol Kinesiol 2022; 7(2):38. doi: 10.3390/jfmk7020038
2. Burtscher J, Millet GP, Place N, Kayser B, Zanou N. The Muscle-Brain Axis and Neurodegenerative Diseases: The Key Role of Mitochondria in Exercise-Induced Neuroprotection. Int J Mol Sci 2021; 22(12):6479. doi: 10.3390/ijms22126479
3. Hansson O. Biomarkers for neurodegenerative diseases. Nat Med 2021; 27(6):954-963. doi: 10.1038/s41591-021-01382-x
4. Lee B, Shin M, Park Y, Won SY, Cho KS. Physical Exercise-Induced Myokines in Neurodegenerative Diseases. Int J Mol Sci 2021; 22(11):5795. doi: 10.3390/ijms22115795
5. Marques-Aleixo I, Beleza J, Sampaio A, Stevanović J, Coxito P, Gonçalves I, Ascensão A, Magalhães J. Preventive and Therapeutic Potential of Physical Exercise in Neurodegenerative Diseases. Antioxid Redox Signal 2021; 34 (8):674-693. doi: 10.1089/ars.2020.8075
6. Ning Y, Chen M, An J, Tang M, Tse G, Chan JSK, Zhao C, Liu Y, Lei X, Qiang H, Bai C, Li H, Yu H, Yan Y, Wang D, Li G. Association between "weekend warrior" physical activity and the incidence of neurodegenerative diseases. Neurotherapeutics 2024; 21(5):e00430. doi: 10.1016/j.neurot.2024.e00430
7. Quan H, Koltai E, Suzuki K, Aguiar AS Jr, Pinho R, Boldogh I, Berkes I, Radak Z. Exercise, redox system and neurodegenerative diseases. Biochim Biophys Acta Mol Basis Dis 2020; 1866(10):165778. doi: 10.1016/j.bbadis.2020.165778
8. Rauf A, Badoni H, Abu-Izneid T, Olatunde A, Rahman MM, Painuli S, Semwal P, Wilairatana P, Mubarak MS. Neuroinflammatory Markers: Key Indicators in the Pathology of Neurodegenerative Diseases. Molecules 2022; 27(10):3194. doi: 10.3390/molecules27103194
9. Ruiz-González D, Hernández-Martínez A, Valenzuela PL, Morales JS, Soriano-Maldonado A. Effects of physical exercise on plasma brain-derived neurotrophic factor in neurodegenerative disorders: A systematic review and meta-analysis of randomized controlled trials. Neurosci Biobehav Rev 2021; 128:394-405. doi: 10.1016/j.neubiorev.2021.05.025
10. Santiago JA, Potashkin JA. Physical activity and lifestyle modifications in the treatment of neurodegenerative diseases. Front Aging Neurosci 2023; 15:1185671. doi: 10.3389/fnagi.2023.1185671
11. Teleanu DM, Niculescu AG, Lungu II, Radu CI, Vladâcenco O, Roza E, Costăchescu B, Grumezescu AM, Teleanu RI. An Overview of Oxidative Stress, Neuroinflammation, and Neurodegenerative Diseases. Int J Mol Sci 2022; 23(11):5938. doi: 10.3390/ijms23115938

12. Terreros-Roncal J, Moreno-Jiménez EP, Flor-García M, Rodríguez-Moreno CB, Trinchero MF, Cafini F, Rábano A, Llorens-Martín M. Impact of neurodegenerative diseases on human adult hippocampal neurogenesis. Science 2021; 374 (6571):1106-1113. doi: 10.1126/science.abl5163