Scope
Volume 15 Number 02 June 2025

Effects of Intermittent Hypoxia Training with Parkinson's Disease

Lee Brown[1], *Dr Prashant Ruchaya[1],Dr Kim Hastings[2],Ellese North[1], Jagrut Shah[1], Brigita Kilip[3], Emma Chapman[4], Dr Andy Galbraith, Dr Richard Buscombe

[1] Health, Sport and Bioscience, University of East London, London, United Kingdom
[2]School of Education, Childhood, Youth and Sport, The Open University, Milton Keynes, United Kingdom.
[3]Kings College, London, United Kingdom
[3] National Health Service, United Kingdom

Corresponding Author: **Lee Brown**

Abstract.

Purpose: This case study investigated the effects of intermittent hypoxia training (IHT) on dopamine (DA) levels in an individual with Parkinson's disease (PD), compared to a healthy control. The aim was to assess the feasibility, safety, and potential dopaminergic response to a six-week IHT intervention. **Methods:** Two female participants (one diagnosed with PD and one age-matched control) completed twice-weekly sessions of low-intensity cycling in a normobaric hypoxia chamber (FiO_2 14.9%) for six weeks. Peripheral oxygen saturation was monitored to ensure safety, and venous blood samples were collected at baseline, midpoint (3 weeks), and endpoint (6 weeks) to evaluate serum dopamine levels using a competitive ELISA. **Results:** The control participant demonstrated a progressive increase in DA concentration, reaching a 104.9% increase by the study endpoint. The PD participant also showed elevated DA levels, with a 39.3% increase from baseline. The intervention was well tolerated by both participants, with no adverse events reported. **Conclusion:** Preliminary findings suggest that IHT may elicit a dopaminergic response in individuals with PD, potentially supporting its use as a novel adjunctive strategy to enhance neuroplasticity and dopaminergic activity. These results support the feasibility and safety of IHT in a clinical context; however, further investigation in larger cohorts is required to determine efficacy.

Keywords: Parkinson's disease, intermittent hypoxia, dopamine, exercise, neuroplasticity, neuroprotection

Introduction.

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder globally (2,16,20,21,22) and is characterized primarily by the progressive degeneration of dopaminergic neurons in the substantia nigra (2). Despite extensive research, the exact etiology of PD remains largely unknown. As an idiopathic and chronic

neurological condition with no known cure, continued investigation is essential to identify effective therapeutic strategies (3,5,16). Both environmental and genetic factors are believed to contribute to PD pathogenesis, although the relative influence of these elements remains uncertain (15). While genetic predisposition may play a role, only 3–5% of PD cases are currently attributed to known PD-associated genetic mutations (3). In contrast, Burtscher et al. (6) suggest that up to 90% of cases are idiopathic, with no identifiable genetic cause. A growing body of evidence supports the hypothesis that PD is driven by the pathological misfolding of the alpha-synuclein protein, which is normally present in neuronal cells (16,21,22). According to Saramowicz et al. (22), these misfolded proteins accumulate intracellularly, leading to neuronal dysfunction and cell death. The consequent damage to the substantia nigra results in a significant decline in dopamine (DA) synthesis and release, which is central to the manifestation of PD's hallmark motor symptoms (Leston et al., 2022; Burtscher et al., 2023).

Dopamine (DA) is a critical neurotransmitter involved in a range of physiological and cognitive functions, including energy regulation, attention, and temporal processing (1,7). DA synthesis primarily occurs in the ventral tegmental area and the substantia nigra, particularly within the hypothalamic nuclei and midbrain regions (21). A reduction in DA levels within the substantia nigra impairs the transmission of neural impulses, thereby disrupting the efficient relay of signals across the brain (Leston et al., 2022; Burtscher et al., 2023). This neural disruption weakens the connectivity between the central nervous system and the peripheral musculature, ultimately resulting in a loss of motor control (Segura-Aguilar, 2020). Motor symptoms, particularly those affecting gait and balance, are among the most recognized clinical features of Parkinson's disease (PD). However, PD is also associated with a broad spectrum of non-motor symptoms. These include dysregulation of autonomic functions such as orthostatic hypotension, gastrointestinal disturbances including constipation and urinary dysfunction, sleep disorders, and various neuropsychiatric manifestations (23). Notably, these clinical symptoms generally emerge following the degeneration of approximately 70% of dopaminergic neurons (3), with disease progression marked by a gradual intensification of both motor and non-motor impairments.

At present, there are no established neuroprotective or neurorestorative therapies capable of halting or reversing the progression of Parkinson's disease (PD) (7,14). However, increasing evidence suggests that various forms of physical exercise can alleviate both motor and non-motor symptoms associated with PD (de Laat), potentially improving overall quality of life (24).One emerging area of interest is exercise conducted under intermittent hypoxia training (IHT) conditions—a protocol characterized by alternating exposure to low oxygen (hypoxia) and normal oxygen

(normoxia) environments (2,4). Over the past two decades, IHT has gathered significant attention due to its reported physiological benefits, including enhanced performance outcomes attributed to increased erythropoietin production, elevated red blood cell count, and higher hematocrit levels, compared with equivalent training under normoxia (sea-level) conditions (9,19,4).During hypoxic exposure, reduced oxygen availability is detected by glomus cells within the carotid body, which respond by releasing dopamine (DA) (16). Interestingly, hypoxia induces the secretion of catecholamines from carotid body glomus cells, but not from adrenal chromaffin cells, indicating a cell-type-specific response to oxygen deprivation. Furthermore, studies suggest that hypoxia influences the secretion profiles of various catecholamines in a differential manner (8). For instance, under specific hypoxic stimuli, DA release from carotid body glomus cells appears to exceed that of noradrenaline, although the underlying mechanisms remain poorly understood and warrant further investigation.

Some studies suggest that IHT may increase the release of neurotransmitters in the brain, including DA, as well as activating tyrosine hydroxylase, a rate limiting enzyme crucial for catecholamine synthesis (Burtscher, Ehrenreich). The implications of such modulations extend to potential long-term neuroprotection and subsequent neuroinflammation due to inhibiting oxidative stress (12). Hypoxia exposure has become increasingly popular amongst athletes for its ability to improve performance, however the effects of hypoxia exposure on individuals with Parkinson's disease remains limited and inconclusive. Therefore, the aims of this case study are to identify if resting DA levels increase over six weeks, when exposed to IHT, and if the protocol is well tolerated, feasible and safe.

Methods.

Approach to the problem.

Two female subjects were recruited for the case study, one with PD (57 years old; 1.6m; 62kg) that was diagnosed four years previous to the study, no other known comorbid conditions were reported. The second female subject was recruited as the control and not diagnosed with PD and no current illnesses (70 years old; 1.61m;70kg), with a minimum of two years light intensity cardiovascular training for health and fitness. Both subjects reported being clear of injury for a minimum of six months free from any ill-health. Participant's stature (Seca 213, Birmingham, UK) and body mass (Seca 761, Birmingham, UK) were measured before testing. All subjects provided written informed consent to participate, and the study was approved by the institutional ethics committee at the University of East London.

This case study design, involving one individual with Parkinson's disease (PD) and one non-PD control, was selected to explore the feasibility, safety, and preliminary physiological responses to intermittent hypoxia training (IHT). Beginning with a

tightly controlled, small-scale format allowed for close monitoring of potential adverse events and helped establish foundational safety data before progressing to larger trials. The design also enabled refinement of key methodological elements such as SpO_2 thresholds, exercise intensity, chamber settings, exposure duration, and rest intervals.

Monitoring dopamine fluctuations and subjective responses provided early insight into the mechanistic effects of hypoxia in PD. The observed increase in serum dopamine levels in the PD participant suggests a potential biological signal, while differences between the PD and control subjects may reflect condition-specific adaptations. As IHT remains relatively underexplored in PD, especially with respect to real-time blood biomarkers, this case study offers preliminary evidence that can inform future hypothesis-driven research.

Furthermore, these early findings contribute to the scientific rationale required for larger interventional trials and provide supportive data for funding applications and ethical approval processes.

Procedures.

Subjects arrived at the laboratory in a rested state, with no exertional work or physical training prior to testing 72 hours before. BASES participation to exercise questionnaire was completed by the subjects, showing no illnesses or injuries, and cleared for testing. Pre and post testing was carried out at the start and end point of the six-week study duration, with bloods analysis observed at midpoint (three weeks) and endpoint (six weeks).

Bloods extraction.

Venous blood samples were collected by a registered nurse practitioner following standard clinical guidelines for phlebotomy. After obtaining informed consent, the participant was positioned appropriately, and a suitable venipuncture site—typically the median cubital vein in the antecubital fossa—was identified. The site was cleansed using a 70% isopropyl alcohol swab and allowed to air dry. A G21sterile needle and vacutainer system were used to collect the required volume of blood into appropriately labelled collection tubes, using vacutainers without anticoagulant (EDTA) present. Following sample collection, haemostasias was achieved by applying pressure to the puncture site with sterile gauze. Samples were immediately inverted, stored at recommended temperatures, and transported to the laboratory for further analysis according to biosafety and handling protocols

Dopamine analysis

A competitive ELISA (ab285238, Dopamine ELISA Kit, Abcam) was used to quantify dopamine in serum samples from two patients, with 12 samples (n=12) across three time

points. The assay was performed in a 96-well plate, starting with two washes using 1X Wash Solution. Then, 50 µL of standards or samples were added to the wells, followed by 50 µL of Biotin-detection antibody. The plate was sealed, mixed, and incubated for 45 minutes at 37°C. After incubation, the plate was washed three times with 1X Wash Solution (350 µL per well, 1-2 min soak), and residual liquid was removed. Next, 100 µL of SABC working solution was added to each well and incubated for 30 minutes at 37°C. The plate was then washed five times, followed by the addition of 90 µL of TMB substrate. After a 15–20-minute incubation at 37°C in the dark, 50 µL of Stop Solution was added to halt the reaction. Absorbance at 450 nm was measured using a microplate reader within 20 minutes.

Intermittent Hypoxia Training Protocol

Intermittent hypoxic exercise was conducted using a normobaric hypoxia chamber fitted by the Altitude Centre (Bank, United Kingdom) at the East London University, UK. Sessions were calibrated to an oxygen concentration of 14.9%. Each training session consisted of five minutes of continuous cycling inside the hypoxia chamber, followed by two minutes of seated rest in normoxia conditions. Two participants (n = 2) cycled at a cadence of 60 revolutions per minute (rpm) on a stationary Monk exercise bike without additional resistance, maintaining a light-intensity workload.

Peripheral oxygen saturation (SpO_2) was continuously monitored using a handheld pulse oximeter (MD300M, ChoiceMMed, Beijing, China) to ensure values did not fall below 86% during exposure. Prior to the intervention, participants completed a familiarization session in which they remained seated in the chamber for 30 minutes at an FiO_2 of 16% to assess potential adverse reactions to hypoxic exposure.

The intervention was carried out twice weekly (Fridays and Saturdays) for a total duration of six weeks, at the same time of day for each session to control for circadian variation. Participants were advised to abstain from physical activity for at least 24 hours and from stimulants (e.g., caffeine) for 48 hours prior to each session.Before commencing the intervention, participants completed a physical activity readiness questionnaire (PAR-Q) to screen for contraindications to exercise. All participants were medically cleared for participation by their general practitioners.

Data analysis

Descriptive statistics for all variables are expressed as a mean ± SD, and the alpha level of statistical significance was set at $p \leq 0.05$ (SPSS Version 21.0; SPSS Inc., IL, USA). Post hoc test, Wilcoxon signed rank test was carried out for significance between subjects and effect sizes (r) were calculated with between timing intervals and baseline. Effect size and the magnitude is rated at 0.1 - 0.3 = small effect; 0.3 - < 0.5 = moderate effect; >0.5 = large effect (10,11).

Results.

This longitudinal study aimed to elucidate the differences in measured variables between a control group and a Parkinson's Disease (PD) group across three distinct time points: baseline, mid-point, and endpoint as shown in Figure.1. To achieve this, a 96-well plate format was employed, allowing for precise and systematic measurements. Each sample, both from the control and PD groups, was measured n=12 at each time point, which ensured a robust and reliable data collection process. The mean values and standard errors of the mean (SEM) were subsequently calculated for both groups at each of the specified time points, providing a comprehensive overview of the data trends. At baseline, the control group exhibited a mean value of 4.926 with an SEM of 0.7044, indicating a relatively stable measurement within this cohort.

In contrast, the PD group presented a significantly higher mean of 7.084 (SEM = 0.9914), suggesting a notable deviation from the control group at the outset of the study. This initial difference raises important questions regarding the underlying pathophysiology of Parkinson's Disease and its impact on the measured variable. As the study progressed to the mid-point, the control group demonstrated a slight increase in % of dopamine which raised to 13.77%. Meanwhile, the PD group showed a modest reduction of 12.44% when compared to the initial timepoint. This slight decrease in the PD group's mean may indicate a potential stabilization of the measured variable. By the endpoint of the study, the control group exhibited a more pronounced increase dopamine percentage value, reaching 104.9% when compared it to the initial timepoint. Conversely, the PD group reported a mean of 39.29%, which, while was comparatively very less than control group, reflects a decline from the mid-point measurement as shown in figure 2. This trend suggests that the control group may be experiencing improvements or compensatory mechanisms over time, while the PD group continues to show persistent differences in the measured variable.

To rigorously evaluate the statistical significance of differences observed between the control and Parkinson's disease (PD) groups, the Wilcoxon Signed Rank Test was employed. This non-parametric test was selected due to its robustness in analyzing paired data where the assumption of normal distribution cannot be assured, making it particularly suitable for small-sample, exploratory case studies involving repeated measures. In this study, matched observations were compared across three time points—baseline, midpoint, and endpoint—to assess within-subject changes in dopamine levels. The results yielded compelling evidence of statistically significant differences between the control and PD groups at all measured intervals. Notably, the test produced a p-value of less than 0.005 at baseline ($p < 0.005$), indicating a highly significant difference in dopamine levels between groups at the outset of the intervention.

This finding suggests that even at the initial stage, there are marked distinctions in the measured variable between individuals with Parkinson's Disease and healthy controls. The mid-point analysis similarly demonstrated a statistically significant difference, with a p-value again falling below the 0.005 threshold ($p < 0.005$). This result reinforces the persistence of the observed differences as the study progressed, indicating that the disparity between the groups was not a transient phenomenon but a consistent feature throughout the experimental timeline. At the endpoint of the study, the statistical analysis once more revealed a significant difference between the control and PD groups, with the p-value remaining below 0.005 ($p < 0.005$).

This final comparison underscores the enduring nature of the observed differences, suggesting that the impact of Parkinson's Disease on the measured variable is sustained even at the conclusion of the study period. The consistency of these highly significant results across all three time points ($p < 0.005$ for baseline, mid-point, and endpoint) provides robust statistical evidence for the persistent and substantial impact of Parkinson's Disease on the measured outcomes. This level of significance ($p < 0.005$) corresponds to a confidence level exceeding
99.5%, which is considerably more stringent than the conventional 95% confidence level often
used in scientific research.

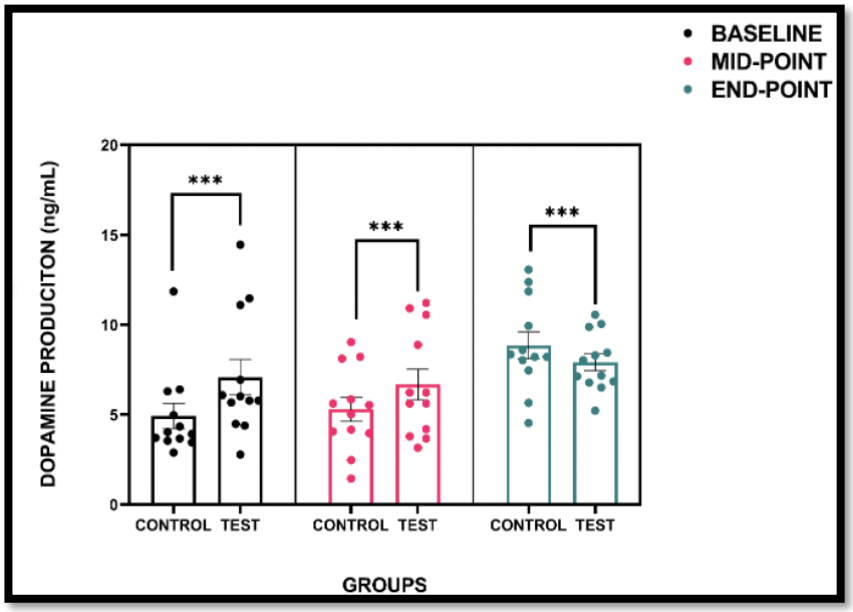

Figure 1. Comparison of Dopamine Levels Between Control and Parkinson's Disease Groups at Baseline, Mid-Point, and End-Point Time Points. Dopamine levels were measured in control and Parkinson's Disease groups using a 96-well plate format, with each sample being analyzed 12 times at each time point (baseline, mid-point, and endpoint). The mean dopamine levels and standard error of the mean (SEM) are presented for both groups. At baseline, the control group had a mean dopamine level of 4.926 (SEM = 0.7044), while the Parkinson's Disease group had a higher mean of 7.084

(SEM = 0.9914). At mid-point, the control group's mean increased to 5.295 (SEM = 0.6649) and the Parkinson's Disease group showed a mean of 6.678 (SEM = 0.8578). By the endpoint, the control group's mean reached 8.86 (SEM = 0.7437), with the Parkinson's Disease group recording a mean of 7.914 (SEM = 0.4658).

Discussion.

This study provides significant insights into the effects of hypoxic exercise on dopamine levels in an individual with Parkinson's Disease (PD) compared to a healthy control subject. The observed trends indicate distinct physiological responses to hypoxia and exercise in PD patients, which may have implications for therapeutic strategies. At the baseline measurement, PD patients exhibited significantly lower dopamine levels compared to the control group. This is consistent with the well-documented dopaminergic deficits in Parkinson's Disease, where the degeneration of dopamine-producing neurons in the substantia nigra leads to reduced dopamine availability in the brain (2,16,20,21,22). This deficit is a hallmark of PD and underlies many of the motor and non-motor symptoms associated with the disease (3,5,16).

During exercise under hypoxic conditions, dopamine levels in the PD subject showed an increase, although they remained lower than those of the control subject. This trend suggests that hypoxic exercise may stimulate certain compensatory mechanisms in PD patients. The increase in dopamine levels could be due to enhanced dopamine synthesis or release triggered by the stress of hypoxia combined with physical activity (8,16). This response might reflect an adaptive mechanism where the body attempts to counteract the dopaminergic deficit by upregulating pathways involved in dopamine production(9,16, 19). In contrast, the control group, which started with higher baseline dopamine levels, also experienced an increase in dopamine during hypoxic exercise but to a lesser extent relative to their baseline.

This suggests that while healthy individuals can further enhance dopamine levels through exercise, the relative change is more pronounced in PD patients, possibly due to their initial lower baseline and greater capacity for adaptive upregulation. The observed trends imply that the combination of hypoxia and exercise could activate neuroprotective pathways that are particularly beneficial for PD patients. These pathways may include increased expression of enzymes involved in dopamine synthesis, improved cerebral blood flow, and enhanced neuroplasticity (2). The stabilization of hypoxia-inducible factors could play a crucial role in these adaptive responses, promoting the survival and function of remaining dopaminergic neurons.

These findings are consistent with recent research exploring the role of hypoxia and exercise in PD (2,6). For instance, studies have shown that hypoxia can stabilize hypoxia-inducible factor 1-alpha (HIF-1α), which upregulates tyrosine hydroxylase, the

enzyme critical for dopamine synthesis (5,6,16). This mechanism may explain the increase in dopamine levels observed during hypoxic exercise in PD patients. High-intensity exercise has been shown to preserve dopamine-producing neurons and enhance dopamine transporter availability, as evidenced by increased neuromelanin and dopamine transporter signals following prolonged exercise regimens (22).

Limitations.

The precise mechanisms underlying these effects that have increased the levels of dopamine require further investigation to optimize treatment protocols, such as timings, levels of hypoxia and frequency of exposure and to ensure safety and efficacy. This case study was designed to test the efficacy and sensitivity of ELISA tests on the neurotransmitter, dopamine, as well as the effects of hypoxia itself, but this is limited by population of subjects. Therefore, it is stated by the authors of this study that to determine definitive outcomes a much larger population of subjects are required to determine the efficacy of treating Parkinson's using IHT. It is also necessary to mention that the blood analysis used to identify DA levels does not differentiate between dopaminergic pathways, but with limited technology, this is the most effective means possible until techniques are developed and identifying other neurotransmitters that work with DA in the nigrostriatal pathway may give better results for PD.

Conclusion.

These findings suggest that exercise can induce brain-protective effects that may slow, symptoms of neurodegeneration associated with PD. The observed increase in dopamine levels during hypoxic exercise in PD patients can be attributed to several physiological adaptations. Hypoxia is known to induce angiogenesis and enhance cerebral blood flow, which may improve oxygen delivery to dopaminergic neurons and support their function. Additionally, the stabilization of HIF-1α under hypoxic conditions can lead to increased expression of genes involved in dopamine synthesis and neuroprotection. Exercise, particularly under hypoxic conditions, may further potentiate these effects by enhancing neuroplasticity and promoting the release of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF). These factors have been shown to support the survival and function of dopaminergic neurons, potentially counteracting some of the neurodegenerative processes in PD. Synergistic effects of hypoxia and exercise observed in this study suggest that hypoxic exercise could serve as a promising therapeutic strategy for enhancing dopaminergic function in Parkinson's Disease, and should therefore be studied with larger cohorts to identify its efficacy and effectiveness in whole.

References:

1. Berke JD. What does dopamine mean? Nature Neuroscience. 2018 Jun;21(6):787–793.
2. Belikova MV, Kolesnikova EE, Serebrovskaya TV. Intermittent hypoxia and experimental Parkinson's disease. In: Serebrovskaya TV, Xi L, editors. Intermittent Hypoxia and Human Diseases. London: Springer; 2012. p. 147–153.
3. Bloem BR, Okun MS, Klein C. Parkinson's disease. The Lancet. 2021 Jun 5;397(10291):2284–2303.
4. Böning D. Altitude and hypoxia training - A short review. International Journal of Sports Medicine. 1997 Oct;18(7):565–570.
5. Burtscher J, Mallet RT, Burtscher M, Millet GP. Hypoxia and brain aging: Neurodegeneration or neuroprotection? Ageing Research Reviews. 2021 Jan;68:101343.
6. Burtscher J, Duderstadt Y, Gatterer H, Burtscher M, Vozdek R, Millet GP, et al. Hypoxia sensing and responses in Parkinson's disease. International Journal of Molecular Sciences. 2024 Feb 1;25(3):1759.
7. de Laat B, Hoye J, Stanley G, Hesepler M, Ligi J, Mohan V, et al. Intense exercise increases dopamine transporter and neuromelanin concentrations in the substantia nigra in Parkinson's disease. NPJ Parkinson's Disease. 2024;10:34.
8. Ehrenreich H, Gassmann DVM, Poustka L, Burtscher M, Hammermann P, Sirén A-L, et al. Exploiting moderate hypoxia to benefit patients with brain disease: Molecular mechanisms and translational research in progress. Neuroprotection. 2023;1:55–65.
9. Faiss R, Girard O, Millet GP. Advancing hypoxic training in team sports: from intermittent hypoxic training to repeated sprint training in hypoxia. British Journal of Sports Medicine. 2013;47 Suppl 1:i45–50.
10. Field A. Discovering Statistics Using IBM SPSS Statistics. 4th ed. London: Sage Publications; 2013.
11. Fritz CO, Morris PE, Richler JJ. Effect size estimates: current use, calculations, and interpretation. Journal of Experimental Psychology: General. 2012 Feb;141(1):2–18.
12. Gangwar A, Pooja, Sharma M, Singh K, Patyal A, Bhaumik G, et al. Intermittent normobaric hypoxia facilitates high altitude acclimatization by curtailing hypoxia-induced inflammation and dyslipidemia. Pflügers Archiv - European Journal of Physiology. 2019 Aug;471(7):949–959.
13. González-Candia A, Candia AA, Paz A, Mobarec F, Urbina-Varela R, Del Campo A, et al. Cardioprotective antioxidant and anti-inflammatory mechanisms induced by intermittent hypobaric hypoxia. Antioxidants. 2022 May;11(6):1043.

14. Gupta A, Dawson VL, Dawson TM. What causes cell death in Parkinson's disease? Annals of Neurology. 2008 Dec;64 Suppl 2:S3–S15.
15. Kalia LV, Lang AE. Parkinson's disease. The Lancet. 2015 Aug 29;386(9996):896–912.
16. Lestón Pinilla L, Ugun-Klusek A, Rutella S, De Girolamo LA. Hypoxia signaling in Parkinson's disease: there is use in asking "What HIF?". Biology. 2021 Jul 29;10(8):723.
17. Levine BD. Intermittent hypoxic training: fact and fancy. High Altitude Medicine & Biology. 2004;3(2):177–193.
18. Nimje MA, Patir H, Tirpude RK, Reddy PK, Kumar B. Physiological and oxidative stress responses to intermittent hypoxia training in Sprague Dawley rats. Experimental Lung Research. 2020 Nov;46(9-10):376–392.
19. Powell FL, Garcia N. Physiological effects of intermittent hypoxia. High Altitude Medicine & Biology. 2004;1(2):125–136.
20. Pringsheim T, Jette N, Frolkis A, Steeves TDL. The prevalence of Parkinson's disease: a systematic review and meta-analysis. Movement Disorders. 2014 Nov;29(13):1583–1590.
21. Segura-Aguilar J, Paris I, Muñoz P, Ferrari E, Zecca L, Zucca FA. Protective and toxic roles of dopamine in Parkinson's disease. Journal of Neurochemistry. 2014 Jun;129(6):898–915.
22. Saramowicz K, Siwecka N, Galita G, Kucharska-Lusina A, Rozpędek-Kamińska W, Majsterek I. Alpha-synuclein contribution to neuronal and glial damage in Parkinson's disease. International Journal of Molecular Sciences. 2024 Jan;25(1):360.
23. Sveinbjornsdottir S. The clinical symptoms of Parkinson's disease. Journal of Neurochemistry. 2016 Oct;139 Suppl 1:318–324.
24. Xu X, Fu Z, Le W. Exercise and Parkinson's disease. International Review of Neurobiology. 2019;147:45–74.