Analysis of the relationship between parkinson's disease and oxidative balance scores in US adults from the 2007-2018 NHANES surveys

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Abstract

Objective: This study set out to investigate the potential association between Parkinson's Disease (PD) and the Oxidative Balance Score (OBS), a measure used to evaluate the systemic level of oxidative stress. As the first large-scale epidemiological study to explore this relationship, it addresses a significant gap in existing research.

Methods: Data of 27,976 participants were obtained from the National Health and Nutrition Examination Survey (NHANES) from the year 2007 to 2018, where PD was identified through self-reported use of anti-PD medications. OBS was computed using 20 dietary and lifestyle variables. Subsequently, participants were categorized into four quartiles based on their OBS: Q1 (3-14), Q2 (15-20), Q3 (21-25), and Q4 (26-36). Weighted multivariable logistic regression and restricted cubic spline (RCS) models were employed to assess the relationship.

Results: In the unadjusted multivariate logistic regression, participants in the Q4 group were found to have a reduced likelihood of developing PD relative to those in the Q1 group [OR=0.553, 95% CI (0.314, 0.974), *P*=0.0433]. After adjusting for age, sex, race and education, the Q4 group continued to demonstrate a decreased risk of PD compared to the Q1 group [OR=0.563, 95% CI (0.332, 0.956), *P*=0.0361]. The RCS models analysis validated the existence of a linear relationship between OBS and PD.

Conclusion: PD is linearly and negatively correlated with OBS. Higher OBS, is associated with a lower risk of PD. This association may be influenced by socioeconomic status, with the PIR being a key indicator.

Background

Parkinson's Disease (PD) ranks as the second most prevalent neurodegenerative disorder of the central nervous system. With the aging of the global population, its prevalence, morbidity, and mortality have garnered extensive attention globally. The incidence and prevalence of PD rise with advancing age, affecting 47 to 77 per 100,000 people aged 45 or older, and 108 to 212 per 100,000 people aged 65 or older [1]. The main clinical symptoms of PD are characterized by motor symptoms, which include resting tremor, muscle rigidity, bradykinesia, and postural instability. Additionally, the disease presents with a range of non-motor symptoms, such as hyposmia, cognitive impairment, urinary and fecal dysfunction, anxiety and/or depression, and sleep disturbances [2], all of which are associated with the mortality of PD, hence severely reducing the quality of life for patients [3]. Relevant studies have shown that the mortality risk of PD is significantly higher than that of the general population (with a standardized mortality ratio of up to 1.84 in PD patients) [4]. As the disease progresses, the mortality rate of PD also gradually increases [5]. In summary, the intensification of population aging and the continuously increasing burden of PD will impose higher demands on public policies and the allocation of medical resources [6].

Oxidative Stress (OS) occurs when oxidants outweigh anti-oxidants, leading to an increase in Reactive Oxygen and Nitrogen Species (RONS). RONS can be produced endogenously by mitochondrial and cytoplasmic enzyme systems or exogenously through diet, lifestyle, medications, and environmental toxins [7]. Excessive ROS can lead to oxidative damage, cellular degeneration, and physiological dysfunction [8]. More studies have shown that OS is associated with various diseases, including metabolic syndrome [9], Cardiovascular Disease (CVD) [10], cancers [11,12], and Alzheimer's Disease (AD) [13]. Thus, OS is also considered one of the critical mechanisms in PD pathogenesis, playing key roles in the onset and progression of PD [14,15]. This may be related to the following two aspects: 1) Dopaminergic neurons are relatively sensitive to oxidative stress. Free radicals generated through neuronal metabolism or other pathways can attack intracellular lipids, proteins, and nucleic acids, leading to cellular dysfunction and death [16]; 2) Oxidative stress can exacerbate neuronal damage by impairing mitochondrial function and triggering neuroinflammation [17,18]. While the majority of PD instances occur randomly, approximately 5-10% of patients have a documented family pedigree [19]. Studies have found that PD-related gene mutations (such as *SNCA*, *PRKN*, *PINK1*, *DJ-1*, and *LRRK2*) are strongly associated with oxidative stress. Mutations in these genes may lead to mitochondrial dysfunction and dysregulation of the antioxidant defense system, thereby increasing the levels of oxidative stress [20,21]. Current studies indicate that PD results from the interaction between environmental and genetic susceptibility factors. Both sporadic and monogenic forms of PD share common pathological, biochemical, and clinical features. Aside from genetic factors, lifestyle may also influence PD risk by altering oxidative balance.

Given the complex interactions and multiple substances involved in the physical oxidant-antioxidant balance, the Oxidative Balance Score (OBS) has been introduced to assess the body's oxidative/antioxidative status, which involves 20 various dietary and lifestyle-related oxidants and antioxidants [22].

To date, no studies have investigated the correlation between OBS and PD. Therefore, this research set out to examine the potential link between OBS and PD among adults in the United States. The study was designed as a cross-sectional analysis utilizing data from the National Health and Nutrition Examination Survey (NHANES). We hypothesized that higher OBS is associated with a reduced risk of developing PD.

Materials and methods

Study population characteristics

NHANES is a population-centric, cross-sectional study funded by the Centers for Disease Control and Prevention (CDC), which collects the health condition data from US adults and children [23]. The survey includes health examinations, laboratory tests, and dietary interviews, aiming to assess and improve the health and nutrition conditions of Americans. Approximately 5,000 adults and children from various US communities participate annually, and a stratified, multistage probability design is used to ensure the samples selected are representative enough to reflect the health and nutrition conditions of the entire US population.

In this study, the data from 6 NHANES survey cycles (2007-2018) were merged, involving 59,842 individuals. Participants under the age of 20 (n=25,072), those with fewer than 16 out of the 20 required items for calculating OBS [24] (n=3,981), and individuals with missing information on covariates (n=2,813) were excluded. As a result, a total of 27,976 eligible adult participants were included in the final analysis (Figure 1).

Oxidative balance score

OBS was computed by integrating 16 dietary elements and 4 lifestyle variables, which together account for 5 oxidants and 15 antioxidants [7]. Dietary intake data were obtained from 24-hour dietary recall interviews in NHANES database, including vitamins B2, B6, B12, niacin, vitamin C, vitamin E, dietary fiber, β-carotene, folate, calcium, magnesium, copper, zinc, selenium, iron, and total fat. Whilst lifestyle factors took into consideration smoking, alcohol consumption, the Body Mass Index (BMI), and Metabolic Equivalent of Task (MET). Serum cotinine levels, obtained from NHANES laboratory tests, were used to assess active and passive tobacco exposure. Physical activity data were derived from questionnaires, calculating MET based on weekly time of vigorous and moderate physical activities, walking, and cycling. All the OBS items, except for alcohol intake were categorized into tertiles. In the calculation of the OBS, antioxidants were rated on a scale of 0 to 2, with the lowest tertile receiving a score of 0, the middle tertile a score of 1, and the highest tertile a score of 2. Conversely, oxidants were scored in an inverted manner, with the highest tertile receiving a score of 0 and the lowest tertile a score of 2. Any missing data points within the OBS, whether they pertained to antioxidants or oxidants, were given a default score of 0. Considering the controversial association between alcohol consumption and PD, and the high prevalence of alcohol abuse in the US population [25], alcohol intake was categorized as <40 g/d, 40-50 g/d, and ≥50 g/d, and assigned scores of 2, 1, and 0, respectively.

Definition and identification of PD

The primary outcome of this study was PD, which was identified through self-reported use of at least one kind of anti-PD medications in the NHANES questionnaires, including benztropine, methyldopa, carbidopa, levodopa, entacapone, amantadine, and ropinirole [26].

Covariates

Information on covariates was derived from demographic data, encompassing basic demographic characteristics such as gender, age, and race, as well as social factors including marital status, education level, and Poverty Income Ratio (PIR).

Statistical analysis

Data from NHANES were analyzed using R 4.2.1 (http://www.r-project.org). Continuous variables were described as mean ± Standard Deviation (SD) or using interquartile range if non-normally distributed, while categorical variables were described as weighted percentages. The χ^2 (chi-square) test was employed to evaluate the statistical significance of variations in categorical variables across different groups. Additionally, a univariate binary logistic regression was performed to investigate the relationship between various variables and the outcome of interest. Subgroup analyses were further conducted, stratifying by gender, age, and ethnicity to delve into these associations. Additionally, based on the quartiles of OBS, the participants were divided into four groups, and four models were constructed to adjust for covariates. Weighted logistic regression and trend tests were employed to verify the linear trend between OBS and PD. Finally, a Restricted Cubic Spline (RCS) method was used to evaluate the potential nonlinear association between

OBS and PD risk. A two-sided *p*-value <0.05 was considered statistically significant.

Results

Baseline characteristics

After collecting data from 59,842 participants, individuals who did not meet the eligibility criteria were excluded, resulting in a final sample of 27,976 adult participants who were included in this study. The table below (Table 1) shows the demographic characteristics. The OBS in the PD group was significantly lower than in the non-PD group (19.01±6.91 vs. 20.52±7.16, *P*=0.017). Regarding demographic characteristics, gender distribution was similar between the PD group and non-PD group (male: 45.69% vs 48.49%, *P*=0.512), while race differed significantly (*P*=0.005). Comparison of the two groups revealed a statistically significant difference in age (*P*<0.001). In terms of social factors, there were also differences between groups in education level (*P*=0.014) and poverty income ratio (*P*=0.034).

OBS and PD risk

The participants were categorized into four distinct groups based on the quartiles of OBS: Q1 (3-14), Q2 (15-20), Q3 (21-25), and Q4 (26-36), whose distribution characteristics were shown in the table below (Table 2). The baseline characteristics, including age, gender, race, marital status, education level, and PIR, differed significantly across these OBS quartiles.

The unadjusted logistic regression revealed that participants in the fourth quartile (Q4) exhibited a reduced likelihood of developing PD when compared to those in the first Quartile (Q1) [OR=0.553, 95% CI (0.314, 0.974), *P*=0.0433]. Each increase in OBS quartile was associated with a 17.7% reduction in PD risk (*P*=0.0024). After being adjusted for gender and age in Mode1, the Q4 group still exhibited a lower risk of PD [OR=0.563, 95% CI (0.332, 0.956), *P*=0.0361], with a decreasing trend in PD risk as OBS increased [OR=0.830, 95% CI (0.712,0.968), *P* =0.0197]. Further adjustments for race and education levels in Model 2 and 3 also showed a decreasing trend in PD risk with higher OBS

(Table 3). However, when the model was adjusted for marriage and poverty income ratio (Model 4), the association lost statistical significance (*P*=0.1047), suggesting that socioeconomic status may substantially influence oxidative balance and its relationship with PD risk.

A dose-response relationship between OBS and PD risk was observed (Figure 2), which was assessed using multivariable-adjusted Restricted Cubic Spline (RCS) regression. The analysis revealed a significant linear negative correlation (P for overall association: 0.017; P for nonlinearity: 0.245).
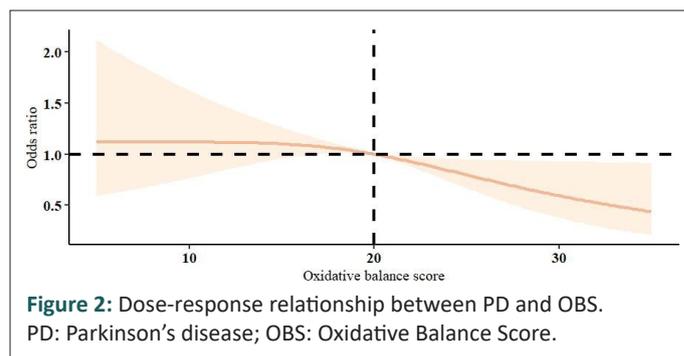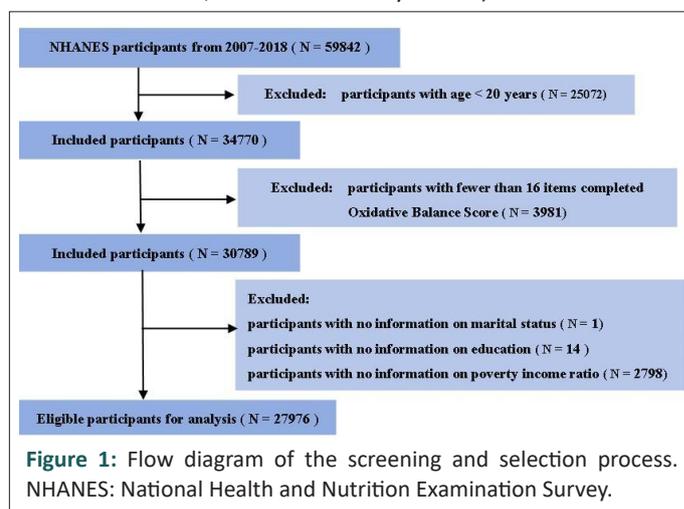

Figure 1: Flow diagram of the screening and selection process. NHANES: National Health and Nutrition Examination Survey.

Figure 2: Dose-response relationship between PD and OBS. PD: Parkinson's disease; OBS: Oxidative Balance Score.

Table 1: Characteristics of participants enrolled in study.

Characteristic	Overall (N=27976)	Non-Parkinson's disease (N=27767)	Parkinson's disease (N=209)	P-value
Age	46.913±0.271			<0.001**
20-39	9430(38.21%)	9410(38.37%)	20(11.97%)	
40-59	9210(36.64%)	9141(36.59%)	69(45.18%)	
≥60	9336(25.15%)	9216(25.04%)	120(42.85%)	
Male	13620(48.47%)	13516(48.49%)	104(45.69%)	0.512
Race				0.005*
Mexican American	4047(8.65%)	4026(8.68%)	21(3.81%)	
Non-Hispanic white	12067(66.69%)	11932(66.60%)	135(80.62%)	
Non-Hispanic black	5929(10.96%)	5899(10.97%)	30(8.91%)	
Other	5933(13.70%)	5910(13.75%)	23(6.66%)	
Education beyond high school	15017(61.95%)	14916(62.01%)	101(51.85%)	0.014*
Marriage				0.312.
Married or living with partner	14307(54.02%)	14192(54.00%)	115(57.42%)	
Never married	5115(19.51%)	5087(19.55%)	28(12.81%)	
Divorced, separated, or widowed	8554(26.47%)	8488(26.45%)	66(29.76%)	
Poverty income ratio	2.9681±0.0371			0.034*
<1.0	6041(15.15%)	5590(15.11%)	51(20.76%)	
1.0-2.9	11544(34.84%)	11443(34.80%)	101(41.87%)	
≥3	10391(50.01%)	10334(50.09%)	57(37.36%)	
OBS	20.507±0.1143	20.52±7.16	19.01±6.91	0.017*

.P<0.5; *P<0.05; **P<0.001. OBS: Oxidative Balance Score.

Table 2: Quartile distribution characteristics of OBS.

Characteristic	Q1(N=7670)	Q2(N=6925)	Q3(N=6152)	Q4(N=7229)	*P*-value
Age					<0.001**
20-39	2494(38.6%)	2183(35.8%)	2135(38.8%)	2618(39.4%)	
40-59	2390(34.8%)	2234(36.2%)	2054(37.0%)	2532(38.2%)	
≥60	2786(26.7%)	2508(27.9%)	1963(24.2%)	2079(22.3%)	
Gender					<0.001**
male	2674(32.9%)	3071(42.4%)	3256(52.2%)	4619(63.5%)	
female	4996(67.1%)	3854(57.6%)	2896(47.8%)	2610(36.5%)	
Race					<0.001**
Mexican American	946(7.9%)	977(8.1%)	968(9.3%)	1156(9.1%)	
Non-Hispanic white	3098(62.5%)	2924(66.1%)	2742(68.3%)	3303(69.3%)	
Non-Hispanic black	2253(17.1%)	1527(11.6%)	1087(8.7%)	1062(7.1%)	
Other	1373(12.5%)	1497(14.1%)	1355(13.6%)	1708(14.5%)	
Education					<0.001**
High school or below	4252(49.8%)	3347(40.6%)	2690(35.5%)	2670(28.2)	
Education beyond high school	3418(50.2%)	3578(59.4%)	3463(64.5%)	4559(71.8%)	
Marriage					<0.001**
Married or living with partner	3292(45.5%)	3486(52.2%)	3363(57.4%)	4167(60.0%)	
Never married	1556(21.5%)	1213(19.3%)	1049(17.6%)	1297(19.5%)	
Divorced, separated, or widowed	2822(33.0%)	2226(28.6%)	1741(25.0%)	1765(20.4%)	
Poverty income ratio					<0.001**
<1.0	2218(22.7%)	1433(14.7%)	1150(12.3%)	1240(11.5%)	
1.0-2.9	3414(40.3%)	2941(36.5%)	2509(34.6%)	2690(29.1%)	
>3	2038(37.0%)	2551(48.8%)	2493(53.0%)	3309(59.4%)	

.*P*<0.5; *P* < 0.05; **P* < 0.001. OBS: Oxidative Balance Score.

Table 3: Odds ratios and quartile trend for associations between OBS and Parkinson's disease (95% CI).

	Q1	Q2	Q3	Q4	OR for trend	P for trend
Un-adjusted	/	0.908(0.571 , 1.443)	0.734(0.432 , 1.248)	0.553(0.314 , 0.974)*	0.823(0.699,0.970)	0.0224 *
Model 1	/	0.878(0.554 , 1.392)	0.740(0.437 , 1.252)	0.563(0.332 , 0.956)*	0.830(0.712,0.968)	0.0197 *
Model 2	/	0.871(0.548 , 1.385)	0.724(0.427 ,1.225)	0.549(0.330 , 0.916)*	0.823(0.709,0.954)	0.0116 *
Model 3	/	0.903(0.566 , 1.441)	0.769(0.462 , 1.280)	0.604(0.345 , 1.058).	0.849(0.724,0.995)	0.0463 *
Model 4	/	0.963(0.610 , 1.520)	0.845(0.511 , 1.396)	0.676(0.393 , 1.160).	0.881(0.758,1.025)	0.1047

Q1 was the reference group.
Model 1 was adjusted for gender, age.
Model 2 was adjusted for gender, age, race.
Model 3 was adjusted for gender, age, race, education.
Model 4 was adjusted for gender, age, race, education, marriage, poverty income ratio.
P<0.5; *P* < 0.05; **P* < 0.001.
OR: Odds ratios; OBS: Oxidative Balance Score; CI: Confidence Interval.

Discussion

This study, aiming to examine the association between OBS and PD, enrolled 27,976 adults from the NHANES dataset. The findings indicated an inverse relationship between OBS and the risk of PD. Additionally, the risk of PD was found to be linked to factors such as age, race, and educational attainment. After adjusting for gender, age, race, and education, the risk of PD was observed to decrease by 15.1% for each ascending quartile of OBS [OR = 0.849, 95% CI (0.724, 0.995), *P*=0.0463].

Several OBS items are related to PD. Among various vitamins, vitamin B12, which is considered a natural Leucine-Rich Repeat Kinase 2 (LRRK2) inhibitor, exhibits the strongest correlation with PD. Mutations in the *LRRK2* gene (such as G2019S mutation) can induce excessive activity of *LRRK2* kinase, which is highly neurotoxic and leads to most autosomal dominant familial PD cases as well as some sporadic cases. Vitamin B12 can protect the nervous system and prevent the onset of PD by modulating *LRRK2* kinase activity [27]. Niacin-derived Nicotinamide Adenine Dinucleotide (NAD+) and NAD participate in dopamine

production. In the rotenone-induced mice model of PD, they increase brain dopamine levels and alter PD pathology through immune modulation and amelioration of oxidative stress [28]. A study showed that a PD patient experienced improvement in symptoms of muscle rigidity and bradykinesia after taking folate [29]. A meta-analysis found that folate and vitamin B12 levels were lower in the PD population [30]. Vitamin B6 has been proven to be associated with inflammation and activation of the Kynurenine Pathway (KP) in PD, and plasma vitamin B6 levels are lower in PD patients compared to the normal population [31]. Another meta-analysis, which included 2,200 individuals with PD, revealed that the most intense levels of total physical activity or moderate to vigorous physical activity were associated with a decreased risk of developing PD, while low level of physical activity did not [32]. However, the roles of smoking and alcohol consumption in the pathogenesis of PD remain controversial. Studies have shown that alcohol drinkers have a lower risk of developing PD [32-34]. While chronic alcohol intake may result in glutamate-induced excitotoxicity, oxidative stress, and irreversible neuronal harm linked to malnutrition, alcohol is paradoxically regarded as a protective element against PD [35]. Smoking has also been shown to have a negative correlation with PD, with some studies suggesting that it may be related to a decreased response to nicotine in the preclinical stages of PD, leading to an increase in smoking cessation [36]. Obesity, on the other hand, has been shown in some studies to be associated with an increased risk of PD. Adipokines secreted by adipose tissue have the potential to enhance systemic inflammation and trigger insulin resistance, which in turn may hasten the advancement of Parkinson's disease [37,38]. A body shape index, which is considered a better indicator of visceral fat content, has been validated to have a non-linear positive correlation with the occurrence of PD [39].

The loss of statistical significance when adjusted for the Poverty Income Ratio (PIR) may be related to the regulation of OBS by socioeconomic status. The family income to poverty ratio is an indicator that reflects the economic status of a household. Due to financial constraints and limited education levels, low-income families often lack nutritional knowledge and place less emphasis on dietary structure, frequently consuming foods with lower nutritional value. Dietary factors constitute a sizable portion of OBS. However, because of limited income, antioxidants (such as vitamin E, vitamin C, and carotenoids), which are primarily derived from fresh fruits, vegetables, and nuts, are typically underrepresented in the diets of low-income families. According to previous studies, levels of vitamin B2, magnesium and OBS increase with a higher PIR, indicating that PIR influences the intake of oxidants and antioxidants [40]. Additionally, low-income families often reside in poorer living conditions, potentially exposed to more air pollutants and environmental stressors, which can increase body oxidative stress levels. Unhealthy lifestyle habits, such as smoking and alcohol consumption, also contribute to elevated oxidative stress levels in low-income households. PIR influences OBS by affecting dietary patterns and lifestyle choices. Lower PIR may place individuals in a continuous state of stress, while chronic stress and emotional disorders can lead to poor physical functions[40]. Poverty also increases anxiety and depression, particularly among females, with OBS showing a significant negative correlation with depression [8]. There is a notable association between low income and chronic diseases. Patients with chronic conditions often face long-term medical expenses, further exacerbating their poverty. Chronic diseases not only increase oxidative stress levels but also disrupt oxidative balance through financial burdens and psychological stress.

This study has several limitations. As the NHANES database is inherently shaped by the US socioeconomic and demographic landscape, extrapolating the results to other populations should be done with caution. Furthermore, the severity of Parkinson's disease in the dataset could not be assessed. Additionally, a substantial number of participants were excluded due to missing questionnaire or laboratory data, an inherent characteristic of NHANES, which may have introduced selection bias.

Conclusion

In conclusion, this nationally representative study of U.S. adults demonstrates a significant negative correlation between OBS and PD risk. Higher OBS is associated with a reduced risk of developing PD. Antioxidative diets and lifestyles may help prevent PD. Therefore, it is crucial to maintain an antioxidant-rich diet pattern, reduce body mass index, and increase high-intensity physical activity, as these measures can help lower the risk of PD. In the future, more experiments and studies should be conducted to further validate the association between OBS and PD, as well as the potential mechanisms.

References

1. Tanner CM, Ostrem JL. Parkinson's disease. N Engl J Med. 2024; 391: 442–452.

2. Tolosa E, Garrido A, Scholz SW, Poewe W. Challenges in the diagnosis of Parkinson's disease. Lancet Neurol. 2021; 20: 385–397.

3. Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, Volkmann J, et al. Parkinson disease. Nat Rev Dis Primers. 2017; 3: 17013.

4. Bäckström D, Granåsen G, Domellöf ME, Linder J, Jakobson Mo S, Riklund K, et al. Early predictors of mortality in parkinsonism and Parkinson disease: a population-based study. Neurology. 2018; 91: e2045–e2056.

5. Okunoye O, Horsfall L, Marston L, Walters K, Schrag A. Mortality of people with Parkinson's disease in a large UK-based cohort study: time trends and relationship to disease duration. Mov Disord. 2021; 36: 2811–2820.

6. Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A. The current and projected economic burden of Parkinson's disease in the United States. Mov Disord. 2013; 28: 311–318.

7. Zhang W, Peng SF, Chen L, Chen HM, Cheng XE, Tang YH. Association between the oxidative balance score and telomere length from the National Health and Nutrition Examination Survey 1999–2002. Oxid Med Cell Longev. 2022; 2022: 1345071.

8. Liu X, Liu X, Wang Y, Zeng B, Zhu B, Dai F. Association between depression and oxidative balance score: National Health and Nutrition Examination Survey 2005–2018. J Affect Disord. 2023; 337: 57–65.

9. Rani V, Deep G, Singh RK, Palle K, Yadav UCS. Oxidative stress and metabolic disorders: pathogenesis and therapeutic strategies. Life Sci. 2016; 148: 183–193.

10. Donia T, Khamis A. Management of oxidative stress and inflammation in cardiovascular diseases: mechanisms and challenges. Environ Sci Pollut Res Int. 2021; 28: 34121–34153.

11. Chikara S, Nagaprashantha LD, Singhal J, Horne D, Awasthi S, Singhal SS. Oxidative stress and dietary phytochemicals: role in cancer chemoprevention and treatment. Cancer Lett. 2018; 413: 122–134.

12. Li W, Guo Y, Zhang C, Wu R, Yang AY, Gaspar J, et al. Dietary phytochemicals and cancer chemoprevention: a perspective on oxidative stress, inflammation, and epigenetics. Chem Res Toxicol. 2016; 29: 2071–2095.

13. Schrag M, Mueller C, Zabel M, Crofton A, Kirsch WM, Ghribi O, et al. Oxidative stress in blood in Alzheimer's disease and mild cognitive impairment: a meta-analysis. Neurobiol Dis. 2013; 59: 100–110.

14. Dionísio PA, Amaral JD, Rodrigues CMP. Oxidative stress and regulated cell death in Parkinson's disease. Ageing Res Rev. 2021; 67: 101263.

15. Chang KH, Chen CM. The role of oxidative stress in Parkinson's disease. Antioxidants (Basel). 2020; 9: 597.

16. Aguirre CA, Concetta Morale M, Peng Q, Sanchez-Alavez M, Cintrón-Colón R, Feng K, et al. Two single nucleotide polymorphisms in IL13 and IL13RA1 from individuals with idiopathic Parkinson's disease increase cellular susceptibility to oxidative stress. Brain Behav Immun. 2020; 88: 920–924.

17. Bhat AH, Dar KB, Anees S, Zargar MA, Masood A, Sofi MA, et al. Oxidative stress, mitochondrial dysfunction and neurodegenerative diseases: a mechanistic insight. Biomed Pharmacother. 2015; 74: 101–110.

18. He J, Zhu G, Wang G, Zhang F. Oxidative stress and neuroinflammation potentiate each other to promote progression of dopamine neurodegeneration. Oxid Med Cell Longev. 2020; 2020: 6137521.

19. Rosner S, Giladi N, Orr-Urtreger A. Advances in the genetics of Parkinson's disease. Acta Pharmacol Sin. 2008; 29: 21–34.

20. Dorszewska J, Kowalska M, Prendecki M, Piekut T, Kozłowska J, Kozubski W. Oxidative stress factors in Parkinson's disease. Neural Regen Res. 2021; 16: 1383–1391.

21. Shen Y, Wu Q, Shi J, Zhou S. Regulation of SIRT3 on mitochondrial functions and oxidative stress in Parkinson's disease. Biomed Pharmacother. 2020; 132: 110928.

22. Hernández-Ruiz Á, García-Villanova B, Guerra-Hernández EJ, Carrión-García CJ, Amiano P, Sánchez MJ, et al. Oxidative balance scores integrating nutrient, food and lifestyle dimensions: development of the NutrientL-OBS and FoodL-OBS. Antioxidants (Basel). 2022; 11: 300.

23. Xu Q, Qian X, Sun F, Liu H, Dou Z, Zhang J. Independent and joint associations of dietary antioxidant intake with risk of post-stroke depression and all-cause mortality. J Affect Disord. 2023; 322: 84–90.

24. Liu F, You F, Yang L, Du X, Li C, Chen G, et al. Nonlinear relationship between oxidative balance score and hyperuricemia: analyses of NHANES 2007–2018. Nutr J. 2024; 23: 48.

25. Kranzler HR. Overview of alcohol use disorder. Am J Psychiatry. 2023; 180: 565–572.

26. Lyra P, Machado V, Proença L, Mendes JJ, Botelho J. Tooth loss and blood pressure in Parkinson's disease patients: an exploratory study on NHANES data. Int J Environ Res Public Health. 2021; 18: 5032.

27. Rekik A, Santoro C, Poplawska-Domaszewicz K, Qamar MA, Batzu L, Landolfo S, et al. Parkinson's disease and vitamins: a focus on vitamin B12. J Neural Transm (Vienna). 2024; 131: 1495–1509.

28. Wuerch E, Urgoiti GR, Yong VW. The promise of niacin in neurology. Neurotherapeutics. 2023; 20: 1037–1054.

29. Alisky JM. Niacin improved rigidity and bradykinesia in a Parkinson's disease patient but also caused unacceptable nightmares and skin rash: a case report. Nutr Neurosci. 2005; 8: 327–329.

30. Dong B, Wu R. Plasma homocysteine, folate and vitamin B12 levels in Parkinson's disease in China: a meta-analysis. Clin Neurol Neurosurg. 2020; 188: 105587.

31. Wilson E, Umans J, Swarovski M, Minhas P, Midttun Ø, Ulvik AA, et al. Parkinson's disease is characterized by vitamin B6-dependent inflammatory kynurenine pathway dysfunction. Res Sq. 2024; rs.3.rs-4980210.

32. Reichmann H, Csoti I, Koschel J, Lorenzl S, Schrader C, Winkler J, et al. Lifestyle and Parkinson's disease. J Neural Transm (Vienna). 2022; 129: 1235–1245.

33. Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. Lancet Neurol. 2016; 15: 1257–1272.

34. Domenighetti C, Sugier PE, Sreelatha AAK, Schulte C, Grover S, Mohamed O, et al. Mendelian randomisation study of smoking, alcohol, and coffee drinking in relation to Parkinson's disease. J Parkinsons Dis. 2022; 12: 267–282.

35. Peng B, Yang Q, Joshi RB, Liu Y, Akbar M, Song BJ, et al. Role of alcohol drinking in Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Int J Mol Sci. 2020; 21: 2316.

36. Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. Lancet Neurol. 2016; 15: 1257–72.

37. Lawton M, Baig F, Toulson G, Morovat A, Evetts SG, Ben-Shlomo Y, et al. Blood biomarkers with Parkinson's disease clusters and prognosis: the Oxford Discovery cohort. Mov Disord. 2020; 35: 279–287.

38. Williams-Gray CH, Wijeyekoon R, Yarnall AJ, Lawson RA, Breen DP, Evans JR, et al. Serum immune markers and disease progression in an incident Parkinson's disease cohort (ICICLE-PD). Mov Disord. 2016; 31: 995–1003.

39. Huang W, Xiao Y, Zhang L, Liu H. Association between a body shape index and Parkinson's disease: a large cross-sectional study from NHANES. Heliyon. 2024; 10: e26557.

40. Fang Y, Dong Z, Huang T, Wang L, Fan W, Wang B, et al. The role of socioeconomic status and oxidative balance score in erectile dysfunction: a cross-sectional study. Heliyon. 2023; 9: e22233.