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Research paper

Exploring the Association of dietary index for gut microbiota with Parkinson's disease and depression: Insights from NHANES

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ABSTRACT

Background: Depression and Parkinson's disease (PD) are important public health issues strongly associated with diet and gut microbiota. The aim of this study was to investigate the association of the dietary index for gut microbiota (DI-GM) with Parkinson's disease and depression.

Methods: This cross-sectional study used data from the National Health and Nutrition Examination Survey (NHANES) database (2007–2020), with a total of 26,473 participants aged 18–80 years, weighted to represent 256 million US adults. Dietary recall data were used to calculate the DI-GM. Weighted logistic regression was used to analyze the relationship between the DI-GM and depression and PD, and to explore the potential mediating role of the DI-GM in depression and PD. Subgroup analyses and restricted cubic spline (RCS) analyses were also performed.

Results: The weighted prevalence of PD combined with depression was approximately 22.99 %. We found a possible inverted U-shaped relationship between DI-GM and depression. Higher DI-GM scores were associated with a lower risk of PD (OR = 0.84, 95 % CI (0.75,0.94)). Mediation modelling indicated no significant role for DI-GM in the relationship between depression and PD. The RCS showed a non-linear association between DI-GM and PD.

Conclusions: A dose-dependent nonlinear association was identified between the DI-GM and PD. Preliminary evidence suggests a potential inverted U-shaped DI-GM-depression relationship requiring validation. This suggests that focusing on DI-GM may be helpful in studying PD and depression.

Research paper

1. Introduction

Parkinson's disease (PD) is the second most prevalent neurodegenerative disease in the world after Alzheimer's disease, with a global prevalence of 1.51 cases per 1000 individuals, reaching 9.34 cases per 1000 individuals over the age of 60 (Ben-Shlomo et al., 2024; Zhu et al., 2024). The potential etiological factors for PD encompass environmental factors (e.g., toxins and infectious microorganisms), lifestyle behaviors (e.g., diet), genetic predisposition, and comorbidities (e.g., diabetes) (Ben-Shlomo et al., 2024). Depression affects approximately 290 million people worldwide, representing the leading global burden of mental illness (Liu et al., 2024). Lifestyle factors, such as diet and smoking, have also been identified as risk factors for depression (Xu et al., 2023). Antidepressant's may increase the risk of PD (Beydoun et al., 2022), and antiparkinsonian medications may also exacerbate depressive symptoms. PD and depression may share certain pathogenetic mechanisms that influence and accelerate disease progression.

The mechanism by which gut microbiota regulates neuropsychiatric disorders through the gut-brain axis has become a research hotspot. Existing evidence indicates that gut microbiota can participate in the pathological processes of depression and PD through neuroendocrine (such as serotonin synthesis), immune regulation (such as inhibition of the IL-6 pathway), and metabolic pathways (such as short-chain fatty acid-mediated changes in blood-brain barrier permeability) (Cryan et al., 2019; Sampson et al., 2016). Notably, diet, as a core environmental factor affecting the structure and function of gut microbiota, may

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indirectly intervene in disease risk by regulating microbiota homeostasis (Garcia-Montero et al., 2021; Valdes et al., 2018). Based on this, Kase et al. (Kase et al., 2024) constructed the Dietary Index of Gut Microbiota (DI-GM), which quantifies the potential impact of dietary patterns on microbiota function by integrating dietary quality scores with microbiota biomarkers (such as the Firmicutes/Bacteroidetes ratio). Its effectiveness has been validated through urinary enterolactone/enteric lactone bioavailability and microbiota diversity. Although gut microbiota dysbiosis has been shown to be associated with common pathological features of depression and PD (such as neuroinflammation and dopamine metabolism disorders) (Qu et al., 2024; Zhang et al., 2024), it is unclear whether DI-GM plays a mediating role in the association between the two; previous studies have focused on the association between diet and a single disease (Kwon et al., 2024), lacking exploration of common mechanisms across diseases. Therefore, this study utilizes data from the National Health and Nutrition Examination Survey (NHANES) to explore the association between DI-GM and PD and depression, and to investigate the potential mediating role of DI-GM in depression and PD.

2. Methods

2.1. Study design and participants

In this cross-sectional study, data from the 2007–2020 NHANES were selected for analysis. The NHANES is produced by the National Center for Health Statistics (NCHS) conducts a nationally representative sample study to assess nutrition and health status in the United States. All subjects participating in the NHANES study were required to sign an informed consent form. The ethical content and data are available for consultation at https://www-cdc-gov-s.libyc.nudt.edu.cn:443/nchs/nhanes/. Exclusion criteria were as follows: age < 18 years, missing medication information, missing DI-GM-related dietary recall data, missing Health Questionnaire-9 (PHQ-9) and missing relevant covariates. The flow chart is shown in Fig. 1.

2.2. Variables

2.2.1. Depression and Parkinson's disease

In this study, the assessment of depressive mood was conducted using the PHQ-9, with a total PHQ-9 score of 9 or greater being indicative of the presence of depression. This definition is frequently employed in epidemiologic studies to identify depression, exhibiting a sensitivity and specificity of 88% (Kroenke et al., 2001). In accordance with the findings of previous studies, patients who self-reported the use of anti-Parkinsonian medications, including Benztropine, Levodopa, Carbidopa, Methyldopa, Ropinirole, Entacapone, and Amantadine, were classified as cases of PD (Lyra et al., 2021).

2.2.2. Di-gm

Kase and colleagues (Kase et al., 2024) selected 14 foods or nutrients from 106 publications to define DI-GM. Among the beneficial components identified were fermented dairy, chickpeas, whole grains, soybeans, fiber, avocados, cranberries, broccoli, coffee, and green tea. Conversely, the unfavorable components included processed meat, red meat, refined grains, and a high-fat diet (≥40 % of energy from fat). The scores for each group were defined as 0–1 based on the median intake, with DI-GM scores ranging from 0 to 13.

2.2.3. Covariates

Covariates were selected from previously explicitly reported factors affecting PD. These factors included demographic information, body mass index (BMI), smoking status, drinking status, hypertension, and diabetes. The demographic information collected included age, sex, race, poverty status, and marital status. The health habits under consideration were smoking and alcohol consumption. The racial categories included non-Hispanic White, Mexican American, non-Hispanic Black, and Other Race. Education was classified into the following categories: less than a high school diploma, high school graduate (including GED), some college or an associate's degree, and college graduate or above. Marital status was classified into the following categories: never married, married (including those who were living with a partner), divorced (including separated), and widowed.

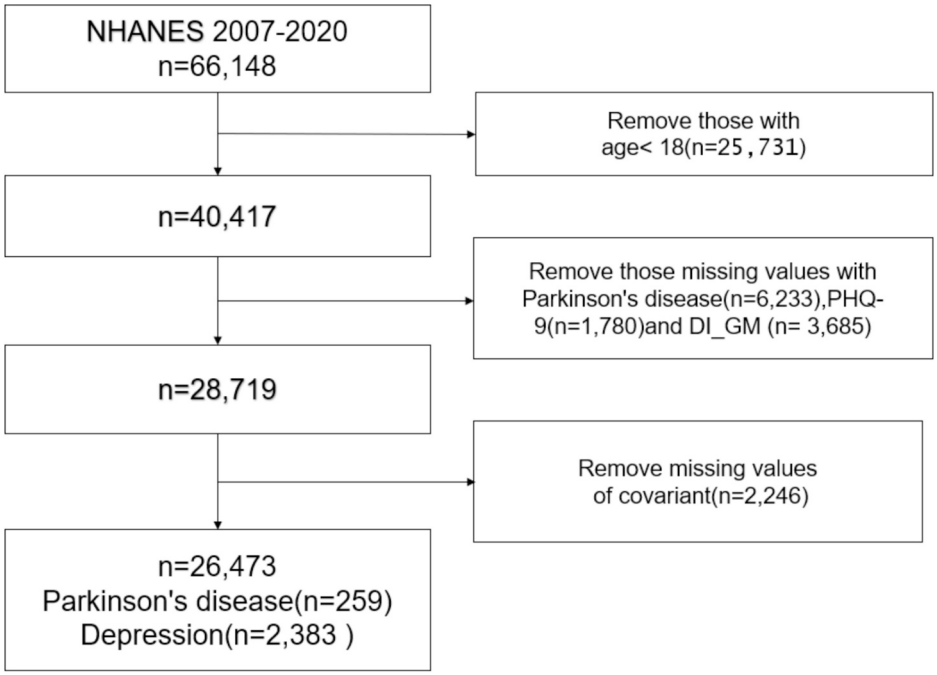

Fig. 1. Flowchart.

2.3. Statistical analysis

To ensure the representativeness of the data set with respect to the US population, the data from the period between 2007 and 2020 were weighted. Descriptive statistics were employed to examine the general characteristics of the U.S. PD and non-PD populations. Categorical variables are expressed as percentages and continuous variables as mean ± standard error (mean ± SE). Weighted Logistic regression models were employed to investigate the interrelationships between depression and DI-GM, PD and DI-GM, and PD and depression. The data were then categorized into quartiles based on the distribution of total DI-GM scores among the population (0–3, 4, 5, and ≥ 6), with the lowest quartile serving as the reference category. The original model was not adjusted for any variables, whereas Model 1 was adjusted for age, gender, and race. Model 2 was adjusted for marital status, educational attainment, and poverty, in accordance with the adjustments made in Model 1. Model 3 adjusted for smoking, alcohol consumption, BMI, hypertension, and diabetes on the basis of Model 2. Subgroup analyses were conducted for age, gender, race, obesity, diabetes, and hypertension groups. Secondly, we also assessed the mediating role of depression in the relationship between DI-GM and PD. Finally, restricted cubic spline (RCS) analysis was conducted on the DI-GM of patients with PD and depression. All data were statistically analyzed using R4.4.1. The Mediation package in R was used for mediation analysis (Wu et al., 2023). A two-sided test was employed, and a *p*-value of <0.05 was deemed statistically significant.

3. Results

3.1. Characteristics of the participant

A total of 26,473 subjects were included in the study, with the data weighted to represent 256 million US adults. The PD and non-PD groups exhibited significant differences in age, DI-GM, gender, race, hypertension, diabetes, alcohol consumption, and depression. No differences were observed in BMI, poverty, marital status, acculturation, or smoking status. A detailed account of the specific results can be found in Table 1.

The relationship between depression and DI-GM, PD and DI-GM, and PD and depression is illustrated in Table 2. In Model 3, the OR was found to be 1.03 (95 % CI: 0.99, 1.06) for DI-GM score and depression. The OR was 1.30 (95 % CI: 1.11, 1.51) for the DI-GM (3,4] group and 1.26 (95 % CI: 1.08, 1.46) for the DI-GM (4,5] group, in comparison to the DI-GM score of [0,3] group. The test for trend was negative (P for trend >0.05). The data suggest the existence of an inverted U-shaped relationship between DI-GM and depression. A positive correlation was observed between higher DI-GM scores and a lower prevalence of PD (OR = 0.84, 95 % CI [0.75, 0.94]). The test for trend yielded a statistically significant result (P for trend <0.01). The odds ratio for depression in PD patients was 3.307 (95 % CI: 2.186, 5.002) compared to non-depressed patients. Furthermore, a non-significant mediating effect of DI-GM between depression and PD was observed ($P > 0.05$).The specific results are shown in Fig. 2. The RCS demonstrated a nonlinear relationship between DI-GM and depression (*P*-value for non-linearity <0.01), as well as DI-GM and PD (P-value for non-linearity <0.01). The specific results are shown in Fig. 3.

The model adjusted for age, sex, race, marital status, education level, poverty, hypertension, diabetes, smoking and drinking status.

3.2. Subgroup analyses

The results of the subgroup analyses are shown in Table 3. Compared with the lowest DI-GM (Q1), the highest DI-GM (Q4) was found in females (0.40, OR; 95 % CI, 0.23,0.69), without Obesity (0.39, OR; 95 % CI, 0.20,0.76), those without diabetes (0.42, OR; 95 % CI, (0.24,0.72) or Hypertension (0.48, OR; 95 % CI, (0.29,0.82)), and those age ≥ 60 years (0.47, OR; 95 % CI,0.26,0.86), Other Race (0.16, OR; 95 % CI, 0.04, 0.59), Non-Hispanic White (0.44, OR; 95 % CI, 0.28,0.70). However, male, Diabetes, Obesity, without Hypertension, Mexican American, Non-Hispanic Black, 40–59 and 18–39 groups had no positive association.

Table 1
Weighted baseline characteristics of patients No-PD or PD.

variable	total	No-PD	PD	*P* value
Age (years)	47.07 ± 0.25	46.96 ± 0.25	57.86 ± 1.32	< 0.0001
BMI (kg/m^2)	29.17 ± 0.08	29.16 ± 0.08	30.30 ± 0.55	0.05
poverty	3.04 ± 0.04	3.04 ± 0.04	2.76 ± 0.15	0.05
DI-GM	4.70 ± 0.02	4.71 ± 0.02	4.32 ± 0.14	0.01
Sex (%)				0.002
Female	50.74	50.62	62.86	
Male	49.26	49.38	37.14	
Eth (%)				< 0.0001
Mexican American	7.95	7.99	3.38	
Non-Hispanic Black	10.59	10.63	6.68	
Non-Hispanic White	69.00	68.87	82.58	
Other Race	12.46	12.51	7.36	
Marital (%)				0.05
Married	63.40	63.39	63.98	
Never married	18.62	18.68	12.29	
Widowed	17.98	17.92	23.73	
Education (%)				0.24
College Graduate or above	30.81	30.88	23.41	
High School Graduate	22.58	22.55	26.23	
less than high school	14.46	14.45	15.05	
Some College or AA degree	32.15	32.12	35.30	
Hypertension (%)				< 0.0001
no	62.66	62.85	43.29	
yes	37.34	37.15	56.71	
Diabetes (%)				0.001
no	85.83	85.92	75.93	
yes	14.17	14.08	24.07	
Smoking (%)				0.76
never	55.52	55.50	57.36	
former	24.95	24.97	22.47	
now	19.54	19.53	20.17	
Drinking (%)				< 0.001
never	10.20	10.17	13.55	
former	12.62	12.53	21.94	
now	77.18	77.3	64.50	
Depression (%)				< 0.0001
no	92.07	92.21	77.01	
Yes	7.93	7.79	22.99	

4. Discussion

The results of this cross-sectional study indicate the potential existence of an inverted U-shaped curve between DI-GM and depression. There is a possibility of a dose-dependent, nonlinear correlation between the DI-GM and PD. The mediating effect of DI-GM between depression and PD was not statistically significant. In this study, the weighted prevalence of PD in conjunction with depression was determined to be 22.99 %.

The modifying effect of diet on the gut microbiota in the context of neurological and psychiatric disorders has been a subject of considerable emphasis in recent research. Plant fiber and dairy products are significant beneficial components of DI-GM, as they positively impact gut microbiota. It has been demonstrated that diets with high fiber content affect biome diversity, while dairy products affect microbial diversity and reduce inflammation levels (Wastyk et al., 2021). Broccoli and whole grains are rich in ferulic acid, and the presence of ferulic esterase in the gut microbiota facilitates the conversion of ferulic acid, which

Table 2
Table Weighted logistic regression analysis between depression and DI-GM, PD and DI-GM, and PD and depression.

	Crude model	Model 1	Model 2	Model 3
Depression				
DI-GM	0.95 (0.92,0.98)	0.94 (0.92,0.97)	1.02 (0.99,1.06)	1.03 (0.99,1.06)
DI-GM [0,3]	ref	ref	ref	ref
DI-GM (3,4]	1.18 (1.01,1.37)	1.17 (1.01,1.36)	1.29 (1.10,1.50)	1.30 (1.11,1.51)
DI-GM (4,5]	1.04 (0.90,1.20)	1.03 (0.89,1.19)	1.24 (1.07,1.44)	1.26 (1.08,1.46)
DI-GM (5,11]	0.83 (0.71,0.98)	0.82 (0.69,0.96)	1.12 (0.94,1.34)	1.15 (0.96,1.37)
P for trend	<0.01	<0.01	0.29	0.18
PD				
DI-GM	0.86 (0.78,0.96)	0.82 (0.74,0.91)	0.84 (0.75,0.94)	0.84 (0.75,0.94)
DI-GM [0,3]	ref	ref	ref	ref
DI-GM (3,4]	0.58 (0.37,0.91)	0.57 (0.36,0.89)	0.59 (0.37,0.94)	0.59 (0.37,0.94)
DI-GM (4,5]	0.42 (0.26,0.68)	0.37 (0.23,0.60)	0.39 (0.24,0.64)	0.39 (0.24,0.64)
DI-GM (5,11]	0.54 (0.37,0.79)	0.43 (0.29,0.63)	0.48 (0.32,0.73)	0.49 (0.32,0.74)
P for trend	<0.01	<0.01	<0.01	<0.01
PD				
No-depression	ref	ref	ref	ref
Depression	3.54 (2.46,5.08)	3.76 (2.60,5.44)	3.35 (2.23,5.04)	3.31 (2.19,5.00)
P	<0.01	<0.01	<0.01	<0.01

Model 1: adjusted for age, sex and race;
Model 2: adjusted for age, sex, race, marital status, poverty, educational level;
Model 3: further adjusted for drinking, smoking status, hypertension, diabetes based on Model 2.

counteracts oxidative stress and reduces the production of free radicals in brain cells, thereby affecting PD (Kunnummal and Khan, 2024). Coffee has been demonstrated to improve gut microbial dysbiosis and confer neuroprotective benefits in individuals with PD (Liu et al., 2022). Green tea is a rich source of catechin, particularly the beneficial compound Eigallocatechin-3-gallate (EGCG), which has been linked to neuroprotective effects in patients with PD. The gut microbiota-TotM pathway has been linked to EGCG-mediated neuroprotection (Xu et al., 2020). A diet high in fat has been demonstrated to disrupt the equilibrium of gut microbiota and affect gut microbial diversity, which in turn leads to inflammation and immune dysfunction, and thus may contribute to the development of PD (Neufeld et al., 2024). It has been demonstrated that individuals diagnosed with PD and those in the general population exhibit differences in their dietary habits, particularly in their consumption of red meat and cereal products. Additionally, the relative abundance of specific bacterial species, namely Streptococcus spp. and Lactobacillus spp., in the oral cavity is higher in individuals with PD compared to healthy controls (Zapala et al., 2022).

A growing body of research has demonstrated an imbalance in the gut microbiota of patients diagnosed with PD (Zhang et al., 2023; Vascellari et al., 2020). A reduction in the number of short-chain fatty acid (SCFA)-producing bacteria has been observed in individuals with PD, which may affect the levels of several metabolites with potential protective effects (Vascellari et al., 2020). Elevated levels of Bifidobacterium have been demonstrated to confer protection against PD, while LachnospiraceaeUCG010, RuminococcaceaeUCG002, Clostridium sensustricto1, *Eubacterium hallii* group, and Bacillales have been identified as PD-protective factors (Jiang et al., 2023). Conversely, Bacillales have been identified as risk factors for PD. Dietary habits exert a significant influence on the diversity of the gut microbiota. A higher prevalence of *Parabacteroides goldsteinii* has been associated with a reduced risk of developing PD (Zeng et al., 2024). This suggests that dietary intervention may be an effective strategy for managing PD. DI-GM is correlated with markers of gut microbiota diversity and may be associated with an imbalance of gut microbiota (Kase et al., 2024). An imbalance in the gut microbiota may affect PD through the microbiota-gut-brain axis (Zhang et al., 2023). Moreover, an imbalance in the gut microbiota may also exert an influence on PD through the mediation of inflammatory factors (Franceschi et al., 2018; Zhang et al., 2023). Our research found that there is a curvilinear relationship between DI-GM and PD, with the lowest risk of PD at DI-GM = 5.93, indicating a possible dose-response relationship. Low dose Maslinic acid (MA) is beneficial for the growth of probiotics in PD mice, thereby increasing the levels of serotonin and gamma aminobutyric acid in the striatum; Although high-dose MA does not affect the composition of gut microbiota in PD mice, it significantly inhibits neuroinflammation. Different doses of MA protect PD through different mechanisms (Cao et al., 2023). Low dose microbial lipolysis (LPS), rather than high dose, altered measurements related to the intensity, distribution, and localization of alpha synuclein, which may have a dose-dependent effect on alpha synuclein the intestinal epithelium of Parkinson's disease (Gorecki et al.,

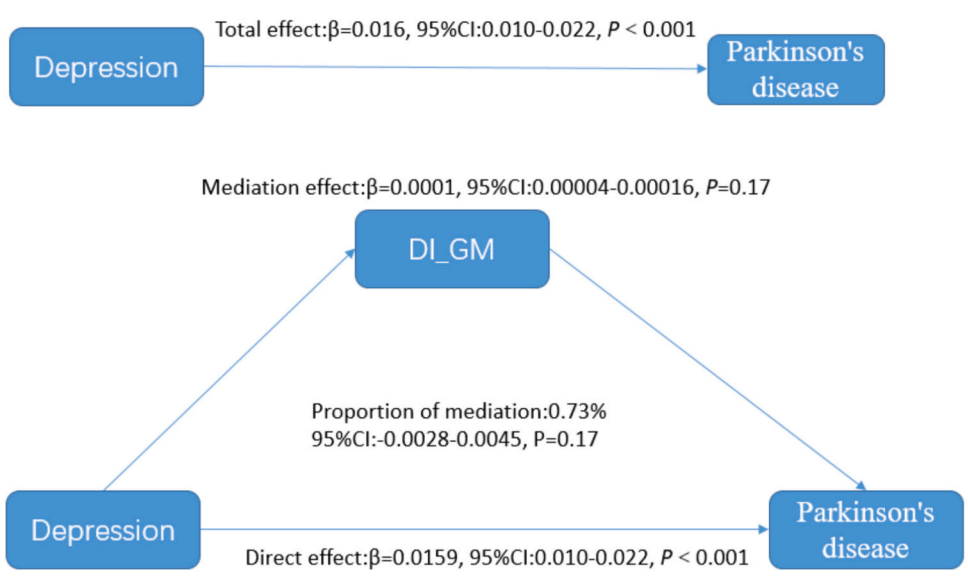

Fig. 2. Mediation analysis of the DI-GM on the risk of depression and PD.

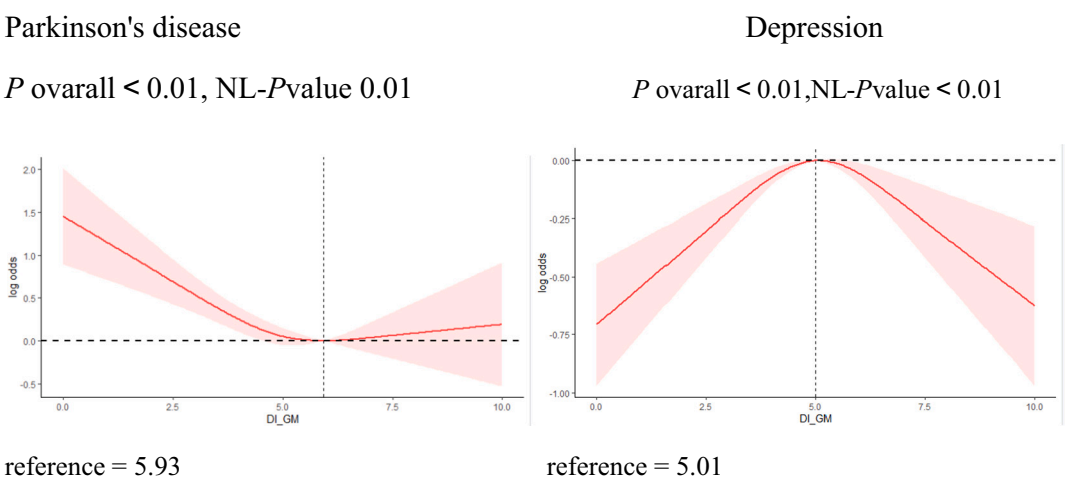

Fig. 3. Association between DI-GM and PD or depression by RCS.

Table 3
Subgroup analysis of PD stratified by sex, obesity, eth, age, diabetes, and hypertension.

character	Q1 [0,3]	Q2 (3,4]	Q3 (4,5]	Q4 (5,11]	*P* for trend	*P* for interaction
Sex						0.48
Female	ref	0.49(0.26,0.93)	0.30(0.15,0.62)	0.40(0.23,0.69)	0.01	
Male	ref	0.83(0.39,1.76)	0.62(0.31,1.23)	0.71(0.31,1.63)	0.35	
Diabetes						0.47
No	ref	0.64(0.37,1.13)	0.37(0.20,0.69)	0.42(0.24,0.72)	0.01	
Yes	ref	0.38(0.15, 0.93)	0.45(0.21, 0.99)	0.76(0.35, 1.63)	0.5	
Obesity						0.71
Yes	ref	0.72(0.36,1.45)	0.37(0.17,0.81)	0.62(0.35,1.10)	0.05	
No	ref	0.48(0.24,0.97)	0.38(0.20,0.75)	0.39(0.20,0.76)	0.01	
Hypertension						0.85
Yes	ref	0.67(0.34,1.29)	0.37(0.20,0.72)	0.48(0.29,0.82)	0.03	
No	ref	0.49(0.23,1.04)	0.41(0.18,0.95)	0.48(0.23,1.03)	0.09	
Eth						0.01
Other Race	ref	1.86(0.52, 6.66)	1.10(0.33, 3.70)	0.16(0.04, 0.59)	0.01	
Non-Hispanic White	ref	0.51(0.29,0.87)	0.35(0.20,0.60)	0.44(0.28,0.70)	0.01	
Mexican American	ref	0.22(0.05, 0.98)	0.17(0.05, 0.55)	0.83(0.26, 2.67)	0.78	
Non-Hispanic Black	ref	1.02(0.42, 2.50)	0.69(0.21, 2.21)	1.59(0.57, 4.44)	0.56	
Age						0.92
≥60	ref	0.44(0.22,0.86)	0.44(0.25,0.79)	0.47(0.26,0.86)	0.03	
40–59	ref	0.72(0.35,1.46)	0.35(0.15,0.83)	0.49(0.21,1.14)	0.06	
18–39	ref	0.73(0.22, 2.44)	0.39(0.08, 1.91)	0.48(0.12, 1.92)	0.22	

Obesity: BMI ≥ 30. Adjusted for age, sex, race, marital status, education level, poverty, hypertension, diabetes, smoking and drinking status except the stratification factor itself.

2025). The nonlinear relationship between DI-GM and PD may be dependent on the dose.

Depression is a common non-motor symptom of PD. The weighted prevalence of PD in conjunction with depression was approximately 22.99 %, a figure that is broadly consistent with the prevalence estimates derived from epidemiologic studies (Goodarzi et al., 2016). The relationship between depression and PD is complex. While depression increases the risk of PD (hazard ratio (HR) = 1.75), PD increases the risk of depression more significantly (HR = 4.35) (Xiang et al., 2025). PD may directly disrupt the emotion regulation network via dopaminergic system dysfunction, extensive neurodegeneration and drug side effects (e.g. long-term levodopa use) (Becker et al., 2011). The promotion of PD by depression may be achieved via neuroinflammation and chronic stress pathways and requires a longer cumulative effect (Jankovic and Tan, 2020; Anderson and Maes, 2014). PD motor symptoms (such as bradykinesia) can lead to social isolation (Terracciano et al., 2023), while abnormalities in 5-HT binding in the basal ganglia (Tan et al., 2011) and certain medications (such as pramipexole) may exacerbate the risk of depression synergistically. Overall, the relationship between the two conditions may be driven by bidirectional interactions or shared pathological mechanisms.

Depression and PD have similar pathogenesis characteristics, depression may be a precursor symptom of PD, and PD is often combined with depression (Zhang et al., 2024). Depression and PD have a shared pathogenesis, with alterations in the gut microbiota interacting with the nervous, immune, and endocrine systems. A reduction in the levels of Faecalibacteria and Prevotella has been observed in individuals with both PD and depression (Zhang et al., 2024). The gut microbiome and its metabolites have the potential to modulate levels of pentraxin, dopamine, and brain-derived neurotrophic factor, increase intestinal permeability, and promote the secretion of inflammatory cytokines such as TNF-alpha and IL-6. This, in turn, affects the brain in the presence of depression (Pizzagalli and Roberts, 2022). The gut microbiota has been demonstrated to enhance the pro-inflammatory stimulatory effects of α-synuclein through multiple pathways, thereby promoting the secretion of pro-inflammatory factors by microglia and ultimately leading to the death of dopamine neurons and the acceleration of PD progression (Qin et al., 2016). It is imperative that potential protective interventions for PD and depression be investigated. The correlation between DI-GM and markers of gut microbiota diversity may provide insights into the

potential role of DI-GM in future studies of PD and depression. In order to investigate the potential mediating role of DI-GM in the relationship between depression and PD, we employed a mediator model. It is regrettable that our findings did not support the hypothesis that DI-GM plays a mediating role.

This study has endeavored to explore the role of the DI-GM in depression and Parkinson's disease. The present study has several notable strengths. Firstly, the results are representative of the population under study, based on data from the NHANES. Moreover, sensitivity analyses were performed to enhance the robustness of the findings. However, there are some limitations to our study. The diagnosis of PD was based on self-reported prescription drug use, a criterion that has been employed similarly in other studies (Lyra et al., 2021). However, this differs somewhat from the clinical diagnosis made by healthcare professionals. Further validation is needed in future clinical samples. A score of 10 or above on the Patient Health Questionnaire-9 (PHQ-9) is a common criterion for diagnosing depression in epidemiological studies (Zhu et al., 2023), although this method differs somewhat from the gold standard for diagnosing depression. In conclusion, cross-sectional studies are unable to establish causal relationships, and further validation in prospective cohorts is required in the future.

5. Conclusion

The present study analyzed representative data from the United States in order to ascertain the relationship between DI-GM and PD. The analysis revealed a U-shaped curve relationship, which may be dose-dependent. The presence of an inverted U-shaped curve between DI-GM and depression is a possibility, while DI-GM does not demonstrate a significant mediating effect between depression and PD. The findings of this study may provide valuable dietary recommendations for the prevention and treatment of PD and depression.

CRediT authorship contribution statement

Yanping Shu: Writing – original draft, Methodology, Data curation. **Wei Hong:** Writing – original draft, Methodology, Data curation. **Jiaoying Liu:** Writing – original draft. **Xianlin Zhu:** Writing – review & editing, Supervision, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare no conflicts of interest.

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Data availability

The dataset generated during and analyzed during the current study are available from the corresponding author on reasonable request.

References

Anderson, G., Maes, M., 2014. Neurodegeneration in Parkinson's disease: interactions of oxidative stress, tryptophan catabolites and depression with mitochondria and sirtuins. Mol. Neurobiol. 49, 771–783. https://doi.org/10.1007/s12035-013-8554-z.

Becker, C., Brobert, G.P., Johansson, S., Jick, S.S., Meier, C.R., 2011. Risk of incident depression in patients with Parkinson disease in the UK. Eur. J. Neurol. 18, 448–453. https://doi.org/10.1111/j.1468-1331.2010.03176.x.

Ben-Shlomo, Y., Darweesh, S., Llibre-Guerra, J., Marras, C., San, L.M., Tanner, C., 2024. The epidemiology of Parkinson's disease. Lancet 403, 283–292. https://doi.org/10.1016/S0140-6736(23)01419-8.

Beydoun, H.A., Saquib, N., Wallace, R.B., Chen, J.C., Coday, M., Naughton, M.J., Beydoun, M.A., Shadyab, A.H., Zonderman, A.B., Brunner, R.L., 2022. Psychotropic medication use and Parkinson's disease risk amongst older women. Ann. Clin. Transl. Neurol. 9, 1163–1176. https://doi.org/10.1002/acn3.51614.

Cao, X., Du, Z.R., Liu, X., Wang, X., Li, C., Zhou, S.N., Liu, J.R., Xu, P.Y., Ye, J.L., Zhao, Q., Zhao, F., Wong, K.H., Dong, X.L., 2023. Low and high doses of oral maslinic acid protect against Parkinson's disease via distinct gut microbiota-related mechanisms. Biomed. Pharmacother. 165, 115100. https://doi.org/10.1016/j.biopha.2023.115100.

Cryan, J.F., O'Riordan, K.J., Cowan, C., Sandhu, K.V., Bastiaanssen, T., Boehme, M., Codagnone, M.G., Cussotto, S., Fulling, C., Golubeva, A.V., Guzzetta, K.E., Jaggar, M., Long-Smith, C.M., Lyte, J.M., Martin, J.A., Molinero-Perez, A., Moloney, G., Morelli, E., Morillas, E., O'Connor, R., Cruz-Pereira, J.S., Peterson, V.L., Rea, K., Ritz, N.L., Sherwin, E., Spichak, S., Teichman, E.M., van de Wouw, M., Ventura-Silva, A.P., Wallace-Fitzsimons, S.E., Hyland, N., Clarke, G., Dinan, T.G., 2019. The microbiota-gut-brain Axis. Physiol. Rev. 99, 1877–2013. https://doi.org/10.1152/physrev.00018.2018.

Franceschi, C., Garagnani, P., Parini, P., Giuliani, C., Santoro, A., 2018. Inflammaging: a new immune-metabolic viewpoint for age-related diseases. Nat. Rev. Endocrinol. 14, 576–590. https://doi.org/10.1038/s41574-018-0059-4.

Garcia-Montero, C., Fraile-Martinez, O., Gomez-Lahoz, A.M., Pekarek, L., Castellanos, A.J., Noguerales-Fraguas, F., Coca, S., Guijarro, L.G., Garcia-Honduvilla, N., Asunsolo, A., Sanchez-Trujillo, L., Lahera, G., Bujan, J., Monserrat, J., Alvarez-Mon, M., Alvarez-Mon, M.A., Ortega, M.A., 2021. Nutritional components in western diet versus mediterranean diet at the gut microbiota-immune system interplay. Implications for health and disease. Nutrients 13. https://doi.org/10.3390/nu13020699.

Goodarzi, Z., Mrklas, K.J., Roberts, D.J., Jette, N., Pringsheim, T., Holroyd-Leduc, J., 2016. Detecting depression in Parkinson disease: a systematic review and meta-analysis. Neurology 87, 426–437. https://doi.org/10.1212/WNL.0000000000002898.

Gorecki, A.M., Anyaegbu, C.C., Fitzgerald, M., Fuller, K.A., Anderton, R.S., 2025. Imaging flow cytometry reveals LPS-induced changes to intracellular intensity and distribution of alpha-synuclein in a TLR4-dependent manner in STC-1 cells. Methods 234, 93–111. https://doi.org/10.1016/j.ymeth.2024.10.009.

Jankovic, J., Tan, E.K., 2020. Parkinson's disease: etiopathogenesis and treatment. J. Neurol. Neurosurg. Psychiatry 91, 795–808. https://doi.org/10.1136/jnnp-2019-322338.

Jiang, L., Li, J.C., Tang, B.S., Guo, J.F., 2023. Associations between gut microbiota and Parkinson disease: a bidirectional Mendelian randomization analysis. Eur. J. Neurol. 30, 3471–3477. https://doi.org/10.1111/ene.15848.

Kase, B.E., Liese, A.D., Zhang, J., Murphy, E.A., Zhao, L., Steck, S.E., 2024. The development and evaluation of a literature-based dietary index for gut microbiota. Nutrients 16. https://doi.org/10.3390/nu16071045.

Kroenke, K., Spitzer, R.L., Williams, J.B., 2001. The PHQ-9: validity of a brief depression severity measure. J. Gen. Intern. Med. 16, 606–613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x.

Kunnummal, S.P., Khan, M., 2024. Diet-gut microbiome interaction and ferulic acid bioavailability: implications on neurodegenerative disorders. Eur. J. Nutr. 63, 51–66. https://doi.org/10.1007/s00394-023-03247-0.

Kwon, D., Zhang, K., Paul, K.C., Folle, A.D., Del, R.I., Jacobs, J.P., Keener, A.M., Bronstein, J.M., Ritz, B., 2024. Diet and the gut microbiome in patients with Parkinson's disease. NPJ Parkinsons Dis. 10, 89. https://doi.org/10.1038/s41531-024-00681-7.

Liu, J., Zhang, Y., Ye, T., Yu, Q., Yu, J., Yuan, S., Gao, X., Wan, X., Zhang, R., Han, W., Zhang, Y., 2022. Effect of coffee against MPTP-induced motor deficits and neurodegeneration in mice via regulating gut microbiota. J. Agric. Food Chem. 70, 184–195. https://doi.org/10.1021/acs.jafc.1c06998.

Liu, J., Liu, Y., Ma, W., Tong, Y., Zheng, J., 2024. Temporal and spatial trend analysis of all-cause depression burden based on global burden of disease (GBD) 2019 study. Sci. Rep. 14, 12346. https://doi.org/10.1038/s41598-024-62381-9.

Lyra, P., Machado, V., Proenca, L., Mendes, J.J., Botelho, J., 2021. Tooth loss and blood pressure in Parkinson's disease patients: an exploratory study on NHANES data. Int. J. Environ. Res. Public Health 18. https://doi.org/10.3390/ijerph18095032.

Neufeld, P.M., Nettersheim, R.A., Matschke, V., Vorgerd, M., Stahlke, S., Theiss, C., 2024. Unraveling the gut-brain axis: the impact of steroid hormones and nutrition on Parkinson's disease. Neural Regen. Res. 19, 2219–2228. https://doi.org/10.4103/1673-5374.391304.

Pizzagalli, D.A., Roberts, A.C., 2022. Prefrontal cortex and depression. Neuropsychopharmacology 47, 225–246.

Qin, X.Y., Zhang, S.P., Cao, C., Loh, Y.P., Cheng, Y., 2016. Aberrations in peripheral inflammatory cytokine levels in Parkinson disease: a systematic review and Meta-analysis. JAMA Neurol. 73, 1316–1324. https://doi.org/10.1001/jamaneurol.2016.2742.

Qu, S., Yu, Z., Zhou, Y., Wang, S., Jia, M., Chen, T., Zhang, X., 2024. Gut microbiota modulates neurotransmitter and gut-brain signaling. Microbiol. Res. 287, 127858. https://doi.org/10.1016/j.micres.2024.127858.

Sampson, T.R., Debelius, J.W., Thron, T., Janssen, S., Shastri, G.G., Ilhan, Z.E., Challis, C., Schretter, C.E., Rocha, S., Gradinaru, V., Chesselet, M.F., Keshavarzian, A., Shannon, K.M., Krajmalnik-Brown, R., Wittung-Stafshede, P., Knight, R., Mazmanian, S.K., 2016. Gut microbiota regulate motor deficits and Neuroinflammation in a model of Parkinson's disease. Cell 167, 1469–1480. https://doi.org/10.1016/j.cell.2016.11.018.

Tan, S.K., Hartung, H., Sharp, T., Temel, Y., 2011. Serotonin-dependent depression in Parkinson's disease: a role for the subthalamic nucleus? Neuropharmacology 61, 387–399. https://doi.org/10.1016/j.neuropharm.2011.01.006.

Terracciano, A., Luchetti, M., Karakose, S., Stephan, Y., Sutin, A.R., 2023. Loneliness and risk of Parkinson disease. JAMA Neurol. 80, 1138–1144. https://doi.org/10.1001/jamaneurol.2023.3382.

Valdes, A.M., Walter, J., Segal, E., Spector, T.D., 2018. Role of the gut microbiota in nutrition and health. BMJ 361, k2179. https://doi.org/10.1136/bmj.k2179.

Vascellari, S., Palmas, V., Melis, M., Pisanu, S., Cusano, R., Uva, P., Perra, D., Madau, V., Sarchioto, M., Oppo, V., Simola, N., Morelli, M., Santoru, M.L., Atzori, L., Melis, M., Cossu, G., Manzin, A., 2020. Gut microbiota and metabolome alterations associated with Parkinson's disease. Msystems 5. https://doi.org/10.1128/mSystems.00561-20.

Wastyk, H.C., Fragiadakis, G.K., Perelman, D., Dahan, D., Merrill, B.D., Yu, F.B., Topf, M., Gonzalez, C.G., Van Treuren, W., Han, S., Robinson, J.L., Elias, J.E., Sonnenburg, E.D., Gardner, C.D., Sonnenburg, J.L., 2021. Gut-microbiota-targeted diets modulate human immune status. Cell 184, 4137–4153. https://doi.org/10.1016/j.cell.2021.06.019.

Wu, Y., Tan, Z., Zhen, J., Liu, C., Zhang, J., Liao, F., Dong, W., 2023. Association between diet soft drink consumption and metabolic dysfunction-associated steatotic liver disease: findings from the NHANES. BMC Public Health 23, 2286. https://doi.org/10.1186/s12889-023-17223-0.

Xiang, L., Xu, R., Zhou, X., Ren, X., Li, Z., Wu, I., 2025. Associations between major depressive disorders and Parkinson's disease and impact of their comorbidity sequence. J. Affect. Disord. 379, 639–646. https://doi.org/10.1016/j.jad.2025.03.065.

Xu, M., Yin, X., Gong, Y., 2023. Lifestyle factors in the Association of Shift Work and Depression and anxiety. JAMA Netw. Open 6, e2328798. https://doi.org/10.1001/jamanetworkopen.2023.28798.

Xu, Y., Xie, M., Xue, J., Xiang, L., Li, Y., Xiao, J., Xiao, G., Wang, H.L., 2020. EGCG ameliorates neuronal and behavioral defects by remodeling gut microbiota and TotM expression in Drosophila models of Parkinson's disease. FASEB J. 34, 5931–5950. https://doi.org/10.1096/fj.201903125RR.

Zapala, B., Stefura, T., Milewicz, T., Wator, J., Piwowar, M., Wojcik-Pedziwiatr, M., Doregowska, M., Dudek, A., Jania, Z., Rudzinska-Bar, M., 2022. The role of the Western diet and Oral microbiota in Parkinson's disease. Nutrients 14. https://doi.org/10.3390/nu14020355.

Zeng, S., Yusufujiang, A., Zhang, C., Yang, C., Li, H., 2024. Correlation between dietary factors and Parkinson's disease revealed by the analysis of Mendelian randomization. Front. Nutr. 11, 1273874. https://doi.org/10.3389/fnut.2024.1273874.

Zhang, P., Jin, W., Lyu, Z., Lyu, X., Li, L., 2024. Study on the mechanism of gut microbiota in the pathogenetic interaction between depression and Parkinson 's disease. Brain Res. Bull. 215, 111001. https://doi.org/10.1016/j.brainresbull.2024.111001.

Zhang, X., Tang, B., Guo, J., 2023. Parkinson's disease and gut microbiota: from clinical to mechanistic and therapeutic studies. Transl. Neurodegener. 12, 59. https://doi.org/10.1186/s40035-023-00392-8.

Zhu, J., Cui, Y., Zhang, J., Yan, R., Su, D., Zhao, D., Wang, A., Feng, T., 2024. Temporal trends in the prevalence of Parkinson's disease from 1980 to 2023: a systematic review and meta-analysis. Lancet Healthy Longev 5, e464–e479. https://doi.org/10.1016/S2666-7568(24)00094-1.

Zhu, X., Zhao, Y., Li, L., Liu, J., Huang, Q., Wang, S., Shu, Y., 2023. Association of non-HDL-C and depression: a cross-sectional analysis of the NHANES data. Front. Psychol. 14, 1274648. https://doi.org/10.3389/fpsyt.2023.1274648.