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Association between added sugars intake and Parkinson's disease status in U.S. adults: a cross-sectional study from NHANES 1990–2020

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Abstract

Background Added sugars intake is common among individuals with Parkinson's disease (PD), yet the link between added sugars intake and PD is not well understood. Our study aims to investigate the association between added sugars intake and PD.

Methods This study utilized data from the National Health and Nutrition Examination Survey (NHANES) from1990 to 2020. Added sugars intake was estimated based on a 24-hour dietary recall from participants. Multivariable logistic regression analysis was employed to explore the relationship between added sugars intake and the prevalence of PD. Restricted cubic spline (RCS) was used to explore the nonlinear association between added sugars intake and PD. To further observe whether the conclusions were consistent across different subgroups, we conducted subgroup analyses to investigate the association of added sugars intake with PD in different populations.

Results The study included 12,489 participants, of which 100 had PD. When weighted, the data represented 136,959,144 participants. The study revealed a positive association between added sugars intake and the prevalence of PD. In multivariable regression models adjusted for all confounding factors, compared with the lowest quartile of added sugars intake, the third quartile (OR = 2.99; 95% CI: 1.43–6.26) and those consuming more than 25% of their calories from added sugars (OR = 3.34; 95% CI: 1.03–10.86) had the highest risk of PD. The RCS curve showed an L-shaped nonlinear association between added sugars intake and PD. Two-segment linear regression by sex revealed that PD prevalence in women was linearly related to sugar intake (nonlinear $P = 0.465$), while men exhibited an L-shaped nonlinear relationship (nonlinear $P = 0.03$). Additionally, subgroup analysis showed that alcohol consumption and diabetes significantly influenced the association between added sugars intake and the prevalence of PD.

Conclusion These results highlight a positive association between added sugars intake and the prevalence of PD, particularly among women, heavy drinkers, and individuals with diabetes.

Keywords Added sugars, Parkinson's Disease, NHANES, Dietary intake, Public Health

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Text box 1. Contributions to the literature

- This study underscores the potential influence of dietary factors on the progression of Parkinson's disease, focusing on non-genetic risk factors in a largely underexplored area.
- We highlight a positive association between added sugar intake and the prevalence of Parkinson's disease, suggesting that dietary modifications may serve as a preventive strategy in public health initiatives aimed at reducing the risk of this condition.
- Public health policies can be customized for diverse populations, particularly targeting women, heavy drinkers, and individuals with diabetes, to implement effective added sugar restriction measures.

Introduction

Parkinson's disease (PD) is a rapidly progressing neurodegenerative disorder [1] that has become a significant global public health concern. In Europe, the prevalence and incidence rates of PD are approximately 108–257 per 100,000 and 11–19 per 100,000 per year, respectively [2]. The global incidence of PD is rising, being more common in older adults and men. The increase in prevalence has exceeded changes in population demographics, placing substantial pressure on healthcare systems [3]. Parkinson's is a heterogeneous disease in its clinical presentation, pathology, and genetics, with its etiological mechanisms remaining unclear [4]. In most cases, non-genetic factors play a significant role. The heterogeneity of Parkinson's begins in the prodromal phase. Although the long prodromal period complicates causal interpretations, some epidemiological studies have identified non-genetic risk factors such as dairy consumption, smoking, caffeine intake, and physical activity (PA) as potential influences on the development of PD [3].

Common dietary sugars, in addition to naturally occurring sugars, include added sugars, free sugars, and sweeteners. Added sugars are those introduced during food processing or preparation, while free sugars encompass both added sugars and sugars naturally found in honey, syrups, and fruit juices [5]. Sweeteners, on the other hand, are sugar substitutes used to provide sweetness without the caloric content, and they can be either artificial or natural [6]. Generally, sugar-sweetened beverages are the most common and largest source of added sugars, and their consumption is steadily increasing in many developing countries [7], which has led to poor health outcomes [8]. It is worth noting that recent large-scale prospective cohort studies have supported the association between added sugars intake and various adverse health outcomes, including the induction of cardiovascular diseases [9], a reduction in handgrip strength [10] and weight gain [11]. Meanwhile, added sugars is common among PD patients, and increased sugar consumption is associated with an increase in non-motor symptoms, including reduced quality of life, increased severity of constipation, and a higher daily requirement for levodopa [12]. However, clinical evidence directly revealing the relationship between added sugars and PD is limited. The latest guidelines from the World Health Organization recommend avoiding the use of non-sugar sweeteners (low-calorie and no-calorie sweeteners) for weight control [11]. Before detailed sugar restriction policies can be formulated, it is necessary to comprehensively evaluate the quality of existing evidence on the association between dietary sugar intake and all health outcomes.

Currently, no treatment can halt the progression of PD [13], underscoring the need for further research into non-genetic factors and the identification of risk or protective factors. In-depth research elucidating the relationship between added sugars intake and PD incidence can help clarify the impact of added sugars on public health, thereby informing the development of appropriate preventive strategies.

Materials and methods

Study participants

The National Health and Nutrition Examination Survey (NHANES) is a series of cross-sectional surveys designed to assess the health status of the entire U.S. population. The study protocol was approved by the NCHS Research Ethics Review Board, and all participants provided written informed consent. We included 10 cycles of NHANES data from 1990 to 2020, with a total of 116,752 participants with information on PD, and 24,045 participants with information on added sugars intake. PD was defined as detailed in the section 'Assessment of Parkinson '. After excluding individuals under 18 years old, those lacking Parkinson's information, and those without added sugar data, covariates were separately extracted for analysis, allowing us to obtain data from 62,524 to 116,876 participants. After merging all variables, 116,876 participants were included. Further exclusions of 104,387 participants with missing covariate data resulted in a final inclusion of 12,489 participants, among which 100 had Parkinson's disease and 12,389 did not. After weighting, these participants represented 136,959,144 individuals (Fig. 1). The main outcome and exposure assessment result is whether participants have PD.

Assessment of added sugars intakes

The primary exposure factor is added sugar, which refers to caloric sweeteners added to foods during preparation, processing, or at the table as ingredients, excluding naturally occurring sugars. In NHANES, added sugars include brown sugar, cane syrup, corn syrup, corn syrup solids, dextrose, fructose, fruit syrup, honey, maple syrup, molasses, pancake syrup, raw sugar, sorghum syrup, and white sugar [14]. All NHANES participants were eligible for two 24-hour dietary recall interviews, which were used to estimate added sugars intake. The average of the two interviews was then used for data analysis. The

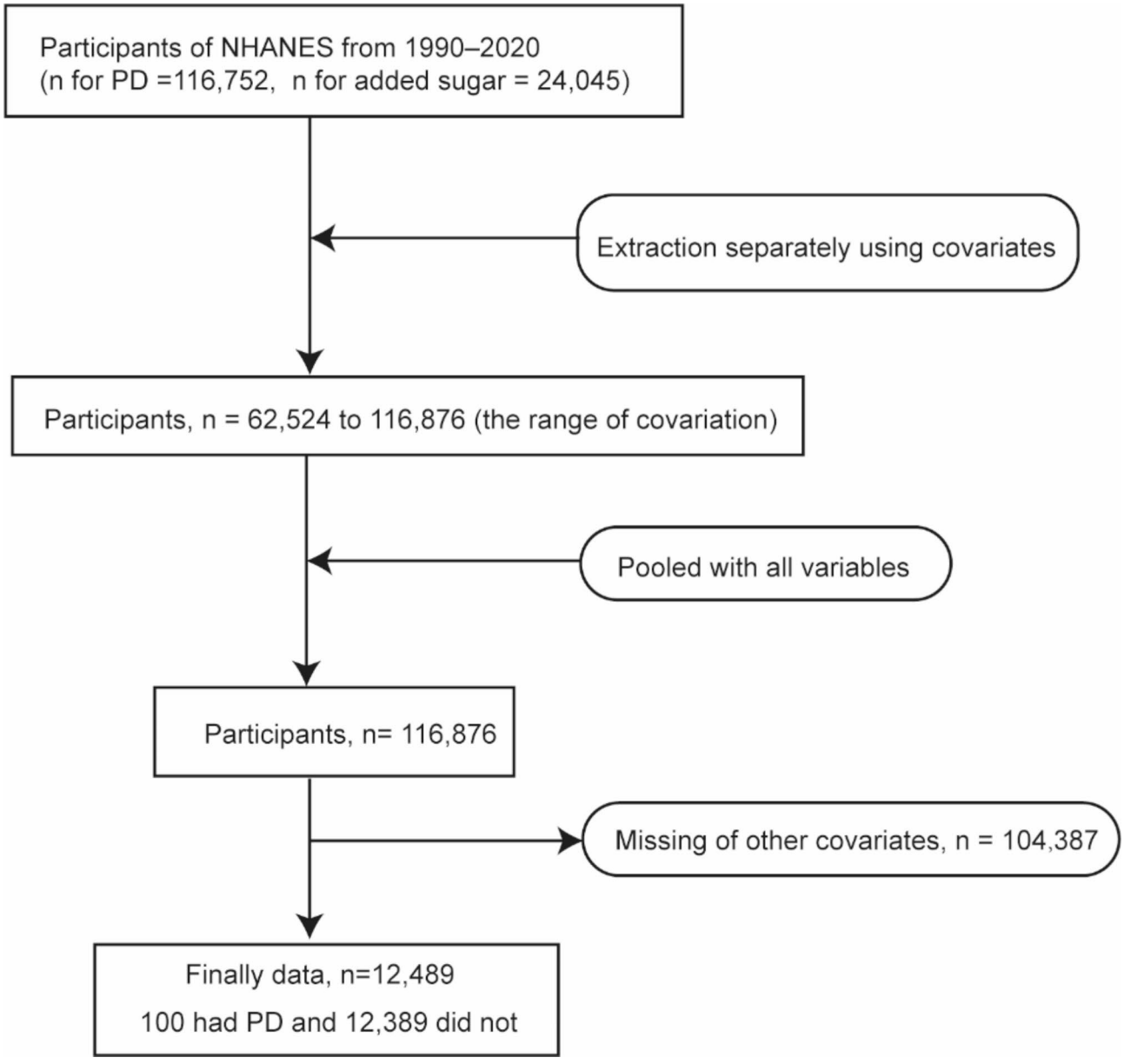

Fig. 1 The flow chart of study population selection: NHANES 1990–2020. NHANES, National Health and Nutrition Examination Survey; PD, Parkinson's disease

first dietary recall interview was collected in person at the Mobile Examination Center (MEC), and the second interview was conducted by telephone 3 to 10 days later. Dietary data, including total energy and added sugars, were extracted from the first day (DR1TOT), the second day (DR2TOT), and the USDA MyPyramid Equivalents Database/Food Patterns Equivalents Database (MPED/FPED) files. In the FPED, one teaspoon equivalent of added sugars is defined as 4.2 g of sugar, with 1 gram of added sugars equaling 3.87 kcal. We calculated added sugars intake as a percentage of total daily energy (% kcal) and categorized the population into quartiles (Q1-Q4) with cut-off points at the 25th (7.35%), 50th (13.83%), and 75th (23.71%) percentiles. Additionally, we classified the percentages into <5%, 5–10%, 10–25%, and ≥25% based on cut-off points recommended by different institutions.

Assessment of Parkinson

Similar to previously published articles based on NHANES, we used self-reported outcomes from the participants' medical condition questionnaires [15]. Participants were asked in the health questionnaire whether they take anti-Parkinson's medication. Those who answered "yes" were considered to have PD, which was defined by the use of medications such as Benztropine, Methyldopa, Carbidopa, Levodopa, Entacapone,

Amantadine, and Ropinirole, while those who selected other responses were considered not to have PD [16].

Study covariates

The epidemiology of PD shows marked variations in age, geography, ethnicity, and sex. Therefore, demographic covariates in this study included age, sex (male, female), race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, other races), marital status (married, widowed, divorced, separated, never married, and living with a partner), education level (less than high school, high school graduate, more than high school), poverty income ratio (PIR).

Underweight was associated with an increased risk of PD incidence [17], while physical exercise, alcohol consumption, and smoking trends are thought to potentially have protective effects against Parkinson's disease [3, 18]. As a result, we included them as covariates in our analysis. Body mass index (BMI, a measure of body fat based on an individual's weight in kilograms divided by the square of their height in meters, categorized as <25, 25–30, and ≥ 30 kg/m^2); PA (measured by the total metabolic equivalent of task (MET) minutes per week, combining work, recreational activities, and walking or bicycling, and categorized as <500 or ≥ 500 MET minutes/week); Personal lifestyle factors based on self-reporting, including smoking status (never: smoked less than 100 cigarettes in life; former: smoked more than 100 cigarettes in life and smoke not at all now; now: smoked more than 100 cigarettes in life and smoke some days or every day) and alcohol-drinking (never: had <12 drinks in lifetime; former: had 12 drinks in 1 year and did not drink last year, or did not drink last year but drank ≥ 12 drinks in lifetime; heavy: men who had ≥ 4 drinks per day or women who had ≥ 3 drinks per day; moderate: men who had 3 drinks per day or women who had 2 drinks per day; others were defined as 'mild').

A review of existing meta-analyses identified a link between added sugars intake and various chronic diseases, prompting us to include the following diseases as covariates [14]. Several self-reported diseases (all classified as yes/no): cancer, diabetes (diagnosed by any of the following: told by a doctor or health professional; HbA1c $\geq 6.5\%$; fasting plasma glucose ≥ 7.0 mmol/L; random plasma glucose ≥ 11.1 mmol/L; 2-hour plasma glucose (oral glucose tolerance test, OGTT) ≥ 11.1 mmol/L; use of antidiabetic medications. Individuals with impaired glucose tolerance and impaired fasting glucose, as well as those self-reporting as "borderline," were considered non-diabetic), hypertension (diagnosed by any of the following: told by a doctor or health professional; use of antihypertensive medication; systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg).

Many genetic risk factors for PD have lipid-related functions [19], and added sugars intake is associated with dyslipidemia [20], prompting us to include laboratory data serum levels related to lipid metabolism as covariates: fasting triglycerides (mmol/L), total cholesterol (mmol/L), HDL-C (high density lipoprotein cholesterol) (mmol/L), and LDL-C (low density lipoprotein cholesterol) (mmol/L). Specific techniques and quality control information for all covariates can be obtained from the NHANES website.

Statistical analysis

All statistical analyses were performed using R statistical software (R 4.3.1), with a two-sided P-value <0.05 considered statistically significant. We combined the sample weights for 10 consecutive cycles as recommended on the NHANES website, and all data were weighted using the variable wtsaf2 year.lipid to account for the sampling design. Normality of the continuous variables was assessed using the Shapiro-Wilk test. In the baseline information table, continuous variables that conformed to a normal distribution were expressed as means (standard deviations), those that did not conform to a normal distribution were expressed as medians (interquartile ranges), and categorical variables were expressed as percentages. Group comparisons for continuous variables that conformed to a normal distribution were performed using t-tests, those that did not conform to a normal distribution were compared using Kruskal-Wallis H tests, and group comparisons for categorical variables were performed using chi-square tests.

In this study, to explore the relationship between added sugars and the prevalence of PD, we conducted multivariable logistic regression analyses. Three models were constructed for analysis: the crude model without any covariates, Model 1 adjusted for sex, age, and race, and Model 2 adjusted for all covariates. Added sugars energy percentage (classified into four categories based on cut-off points of 5%, 10%, and 25%) and the quartiles of the percentage of total daily energy from added sugars (Q1-Q4) were used as categorical variables, with the lowest category serving as the reference group for trend tests, yielding the corresponding odds ratios and p-values. Additionally, we employed restricted cubic spline (RCS) analyses to assess potential nonlinear associations between added sugars and PD, incorporating all covariates.

Finally, we used stratified logistic regression models and interaction tests based on all potential confounders in the baseline table to determine the consistency of these associations across different subgroups, including sex, age, race, education level, smoking status, diabetes status, and hypertension status.

Results

Population, outcome and exposure factors characteristics

Table 1 shows the baseline characteristics of the overall population, along with the characteristics of each quartile of %kcal added sugars and the percentage of energy from added sugars. A total of 12,489 Americans aged were included, with a weighted mean age of 45.32 years, of which 51.72% were male and 48.28% were female. The overall prevalence of PD was 0.74%.

The weighted mean age for participants in the Q1 quartile of added sugars calorie percentage was 48.21, Q2: 47.63, Q3: 45.09, and Q4: 40.83 years, respectively. Additionally, there were significant differences ($P<0.05$) in BMI, age, PIR, triglycerides, total cholesterol, HDL-C, alcohol-drinking, tumor presence, sex, race, marital status, education, diabetes, hypertension, and smoking status among the different quartiles of added sugars calorie percentage and between the quartiles of added sugars intake. An increase in added sugars intake was associated with a higher prevalence of PD, a lower age, a lower probability of chronic diseases, and sex differences (more males, fewer females).

Multivariate regression analysis

In this study, three models were constructed to examine the relationship between added sugars and PD (Table 2). We found a positive correlation between the percentage of calories from added sugars and PD. In Model 1, which adjusted for some confounding factors, the odds ratio (OR) was 1.02 (95% CI 1.01–1.03; $P=0.004$), indicating that for each unit increase in added sugars, the risk of PD increased by 2%. This relationship remained in Model 2 (OR = 1.02; 95% CI 1.01–1.03; $P<0.05$).

Through multivariate regression analysis, compared with the first quartile of the percentage of calories from added sugars, in the fully adjusted model, the third quartile had the highest prevalence of PD (OR = 2.99; 95% CI: 1.43–6.26; $P=0.004$), and the fourth quartile also had a higher prevalence of PD (OR = 2.99; 95% CI: 1.43–6.26; $P=0.01$), with a trend p-value < 0.05. Additionally, compared to those consuming less than 5% of their calories from added sugars, in the fully adjusted model, those consuming 10–25% of their calories from added sugars had a higher prevalence of PD (OR = 2.72; 95% CI: 1.07–6.95; $P=0.04$). The same trend was observed in those consuming more than 25% of their calories from added sugars (OR = 3.34; 95% CI: 1.03–10.86).

RCS analysis

RCS was used to fit a smooth curve, indicating an L-shaped nonlinear relationship between added sugars intake and PD (nonlinear $P=0.021$; Fig. 2A), with a turning point at 13.83. As the proportion of calories from added sugars increased, the prevalence of PD significantly increased, but this increase was more pronounced at lower levels of added sugars intake.

The threshold effects of added sugars on PD were further analyzed using two-segment linear regression by sex. As shown in Fig. 2B, the prevalence of PD in women was linearly related to added sugars intake (nonlinear $P=0.465$), while men remained an L-shaped nonlinear association with added sugars intake (nonlinear $P=0.03$). After the cut point (15.97), the association between added sugars and PD showed different trends in men and women.

Subgroup analysis and interactions

To further observe whether the conclusions were consistent across different subgroups, we analyzed the association between added sugars intake and PD in various subpopulations. All variables recorded in Model 2 were retained in this analysis, and the entire population was stratified based on age, sex, BMI, hypertension, diabetes mellitus (DM), alcohol-drinking, and smoking status. Considering potential differences among these populations and specific environmental factors, we also tested their interactions. Continuous stratified analysis revealed no interaction between added sugars and sex, BMI, age, hypertension, or smoking (interaction $P>0.05$) after adjusting for other covariates. However, alcohol consumption and diabetes were effect modifiers in the relationship between added sugars and PD. For individuals with diabetes, the OR was 1.08 (95% CI: 1.03–1.13; $P=0.003$), while for those without diabetes, the OR was 1.02 (95% CI: 1.00–1.03; $P=0.02$), with an interaction p-value < 0.001. For moderate drinkers, the OR was 1.04 (95% CI: 1.01–1.06; $P=0.003$), and for heavy drinkers, the OR was 1.06 (95% CI: 1.01–1.12; $P=0.02$), with an interaction $P=0.05$. (Fig. 3)

Discussion

Previous research has suggested that the onset of PD is related to dietary habits, with certain phenotypes being modifiable through diet [12, 21]. However, the association between added sugars intake and PD remains unclear. This cross-sectional study aims to investigate the potential impact of added sugars intake on the prevalence of PD by analyzing data from ten consecutive cycles of NHANES, as well as exploring whether this association is consistent across different populations.

Growing evidence indicates that added sugars, particularly high-fructose corn syrup, are associated with the global rise in obesity rates [22]. Recent studies suggest that consuming high-sugar foods can lead to increased insulin levels, which may positively impact dopamine concentrations in the brain, compensating for the dopamine deficiency in PD [23]. The Dietary Guidelines for Americans (DGA) 2020–2025 report recommends

Table 1 Baseline characteristics of participants according to added sugars intake quartiles of %kcal and energy percentage: NHANES 1990–2020 (weighted *N* = 136,959,144)

Variables		Percentage of energy from added sugars					Quartile of %kcal added sugars				
	Total	**< 5**	**5–10**	**10–25**	**> 25**	***P***	**Q1**	**Q2**	**Q3**	**Q4**	***P***
Age (years)	45.32(0.26)	47.81(0.54)	48.33(0.44)	45.78(0.34)	40.66(0.37)	**< 0.0001**	48.21(0.46)	47.63(0.37)	45.09(0.39)	40.83(0.35)	**< 0.0001**
Age category (%)						**< 0.0001**					**< 0.0001**
=<60	80.41	74.00	74.71	79.59	90.15		73.60	75.89	81.20	89.91	
>60	19.59	26.00	25.29	20.41	9.85		26.40	24.11	18.80	10.09	
Sex (%)						**< 0.0001**					**< 0.0001**
Male	51.72	43.36	41.96	50.45	66.64		42.09	45.58	51.26	66.40	
Female	48.28	56.64	58.04	49.55	33.36		57.91	54.42	48.74	33.60	
Race (%)						**< 0.0001**					**< 0.0001**
Non-Hispanic white	72.63	70.70	73.01	72.91	72.98		71.67	73.56	72.08	73.12	
Mexican American	6.82	6.84	6.02	7.09	7.02		6.35	6.54	7.31	7.06	
Non-Hispanic black	9.64	7.03	7.88	10.07	11.85		6.93	8.31	11.17	11.85	
Other	10.91	15.43	13.09	9.93	8.15		15.06	11.60	9.43	7.97	
Marital (%)						**< 0.0001**					**< 0.0001**
Married	58.17	60.53	60.39	58.83	53.87		60.55	59.61	58.81	54.12	
Widowed	3.94	4.99	5.72	3.91	1.94		5.32	4.99	3.68	1.97	
Divorced	9.51	9.08	8.65	9.68	10.16		9.09	9.85	8.78	10.25	
Separated	2.10	2.27	1.37	1.93	2.88		1.81	1.75	2.03	2.75	
Never married	18.29	16.05	16.57	18.13	21.27		16.46	16.39	18.86	21.17	
Living with partner	7.99	7.07	7.29	7.53	9.88		6.77	7.41	7.85	9.74	
Education (%)						**< 0.0001**					**< 0.0001**
Under high school	13.06	12.42	11.85	11.94	16.33		11.60	11.80	12.69	15.89	
High school or equivalent	23.45	19.49	20.10	22.62	29.88		20.02	20.22	23.41	29.53	
Above high school	63.49	68.09	68.05	65.44	53.79		68.38	67.98	63.89	54.58	
PIR	3.17(0.03)	3.32(0.05)	3.27(0.04)	3.24(0.04)	2.85(0.04)	**< 0.0001**	3.33(0.04)	3.29(0.04)	3.19(0.05)	2.88(0.04)	**< 0.0001**
BMI (kg/m^2)	28.42(0.09)	28.51(0.21)	28.47(0.16)	28.30(0.11)	28.53(0.15)	**< 0.0001**	28.57(0.17)	28.03(0.15)	28.56(0.14)	28.51(0.15)	**0.02**
Smoking status (%)						**< 0.0001**					**< 0.0001**
Never	53.75	55.54	56.08	55.00	48.71		56.16	54.79	55.43	49.09	
Former	25.42	27.62	28.68	26.46	19.74		28.15	28.30	25.61	20.14	
Now	20.83	16.84	15.24	18.54	31.55		15.69	16.91	18.96	30.78	

Table 1 (continued)

Variables		Percentage of energy from added sugars					Quartile of %kcal added sugars				
	Total	**< 5**	**5–10**	**10–25**	**> 25**	***P***	**Q1**	**Q2**	**Q3**	**Q4**	***P***
Alcohol-drinking (%)						**< 0.0001**					**< 0.0001**
Never	9.33	10.41	10.09	9.51	7.79		10.50	8.81	10.20	7.99	
Former	12.61	11.83	11.02	11.83	15.68		11.88	10.55	12.17	15.61	
Mild	38.47	36.89	40.11	39.88	35.69		37.88	41.86	38.46	35.83	
Moderate	17.97	21.07	19.40	17.95	15.03		20.76	18.34	17.98	15.15	
Heavy	21.61	19.80	19.40	20.82	25.80		18.98	20.44	21.20	25.42	
PA (MET minutes/week)	1225.00 (413.23,3643.50)	1288.00 (480.00,3240.00)	1200.00 (425.25,3120.00)	1260.00 (444.85,3600.00)	1200.00 (360.00,4800.00)	0.49	1220.50 (420.00,3240.00)	1220.00 (480.00,3360.00)	1274.00 (413.23,3780.00)	1200.00 (378.00,4800.00)	0.5
Cancer (%)						**0.001**					**0.001**
No	91.67	92.12	90.54	90.82	93.75		91.64	89.86	91.54	93.50	
Yes	8.33	7.88	9.46	9.18	6.25		8.36	10.14	8.46	6.50	
DM (%)						**< 0.0001**					**< 0.0001**
No	92.66	86.46	89.51	93.96	96.64		87.20	91.91	94.45	96.52	
Yes	7.34	13.54	10.49	6.04	3.36		12.80	8.09	5.55	3.48	
Hypertension (%)						**< 0.0001**					**< 0.0001**
No	66.33	61.42	61.31	68.03	70.37		61.02	64.86	68.18	70.69	
Yes	33.67	38.58	38.69	31.97	29.63		38.98	35.14	31.82	29.31	
Lipids											
Fast triglyceride (mmol/L)	1.14 (0.79,1.67)	1.15 (0.78,1.68)	1.12 (0.76,1.64)	1.12 (0.78,1.65)	1.21 (0.86,1.75)	**< 0.0001**	1.14 (0.77,1.64)	1.11 (0.78,1.65)	1.11 (0.78,1.66)	1.21 (0.86,1.75)	**< 0.0001**
Fast total cholesterol (mmol/L)	4.94 (4.29,5.64)	4.99 (4.34,5.74)	4.97 (4.34,5.72)	4.91 (4.29,5.64)	4.89 (4.24,5.56)	**< 0.001**	4.97 (4.32,5.72)	5.02 (4.34,5.77)	4.91 (4.29,5.59)	4.89 (4.24,5.56)	**< 0.001**
HDL-C(mmol/L)	1.34 (1.11,1.63)	1.42 (1.14,1.74)	1.42 (1.16,1.73)	1.34 (1.11,1.63)	1.22 (1.03,1.45)	**< 0.0001**	1.45 (1.16,1.73)	1.40 (1.16,1.71)	1.32 (1.11,1.61)	1.22 (1.03,1.45)	**< 0.0001**
LDL-C (mmol/L)	2.92 (2.35,3.57)	2.90 (2.33,3.57)	2.90 (2.33,3.54)	2.92 (2.38,3.54)	2.97 (2.40,3.57)	0.21	2.90 (2.30,3.52)	2.95 (2.38,3.59)	2.92 (2.38,3.54)	2.97 (2.40,3.57)	**0.03**
PD (%)						0.45					0.2
No	99.26	99.63	99.27	99.17	99.17		99.57	99.35	99.01	99.12	
Yes	0.74	0.37	0.73	0.83	0.83		0.43	0.65	0.99	0.88	

Variables are presented as median (IQR) or numbers (percentages). *P*-value of the T-test or Chi-square test. NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio; BMI, body mass index; PA, physical activity; MET, metabolic equivalent of task; DM, diabetes mellitus; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PD, Parkinson's disease; Bold value: the value has statistical significance

Table 2 Weighted multivariate logistic regression results of the associations between added sugars intake and PD: NHANES 1990–2020

Characters	Crude model		Model 1		Model 2	
	OR (95%CI)		OR (95%CI)		OR (95%CI)	
	95%CI	*P*-value	95%CI	*P*-value	95%CI	*P*-value
Quartile %kcal added sugars						
Q1	1.00 (Ref)		1.00 (Ref)		1.00 (Ref)	
Q2	1.52 (0.73,3.17)	0.26	1.57 (0.74,3.33)	0.24	1.68 (0.78,3.60)	0.18
Q3	2.31 (1.13,4.74)	**0.02**	2.82 (1.38,5.75)	**0.005**	2.99 (1.43,6.26)	**0.004**
Q4	2.04 (0.86,4.87)	0.11	3.30 (1.33,8.16)	**0.01**	3.28 (1.29,8.34)	**0.01**
***P*-value for trend**		0.08		**0.004**		**0.01**
Percentage of energy from added sugars						
<5	1.00 (Ref)		1.00 (Ref)		1.00 (Ref)	
5–10	1.99 (0.84,4.71)	0.12	1.92 (0.81, 4.55)	0.14	1.94 (0.81,4.61)	0.13
10–25	2.28 (0.92,5.64)	0.08	2.55 (1.02, 6.35)	**0.05**	2.72 (1.07,6.95)	**0.04**
>25	2.26 (0.76,6.75)	0.14	3.50 (1.12,10.93)	**0.03**	3.34 (1.03,10.86)	**0.05**
***P*-value for trend**		0.2		**0.03**		**0.04**

Odds ratios (95% CIs) for risk of PD were analyzed using logistic regression models. Crude model: No covariates were adjusted; Model 1: age, sex, race; Model 2: alcohol-drinking, BMI, cancer, age, sex, race, marital, PIR, education, DM, lipids, PA, hypertension, smoking status. OR, odds ratio; CI, confidence intervals. Q1, 1st quartile; Q2, 2nd quartile; Q3, 3rd quartile; Q4, 4th quartile

Bold value: the value has statistical significance

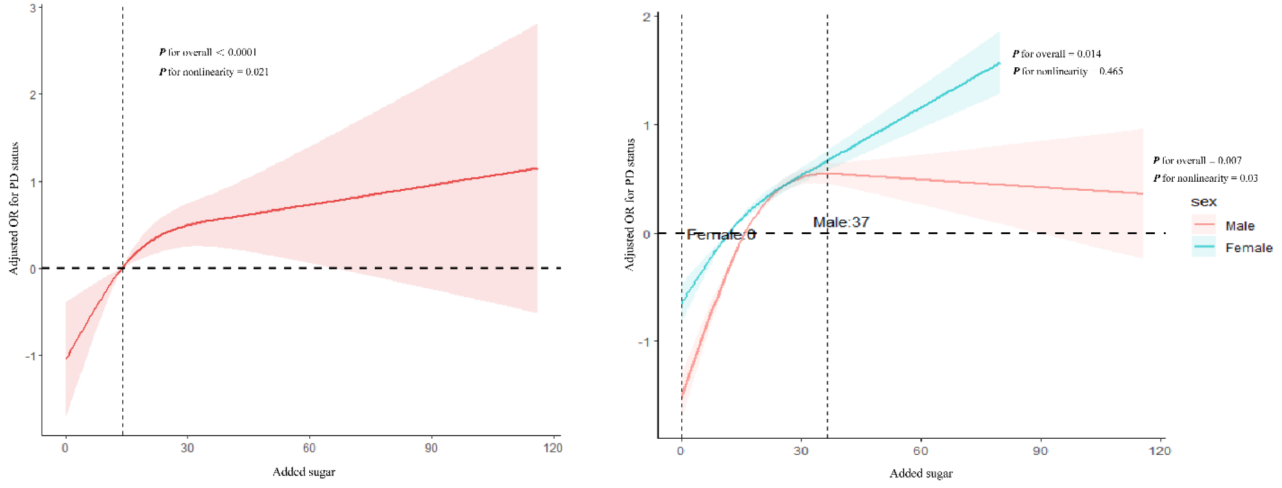

Fig. 2 Dose-response relationships between added sugars intake with PD: NHANES 1990–2020. Odds ratios (ORs) and 95% confidence intervals (CIs) are based on a logistic regression model adjusted for variables in Model 2. The solid lines represent ORs, and the shaded areas represent 95%CIs. **(A)** Nonlinear relationship between added sugars intake and PD. **(B)** Two-segment linear regression by sex. PD, Parkinson's disease

reducing the limit on added sugars from 10% of total energy intake to 6% [24]. In our baseline data, we indeed observed that populations in the higher quartiles of added sugars intake and percentage groups exhibited a correspondingly higher prevalence of PD, which aligns with the existing literature. Clinical research has confirmed that PD patients tend to consume more added sugars, which may exacerbate oxidative damage in the brain, such as inducing neuroinflammation, oxidative stress, synaptic loss, and the degeneration of specific neuronal populations [25]. A study involving 5,824 participants from the NHANES database found that increased adherence to the Mediterranean diet (especially with reduced sweets intake) was associated with a lower probability of PD prevalence [26]. Although there are few existing studies on the association between added sugars and PD, the impact of dietary patterns on PD is well-established [27]. Previous studies have found that the complex bidirectional communication between the gut and brain is regulated by dietary patterns, playing a crucial role in the pathogenesis of PD [28], and caloric restriction can reduce its incidence [29]. Meanwhile, another cross-sectional study discovered significant associations between PD and dietary factors such as sugar, fish, and milk [30].

Furthermore, our multivariate regression analysis, adjusted for potential confounders such as BMI, blood lipids, smoking, and socioeconomic status, revealed a

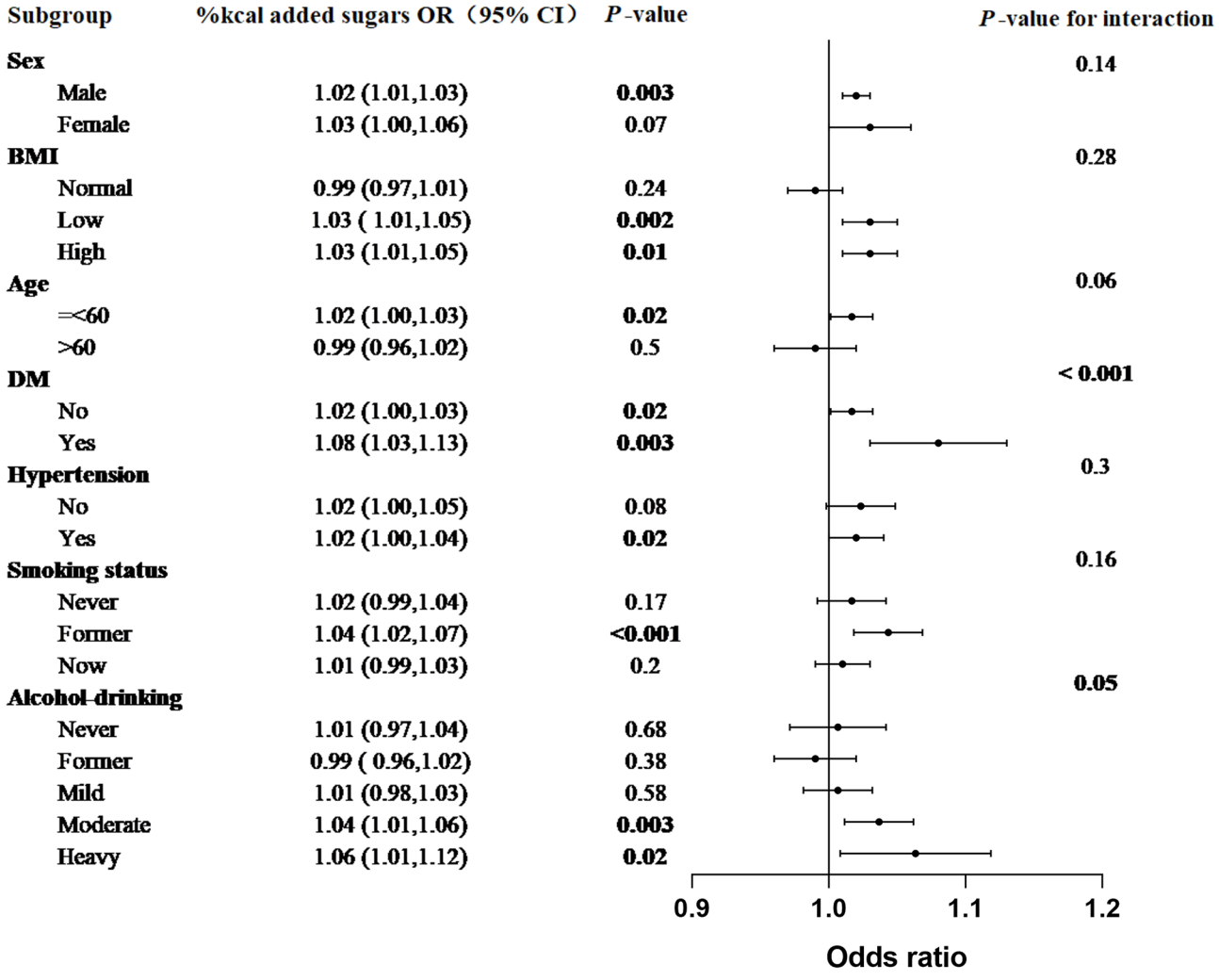

Fig. 3 Forest plot: Continuous stratified analysis of the association between added sugars (%kcal) and PD stratified by population characteristics. Odds ratios (ORs) and 95% confidence intervals (CIs) are based on a logistic regression model adjusted for variables in Model 2, stratified by the key risk factors. PD, Parkinson's disease; BMI, body mass index; DM, diabetes mellitus. Likelihood ratio tests were used to assess the significance of interaction terms in the model, and two-sided *P* values are reported. Bold value: the value has statistical significance

strong association in which individuals in the highest quartile of added sugars intake exhibited nearly three times the prevalence of PD compared to those in the lowest quartile. This correlation underscores the significant positive relationship between added sugars intake and PD revealed by our study. From the perspective of the pathological mechanism, neuronal homeostasis relies on monosaccharides and complex sugars, and their metabolic dysregulation can impair neural function, leading to neurodegenerative diseases [31]. Recent research suggests that high-sugar diets may alter neurochemical pathways and modulate neuroinflammation or oxidative stress, which are key mechanisms in neurodegenerative diseases like PD, further impacting disease progression [32, 33]. Moreover, excessive carbohydrate metabolism has been identified as a cause of mitochondrial dysfunction in PD [34]. In line with this, animal studies have found a strong association between fructose and neurodegenerative diseases, with high-fructose intake inducing early signs of neurodegeneration in the hippocampus [35]. The aforementioned research supports the findings of our study.

The inclusion of all covariates in the RCS analysis further supports the robustness of these findings, indicating an L-shaped nonlinear association between added sugars intake and PD. As added sugars intake surpasses certain thresholds, the positive correlation continues to rise, albeit at a slower rate, suggesting a plateau effect at higher levels of intake. This nonlinear relationship underscores the complexity of the association between diet and PD,

highlighting the importance of considering nonlinearity in dietary studies. We further analyzed the threshold effects of added sugars on PD using two-segment linear regression by sex. Interestingly, after the cut point, the association between added sugars and PD was more significant in females than in males. This suggests that while males are the primary demographic for PD onset, females may experience greater negative impacts on PD risk and progression with increased added sugars intake. Despite the biological reasons behind this finding remain unclear, a multimodal biomarker study has found that gonadotropins may mediate the age-dependent phenomena of amyloid deposition and cognitive decline [36]. Similarly, a large-scale prospective study found that women exhibit greater susceptibility to weight changes following carbohydrate intake [11]. Future research should explore how these associations may vary across different demographics and health profiles, further clarifying the role of dietary sugars in the context of PD.

Increased added sugars intake is a major factor contributing to common diseases related to metabolic dysfunction, such as obesity and diabetes, both of which are common risk factors for PD [37].Considering potential differences among populations, our subgroup analysis adjusted for other covariates and found no interaction between added sugars and sex, BMI, age, hypertension, or smoking (interaction $P>0.05$). However, alcohol consumption and DM were effect modifiers in the relationship between added sugars and PD. Previous research has shown an association between PD and DM in both molecular and epidemiological studies, including links between α-synuclein and amyloid aggregation [38]. A high intake of rapid-acting carbohydrates can also affect insulin metabolism, which has recently been considered a potential factor influencing the progressive neurodegeneration in PD [39]. Understanding these nuances can help in developing targeted dietary interventions aimed at reducing the risk of PD in susceptible populations. To build on this, it's essential to consider the underlying mechanisms that may drive this relationship, such as the impact of added sugars on inflammation and insulin resistance, which could exacerbate neurodegenerative processes. Excessive levels of pro-inflammatory agents in insulin resistance can induce abnormal neuroinflammation, suggesting that a similar mechanism may apply to PD [40]. Our study also indicated that heavy drinkers have a higher risk of PD. Alcohol is a psychoactive substance with dependence-producing properties. Contrary to our findings, previous studies have shown a significant negative association between alcohol consumption and PD risk [41], or no association at all [42]. This discrepancy may be due to individuals with PD reducing their alcohol consumption due to symptoms or substituting alcoholic beverages for sugary drinks, which could explain the inconsistent results.

This is the first study to explore the relationship between added sugar intake and Parkinson's disease incidence using a large clinical sample, which indicates a significant positive correlation between increased added sugar intake and higher prevalence of Parkinson's disease in the U.S. population. Second, the robustness of the findings was confirmed after adjusting for confounding factors in the model. We also analyzed the association between added sugars intake and PD across different population groups, taking into account potential differences and specific environmental factors, and tested for interactions between these variables. Nevertheless, the study has limitations. These include potential bias in the questionnaire collection, possible confounding effects from other chemicals in sugary drinks, and the cross-sectional design's inability to establish causality between added sugars intake and PD prevalence. Furthermore, we did not control for overall diet quality, including intake of other nutrients (e.g., fiber, fats, protein) or specific foods like fruits and vegetables, which could have influenced the associations observed. Finally, PD diagnoses were based on self-reported data, which may introduce bias.

Conclusion

In this cross-sectional study, our data indicated a positive association between added sugars intake and the prevalence of PD, particularly among women, heavy drinkers, and individuals with diabetes. Future research should adopt a longitudinal design and comprehensive dietary assessments to clarify the link between added sugars and PD.

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We thank the respondents in the NHANES database for providing data for this study. This study complies with the ethical requirements of the Declaration of Helsinki and its subsequent amendments. The NHANES public database is approved by the CDC, and all participants provided consent.

Author contributions

XC and GH conceived and designed the study. LH is responsible for data management and retrieval, and GH contributes to initial data analysis and graphing. XC and GH drafted and revised the manuscript. TS, GH and TW assisted in the manuscript review. All authors contributed to this paper and approved the submitted version.

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Data availability

Data is provided within the manuscript or supplementary information files. All information can be obtained on the NHANES official website.

Declarations

Ethics approval and consent to participate
The study was reviewed and approved by the Ethics Review Board of the National Center for Health Statistics and participants all provided informed consent.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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