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La adherencia a una dieta antioxidante se asocia a un riesgo reducido de epilepsia entre los adultos estadounidenses: NHANES 2013-2018

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ABSTRACT

Background: oxidative stress is correlated with epilepsy. Oxidative Balance Scores (OBS) serve as a systematic approach for evaluating oxidative stress in relation to dietary and lifestyle factors. The relationship between OBS and epilepsy is unclear. An investigation of the relationship between OBS and epilepsy was conducted in this study.

Methods: in this cross-sectional study, we employed weighted logistic regression and conducted sensitivity analysis to examine the correlation between OBS and epilepsy. Additionally, we performed subgroup analysis and an interaction test to ascertain the consistency of this relationship across different demographic groups.

Results: 11,910 participants from the National Health and Nutrition Examination Survey (NHANES) conducted between 2013 and 2018 were included in this study. The results indicated a statistically significant inverse relationship between OBS and the prevalence of epilepsy [0.95 (0.92, 0.99)]. Furthermore, when OBS was converted into a quartile variable, individuals with OBS values greater than 25 had an adjusted OR of 0.47 compared to the lowest (95 % CI: 0.24, 0.92). Specifically, dietary OBS showed a consistent negative correlation with epilepsy risk across all models, while lifestyle OBS did not exhibit an association. The results of our study revealed a notable interaction between serum UA levels and race and diabetes

($p < 0.05$ for interaction).

Conclusions: the study revealed a noteworthy inverse correlation between OBS and epilepsy among American adults. These findings underscore the potential protective effect of adherence to an antioxidant diet in reducing the prevalence of epilepsy.

Keywords: Epilepsy. Oxidative balance score. Oxidative stress. NHANES. Diet. Lifestyle.

RESUMEN

Introducción: el estrés oxidativo se correlaciona con la epilepsia. Las puntuaciones de balance oxidativo (OBS) sirven de enfoque sistemático para evaluar el estrés oxidativo en relación con los factores dietéticos y del estilo de vida. La relación entre OBS y síndrome epiléptico no está clara. En este estudio se ha llevado a cabo una investigación sobre la relación entre la OBS y el síndrome epiléptico.

Métodos: en este estudio transversal se emplearon la regresión logística ponderada y el análisis de sensibilidad para examinar la correlación entre la OBS y el síndrome epiléptico. Adicionalmente se realizaron un análisis de subgrupos y una prueba de interacción para determinar la consistencia de esta relación entre los diferentes grupos demográficos.

Resultados: se incluyeron 11.910 participantes de la encuesta nacional del examen de salud y nutrición (NHANES) realizada entre 2013 y 2018. Los resultados indicaron una relación inversa estadísticamente significativa entre la OBS y la prevalencia de la epilepsia [0,95 (0,92, 0,99)]. Además, al convertir la OBS en una

variable cuartílica, los individuos con valores de OBS mayores de 25 tuvieron una OR ajustada de 0,47 en comparación con el cuartil más bajo (IC 95 %: 0,24, 0,92). Específicamente, las OBS dietéticas mostraron una correlación negativa consistente con el riesgo de epilepsia en todos los modelos, mientras que las OBS del estilo de vida no exhibieron ninguna asociación. Los resultados de nuestro estudio revelan una notable interacción entre niveles séricos de AU, raza y diabetes ($p < 0,05$ para la interacción).

Conclusiones: el estudio reveló una notable correlación inversa entre la OBS y la epilepsia en adultos estadounidenses. Estos hallazgos subrayan el efecto protector potencial de la adherencia a una dieta antioxidante sobre la reducción de la prevalencia de la epilepsia.

Palabras clave: Epilepsia. Puntuación de equilibrio oxidativo. Estrés oxidativo. NHANES. Dieta. Estilo de vida.

INTRODUCTION

Epilepsy is a neurological condition distinguished by a chronic vulnerability to experience epileptic seizures (1). Symptoms of epilepsy encompass frequent muscular twitches, transient sensory abnormalities, disturbances in consciousness, and additional manifestations (2). This condition can manifest in individuals of all ages, geographical locations, and ethnic backgrounds. Currently, epilepsy ranks as the second most prevalent neurological ailment, impacting approximately 20-70 individuals per 100,000 annually (3). Consequently, patients afflicted with epilepsy may experience substantial physical and mental health challenges, placing a

considerable burden on both their families and society as a whole. Hence, the effective management and prevention of epilepsy assume paramount importance.

Epilepsy, being a highly prevalent neurological disorder, exhibits a strong association with oxidative stress (OS) and neuroinflammation (4). Accumulated evidence (5,6) suggests that OS is potentially involved in epileptogenesis and epilepsy development. Many studies (7-9) indicated that specific antioxidants, including vitamin E, selenium, and melatonin, could be considered as adjunctive therapies for individuals suffering from drug-resistant epilepsy. The ketogenic diet (KD) has been shown to be a viable, efficient, and secure therapeutic option for drug-resistant epilepsy in pediatric patients (10). The main mechanisms of action of KD include scavenge ROS, bolster endogenous antioxidant mechanisms, and reduce the production of free radicals (11).

The Oxidative Balance Score (OBS) is a significant epidemiological methodology for assessing the collective impact of antioxidants and pro-oxidants, particularly in relation to chronic ailments (12). In 2002, Van Hoydonck and colleagues (13) proposed the use of OBS as a means to investigate the potential association between oxidative imbalance and increased susceptibility to all-cause and cause-specific mortality. Subsequently, many studies have explored the correlation between OBS and chronic conditions, revealing significant connections with disorders such as depression (14), cardiovascular disease (15), and chronic renal disease (16). However, research on the connection between OBS and epilepsy has not been done.

A cross-sectional study was conducted utilizing data from the National Health and Nutrition Examination Survey (NHANES) spanning the years 2013 to 2018, with the aim of examining the association

between OBS and epilepsy in American adults. This research endeavor holds potential to provide valuable insights for the management and prevention of epilepsy.

METHODS

Study population

The study population consisted of subjects selected from the nationally representative consecutive NHANES cycles conducted during the aforementioned period, specifically chosen due to the presence of reported cases of epilepsy. NHANES, a cross-sectional survey, was originally intended to assess American nutrition and health. All participants in the NHANES study provided written informed consent, which was approved by the Ethics Review Board of the National Center for Health Statistics. In the NHANES 2013–2018, with a total of 29,400 individuals, 12,343 participants under the age of 20 were not included due to the presence of certain variables that were only applicable to individuals aged 20 and above. Among the remaining 17,057 individuals, data on OBS and epilepsy were missing for 5139 and 8 participants, respectively. Ultimately, the research included 11,910 participants, including 93 individuals with epilepsy (Fig. 1). The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting (17).

Definition of epilepsy

Data on epilepsy was collected through face-to-face interviews conducted by researchers. Participants were asked to provide a comprehensive list of prescription medications prescribed by healthcare providers in the past month, accompanied by a rationale

for each prescription. Individuals were categorized as epilepsy patients if they were taking any medication for the treatment of "epilepsy and recurrent seizures" as defined by the International Classification of Diseases (G40) (18).

Oxidative Balance Score

OBS was calculated by amalgamating 16 dietary components and 4 lifestyle factors, encompassing 15 antioxidants and 5 pro-oxidants, as per a previous investigation (12,19). The initial dietary assessment interview furnished data on the consumption of sixteen elements, including dietary fiber, carotene, riboflavin, niacin, vitamin B6, total folate, vitamin B12, vitamin C, vitamin E, calcium, magnesium, zinc, copper, selenium, total fat, and iron. The four lifestyle factors considered are alcohol use, smoking, body mass index (BMI), and physical activity. The quantity of smoking is quantified in terms of cotinine. A comprehensive breakdown of the OBS components can be found in table I. The quantification of physical activity was conducted by considering the Metabolic equivalent (MET) value, activity type, weekly frequency, and duration (20). The allocation of points for alcohol consumption varied depending on the individual's drinking habit: nondrinkers were assigned 2 points, nonheavy drinkers (0 to 15 g/d for females and 0 to 30 g/d for males) were assigned 1 point, and heavy drinkers (> 15 g/d for females and > 30 g/d for males) were assigned 0 points. Subsequently, the remaining components were classified into three groups based on sex-specific tertiles. Antioxidants were assigned points ranging from 0 to 2, corresponding to tertile 1 to tertile 3, respectively. The scoring of prooxidants was conducted in a reverse manner, with the highest tertile being assigned a score of 0 and the lowest tertile receiving a score of 2. The

overall OBS was calculated by summing the scores assigned to each component, whereby a higher OBS indicates a greater intake of antioxidants.

Covariate assessment

The selection of covariates for the present study was informed by established confounders identified in previous research and clinical experience. The covariates encompassed age, gender, race, marital status, education level, poverty income ratio (PIR), diabetes, hypertension, general health, depression, and sleep disorders (Supplementary Table I). The depression score was assessed using the Patient Health Questionnaire (PHQ-9). In accordance with previous research (21,22), depression was classified as a total PHQ-9 score of ≥ 10 in this current study.

Statistical analysis

Continuous variables were characterized by their weighted mean ± standard deviation (SD) and analyzed using weighted linear regression. Categorical variables were presented as weighted percentages and compared using the weighted chi-square test. The association between OBS and epilepsy was assessed using weighted logistic regression models. The ultimate model was adjusted for a comprehensive set of variables, encompassing age, gender, race, marital status, education level, PIR, diabetes, hypertension, general health, depression, and sleep disorders. Furthermore, subgroup analysis was carried out to assess the impact of age, gender, race, education level and diabetes on the result. To determine whether the association was consistent across subgroups, interaction tests were performed.

The statistical analyses were performed using the R software (http://www.R-project.org, The R Foundation, Austria), Empowerstats (http://www.empowerstats.com, X&Y Solutions, Inc., CA, USA), and STATA 16.0 (StataCorp, College Station, TX, USA). The individual sample weights for the NHANES study were determined using the recommended sample weight for dietary day one (WTDRD1) data, which was calculated as one-third of WTDRD1. Statistical significance was defined as a two-sided *p*-value less than 0.05.

RESULTS

Characteristics of participants

The study included a total of 11,910 participants, with an average age of 47.1 years and a gender distribution of 50.7 % males and 49.3 % females. Table II shows the overall characteristics of the study participants, categorized by OBS quartiles. The highest OBS quartile had a higher percentage of non-Hispanic white participants compared to the lowest OBS quartile. Regarding socioeconomic circumstances, individuals with higher OBS scores exhibited higher levels of educational attainment and incomes. Furthermore, participants in the lowest OBS quartile demonstrated a higher prevalence of hypertension, diabetes, depression, and sleep disorders.

The characteristics of participants categorized by epilepsy status are presented in supplementary table II. Individuals with epilepsy exhibited lower OBS, educational achievement, and income, as well as lower rates of marriage, poorer health status, and a higher prevalence of hypertension and depression.

Association between OBS and epilepsy

The correlation between OBS and epilepsy was presented in table III.

Following the adjustment for all covariates, a reduction in epilepsy risk was found to be associated with overall and dietary OBS, but not lifestyle OBS [overall OBS: OR (odds ratios) = 0.95, $p = 0.006$; dietary OBS: OR = 0.95, $p = 0.014$; lifestyle OBS: OR = 0.95, $p = 0.535$]. Sensitivity analyses were conducted subsequent to the conversion of the OBS variable from a continuous to a categorical form. For overall OBS in model 3, utilizing the first OBS category as a reference point, the OR (95 % confidence intervals) for the remaining OBS groups were found to be 0.45 (0.19, 1.06), 0.54 (0.27, 1.10), and 0.47 (0.24, 0.92). As categorical variables, dietary OBS in Quartile 2 (OR = 0.35, $p = 0.020$), Quartile 3 (OR = 0.47, $p = 0.026$) and Quartile 4 (OR = 0.41, $p = 0.015$) (compared to Quartile 1) was significantly associated with a lower risk of epilepsy in model 3. However, lifestyle OBS in Quartile 2, Quartile 3, and Quartile 4 (compared to Quartile 1) was not significantly associated with the risk of epilepsy in all models.

Subgroup analyses

The relationship between OBS and epilepsy, as determined through multiple logistic regression, is presented in table IV, stratified by age, gender, race, education level, and diabetes. There were no statistically significant differences in demographic data, such as age, gender, and education level. Among non-Hispanic white individuals, a one-unit increase in OBS was found to be correlated with a 7 % reduction in the probability of epilepsy [0.93 (0.89, 0.97)]. Additionally, individuals without diabetes exhibited a significantly stronger negative association effect [0.94 (0.89, 0.98)] compared to those with diabetes [1.01 (0.90, 1.15)]. However, the small sample size in this category prevented the performance of a subgroup analysis on the age-epilepsy association. It was interesting to note

that there was an interaction of OBS with race (p for interaction = 0.025) or diabetes (p for interaction = 0.020).

DISCUSSION

This study involved a cross-sectional analysis of a cohort consisting of 11,910 individuals aged 20-80 from the NHANES dataset to elucidate the association between OBS and epilepsy. Our findings revealed a significant inverse correlation between OBS and epilepsy. These results underscore the crucial influence of an antioxidant-rich diet in mitigating the risk of epilepsy, thereby bearing implications for public health policy.

OS arises from an imbalance in the creation and clearance of reactive oxygen species (ROS), which include superoxide radicals, hydrogen peroxide, hydroxyl radicals, and singlet oxygen. ROS are byproducts of cellular metabolism that can be neutralized through enzymatic (such as superoxide dismutase and glutathione peroxidase) and non-enzymatic (such as vitamin C, vitamin E, and reduced form glutathione) antioxidant mechanisms. Elevated levels of ROS, stemming from either heightened production or diminished antioxidant defenses, can induce oxidative stress, potentially playing a role in the pathogenesis and advancement of epilepsy (23). The blood antioxidant status of epileptic patients is lower than those of controls, according to a meta-analysis (24). In acquired epilepsies like post-traumatic epilepsy, tissue and cellular damage lead to increased ROS production, mitochondrial damage, lipid peroxidation, and oxidative modifications (25). It is important to note that antioxidants function synergistically and assessing their individual components in isolation may not adequately capture their overall impact on the body's antioxidant activity. Our investigation encompasses a

composition of 15 antioxidants and 5 pro-oxidants within OBS, potentially offering a more precise depiction of the overall oxidative stress levels within the body. Our findings indicate a significant inverse correlation between OBS and epilepsy, as evidenced by a linear trend analysis using OBS quartiles.

This study represents the initial investigation known to us that examines the association between OBS and epilepsy. Although direct evidence is lacking, many studies have explored the link between diet and epilepsy. A study (26) examining the impact of vitamins on epilepsy indicated that vitamins have a crucial role in seizure management. Patients treated with antioxidant vitamin E demonstrated improved pathological symptoms and a reduction in seizure frequency through the depletion of lipid peroxidation levels (27). Multiple studies (28,29) have demonstrated that Vitamin E has the potential to effectively mitigate the severity and adverse consequences of seizures by mitigating OS in the brain. Furthermore, a 22-year follow-up study (30) showed a correlation between higher oral magnesium intake and a decreased risk of adult epilepsy. Overall, the findings indicate that targeted intake of dietary antioxidants may potentially reduce the prevalence of epilepsy by enhancing antioxidant defense mechanisms.

A notable discovery from our study on the correlation between epilepsy and distinct types of OBS revealed that dietary OBS were linked to decreased risks of epilepsy, whereas lifestyle OBS did not show similar associations. Previous research has shown mixed results regarding the relationship between alcohol consumption, smoking, BMI, physical activity, and the occurrence of epilepsy. A recent meta-analysis of case-control studies (31) revealed a 161 % higher risk of epilepsy associated with alcohol use. However, cohort studies (31) did

not identify a significant correlation between alcohol use and epilepsy. Devetag et al. (32) found that heavy drinkers typically require a minimum of five years to manifest repetitive unprovoked seizures. In light of this temporal association, alcohol may not actually increase the risk of epilepsy, whereas dietary choices may primarily affect brain health during the preventative or initial phases. People with epilepsy engage in less physical activity than peers, which may be attributed to the perceived increased risk of seizure activity, apprehension of seizure-related harm, and the dissemination of misguided guidance from healthcare providers (33). Therefore, in comparison to dietary influences, the effects of lifestyle factors on epilepsy may be more nuanced and indirect. These results emphasize the importance of tailored approaches in designing prevention and intervention tactics for individuals with epilepsy, with further research needed to explore underlying mechanisms.

Based on the subgroup analysis and interaction test, a notable interaction was found between OBS and diabetes. Previous studies (34,35) have demonstrated a correlation between diabetes and epilepsy with oxidative stress. Advanced glycation end products (AGE), which result from prolonged hyperglycemia, play a significant role in the advancement of diabetes mellitus and its chronic complications (36). Through an experimental investigation (34), it was observed that upregulation of AGE led to an increase in ROS production, and the receptor for AGE contributed to heightened excitability in both acute and chronic seizure occurrences. Our findings from the interaction test align with the aforementioned research. Furthermore, our findings indicate the presence of racial disparities in the impact of OBS on epilepsy. Non-Hispanic black individuals exhibit a comparatively elevated mortality rate attributed

to epilepsy in comparison to individuals of other racial backgrounds (37). A study (38) has identified the black race as a risk factor for undifferentiated post-traumatic epilepsy. Subsequent research (39) has also revealed that Black patients exhibit a significantly elevated risk of epilepsy following subdural hematomas compared to White patients. Various social factors, such as socioeconomic status, post-injury resources, and pre-injury factors, may contribute to the observed racial disparities in epilepsy risks (39). Specifically, our findings suggest that non-Hispanic white individuals may experience greater advantages in epilepsy prevention through dietary and lifestyle modifications.

The current study possesses several strengths. Firstly, the NHANES data were obtained through a multi-stage probability sampling technique, enabling the findings to be applicable to the entire non-institutionalized American population. Secondly, our investigation represents the inaugural exploration into the role of OBS in epilepsy, wherein we adopt a composite indicator approach to comprehensively examine the intricate interconnections among its components. Moreover, our research conducted a comprehensive stratified analysis, revealing the existence of racial disparities in the impact of OBS on epilepsy. These findings can potentially inform future investigations into antiepileptogenesis interventions and shed light on the specific racial factors that contribute to this association. However, it is important to acknowledge the limitations of our study. Firstly, due to its cross-sectional design, we were unable to establish causality, thus warranting caution in interpreting the findings. Furthermore, potential confounding factors may have influenced the results. Another limitation is the lack of a clinical examination for diagnosing epilepsy, as well as the failure to consider the various subtypes and

causes of epilepsy in each individual. Nevertheless, the stability of the correlation between OBS and epilepsy, as evidenced by sensitivity analysis, suggests that the influence of excluded factors was minimized.

CONCLUSION

In summary, maintaining a diet rich in antioxidant could potentially decrease the incidence of epilepsy in the adult population in the United States. This research will be a useful reference for the dietary management of individuals with epilepsy. Nevertheless, further investigation is necessary to validate our conclusions. It is recommended that additional research be conducted to elucidate the physiological mechanisms and establish a causal link between OBS and epilepsy.

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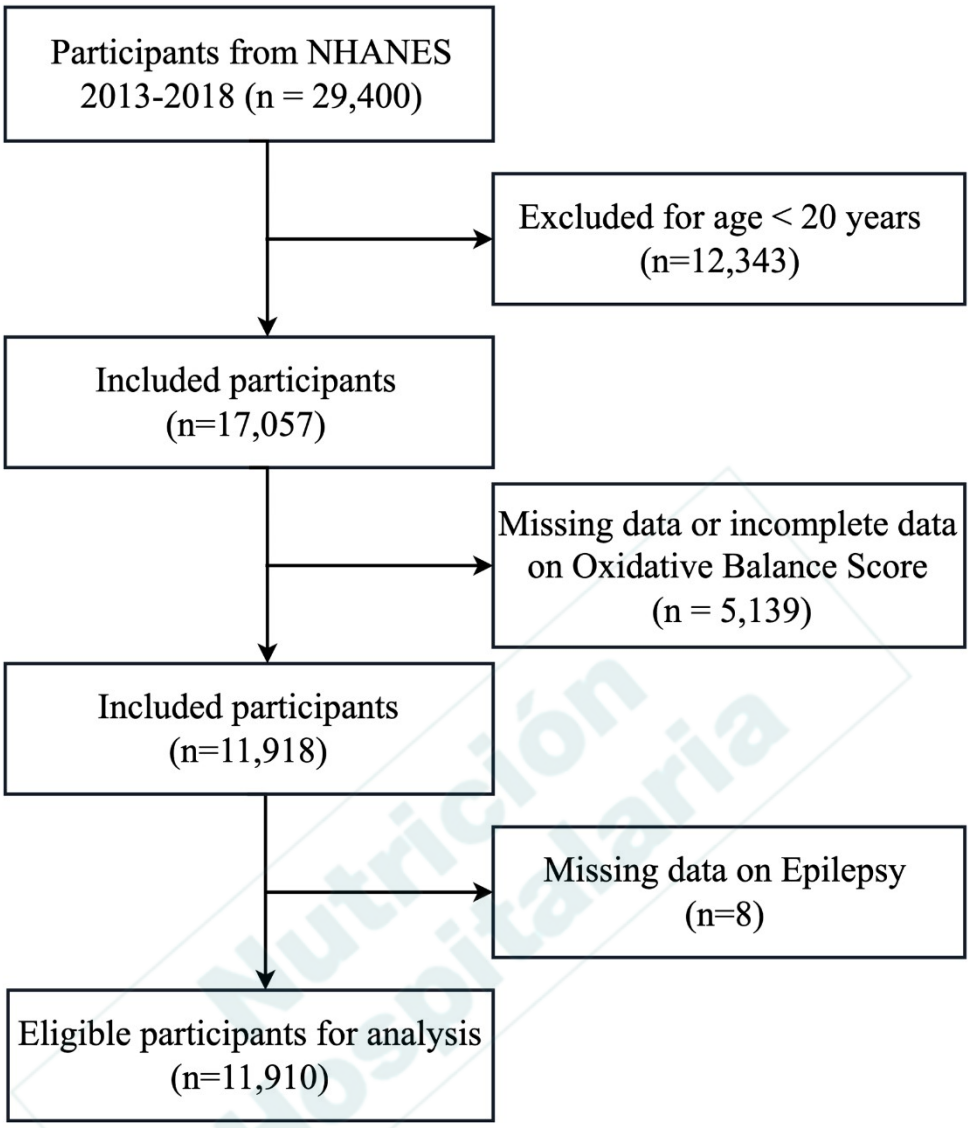

Figure 1. Flow chart of participants selection.

Table I. Oxidative Balance Score assignment scheme

OBS components	**Property**	**Male**			**Female**		
		0	**1**	**2**	**0**	**1**	**2**
Dietary OBS components							
Dietary fiber (g/d)	A	< 12.01	12.01-20.80	> 20.80	< 10.60	10.60-17.40	> 17.40
Carotene (RE/d)	A	< 35.63	35.63-126.54	> 126.54	< 36.21	36.21-149.13	> 149.13
Riboflavin (mg/d)	A	< 1.62	1.62-2.53	> 2.53	< 1.29	1.29-1.95	> 1.95
Niacin (mg/d)	A	< 21.24	21.24-32.95	> 32.95	< 15.32	15.32-25.55	> 25.55
Vitamin B6 (mg/d)	A	< 1.59	1.59-2.54	> 2.54	< 1.17	1.17-1.91	> 1.91
Total folate (mcg/d)	A	< 297.00	297-480.00	> 480.00	< 235.00	235.00-379.00	> 379.00
Vitamin B12 (mcg/d)	A	< 2.95	2.95-5.80	> 5.80	< 2.06	2.06-4.11	> 4.11
Vitamin C (mg/d)	A	< 28.00	28.00-90.40	> 90.40	< 27.10	27.10-83.20	> 83.20
Vitamin E (ATE) (mg/d)	A	< 5.91	5.91-10.33	> 10.33	< 5.15	5.15-8.77	> 8.77
Calcium (mg/d)	A	< 667.00	667.00-1144.00	> 1144.00	< 573.00	573.00-947.00	> 947.00
Magnesium (mg/d)	A	< 245.00	245.00-373.00	> 373.00	< 205	205.00-297.00	> 297.00
Zinc (mg/d)	A	< 8.73	8.73-14.01	> 14.01	< 6.58	6.58-10.27	> 10.27
Copper (mg/d)	A	< 0.95	0.95-1.43	> 1.43	< 0.80	0.80-1.20	> 1.20
Selenium (mcg/d)	A	< 96.40	96.40-148.00	> 148.00	< 72.20	72.20-109.70	> 109.70
Total fat (g/d)	P	> 105.84	66.79-105.84	< 66.79	> 83.07	52.67-83.07	> 83.07

Iron (mg/d)	P	> 17.53	11.20-17.53	< 17.53	> 13.55	8.71-13.55	> 13.55
Lifestyle OBS components							
Physical activity (MET-minutes/week)	A	< 720.00	720.00-4280.00	> 4280.00	< 240.00	240.00-2000.00	> 2000.00
Alcohol (g/d)	P	> 30	≤30	None	> 15	≤15	None
Body mass index (kg/m^2)	P	> 30.50	25.90-30.50	< 25.90	> 32.00	25.80-32.00	< 25.80
Cotinine (ng/mL)	P	> 1.960	0.018-1.960	< 0.018	> 0.087	0.015-0.087	< 0.015

OBS: oxidative balance score; A: antioxidant; P: prooxidant; RE: retinol equivalent; ATE: alpha-tocopherol equivalent; MET: metabolic equivalent.

Table II. Baseline characteristics of participants by Oxidative Balance Score quartile

Characteristics	**Total (*n* = 11910)**	**Q1 (4-13) (*n* = 2807)**	**Q2 (14-19) (*n* = 2917)**	**Q3 (20-24) (*n* = 2690)**	**Q4 (25-37) (*n* = 3496)**	***p*-Value**
Age (years)	47.1 ± 17.0	47.3 ± 17.5	47.8 ± 17.2	47.2 ± 16.9	46.5 ± 16.5	*0.029*
Age (years), (%)						*< 0.001*
20-39	37.6	37.9	37.0	37.0	38.4	
40-59	36.4	34.7	34.5	36.4	38.7	
60-80	26.0	27.4	28.5	26.6	22.9	
Gender, (%)						0.715
Male	50.7	49.9	51.5	50.6	50.6	
Female	49.3	50.1	48.5	49.4	49.4	
Race/ethnicity, (%)						*< 0.001*
Hispanic	15.2	13.8	15.9	14.5	16.0	
Non-Hispanic white	65.1	60.5	63.7	67.2	67.5	
Non-Hispanic black	10.5	17.4	11.1	8.9	6.9	
Non-Hispanic Asian	5.5	3.8	5.9	6.2	5.7	
Other races	3.7	4.5	3.4	3.2	3.9	

Education level, (%)						*< 0.001*
More than high school	64.5	52.3	61.9	66.0	73.2	
High school or equivalent	23.6	32.1	25.4	22.9	17.5	
Less than high school	11.9	15.6	12.7	11.1	9.3	
Marital status, (%)						*< 0.001*
Married/living with partner	62.8	54.7	62.7	62.4	68.4	
Never married	19.7	23.3	17.6	20.5	18.3	
Divorced/separated/widowed	17.5	22	19.7	17.1	13.3	
PIR, (%)						*< 0.001*
< 1.3	19.6	28.7	20.9	17.3	14.4	
1.3-1.8	8.5	10.3	8.9	7.9	7.4	
> 1.8	64.6	52.7	63	67.2	71.6	
Not recorded	7.3	8.3	7.2	7.6	6.6	
Diabetes, (%)						*< 0.001*
Yes	12.5	16.3	14.7	12.6	8.4	
No	87.5	83.7	85.3	87.4	91.6	
Hypertension, (%)						*< 0.001*
Yes	38.7	43.5	42.3	37.7	33.7	
No	61.3	56.5	57.7	62.3	66.3	

Depression, (%)						*< 0.001*
Yes	8.2	13.1	8.7	6.5	6.0	
No	90.9	85.9	90.2	92.8	93.1	
Not recorded	0.9	1.0	1.1	0.7	0.9	
General health condition, (%)						*< 0.001*
Excellent	9.9	6.3	8.3	9.2	13.9	
Very good/good	72.1	69.0	71.4	73.9	73.3	
Fair/poor	17.5	24.3	19.7	16.6	12.2	
Not recorded	0.5	0.4	0.6	0.3	0.6	
Sleep disorders (%)						*< 0.001*
Yes	29.8	34.5	30.6	28.7	27.1	
No	70.2	65.5	69.4	71.3	72.9	
Epilepsy, (%)						*< 0.001*
Yes	0.7	1.5	0.6	0.7	0.5	
No	99.3	98.5	99.4	99.3	99.5	

Mean ± SD for continuous variables: the *p*-value was calculated by the weighted linear regression model. (%) for categorical variables: the *p* value was calculated by the weighted chi-square test. Q: quantile of poverty income ratio.

Table III. The associations between Oxidative Balance Score and epilepsy

Exposure	**Model 1**		**Model 2**		**Model 3**	
	OR (95 % CI)	***p*-value**	**OR (95 % CI)**	***p*-value**	**OR (95 % CI)**	***p*-value**
OBS (continuous)	0.93 (0.90, 0.96)	*< 0.001*	0.93 (0.89, 0.97)	*0.001*	0.95 (0.92, 0.99)	*0.006*
OBS (quartile)						
Quartile 1 (4-13)	reference		reference		reference	
Quartile 2 (14-19)	0.38 (0.16, 0.89)	*0.026*	0.38 (0.16, 0.90)	*0.030*	0.45 (0.19, 1.06)	0.066
Quartile 3 (20-24)	0.44 (0.20, 0.97)	*0.043*	0.44 (0.19, 1.04)	*0.061*	0.54 (0.27, 1.10)	0.087
Quartile 4 (25-37)	0.32 (0.17, 0.57)	*< 0.001*	0.31 (0.17, 0.58)	*< 0.001*	0.47 (0.24, 0.92)	*0.028*
P for trend		*0.001*		*0.002*		*0.031*
OBS.DIETARY (continuous)	0.93 (0.89, 0.97)	*0.002*	0.93 (0.89, 0.98)	*0.004*	0.95 (0.92, 0.99)	*0.014*
OBS.DIETARY (quartile)						
Q1	reference		reference		reference	
Q2	0.3 (0.13, 0.74)	*0.010*	0.3 (0.12, 0.75)	*0.010*	0.35 (0.15, 0.84)	*0.020*
Q3	0.38 (0.18, 0.81)	*0.013*	0.38 (0.17, 0.85)	*0.020*	0.47 (0.24, 0.91)	*0.026*
Q4	0.3 (0.16, 0.57)	*< 0.001*	0.29 (0.15, 0.57)	*< 0.001*	0.41 (0.21, 0.84)	*0.015*
p for trend		*0.001*		*0.002*		*0.012*

OBS.LIFESTYLE (continuous)	0.85 (0.70, 1.02)	0.082	0.86 (0.71, 1.03)	0.102	0.95 (0.80, 1.12)	0.535
OBS.LIFESTYLE (quartile)						
Q1	reference		reference		reference	
Q2	0.72 (0.27, 1.87)	0.489	0.72 (0.28, 1.86)	0.494	0.72 (0.39, 1.34)	0.295
Q3	0.56 (0.25, 1.23)	0.145	0.57 (0.26, 1.24)	0.152	0.69 (0.33, 1.45)	0.320
Q4	0.53 (0.24, 1.16)	0.109	0.56 (0.26, 1.20)	0.135	0.86 (0.45, 1.66)	0.654
p for trend		0.073		0.092		0.591

Model 1: no covariates were adjusted. Model 2: age, gender and race were adjusted. Model gender, race, education, marital status, PIR, hypertension, diabete condition, sleep disorders. OBS: oxidative balance score; OR: odds ratio; CI: confidence interval; PIR: poverty income ratio.

Table IV. Subgroup analysis of the association between Oxidative Balance Score and epilepsy

Subgroup	**Full adjustment model**	***p***	***p* for interaction**
	OBS [OR (95 % CI)]		
Age (years)			0.105
20-39	0.92 (0.85, 1.00)	0.052	
40-59	0.98 (0.92, 1.05)	0.632	
60-80	0.96 (0.90, 1.02)	0.163	
Gender			0.102
Male	0.94 (0.89, 1.00)	0.052	
Female	0.97 (0.90, 1.05)	0.439	
Race/ethnicity			*0.025*
Hispanic	1.03 (0.96, 1.10)	0.408	
Non-Hispanic white	0.93 (0.89, 0.97)	*0.002*	
Non-Hispanic black	1.00 (0.94, 1.05)	0.930	
Non-Hispanic Asian	0.85 (0.69, 1.06)	0.140	
Education level			0.696
More than high school	0.98 (0.92, 1.04)	0.432	
High school or equivalent	0.92 (0.82, 1.02)	0.119	
Less than high school	0.98 (0.89, 1.08)	0.696	
Diabetes			*0.020*
Yes	1.01 (0.90, 1.15)	0.824	
No	0.94 (0.89, 0.98)	*0.011*	

Full adjustment model adjusted for: age, gender, race, education, marital status, PIR, hypertension, diabetes, depression, general health condition, sleep disorders. OBS: oxidative balance score; OR: odds ratio; 95 % CI: 95 % confidence interval; PIR: poverty income ratio.

Supplementary Table I. The classifications of covariates

Covariates	Classification
Age	20-39; 40-59; 60-80
Sex	Male; Female
Race	Hispanic; Non-Hispanic white; Non-Hispanic black; Non-Hispanic Asian; Other races
Education level	More than high school; High school or equivalent; Less than high school
Marital status	Married/living with partner; never married; divorced/separated/widowed
Poverty-income ratio (PIR)	< 1.3; 1.3-1.8; > 1.8
Diabetes[a]	Yes; No
Hypertension[b]	Yes; No
Depression[c]	Yes; No
General health condition[d]	Excellent; Very good/good; Fair/poor
Sleeping disorder[e]	Yes; No

[a]Diabetes was defined as self-reported physician diagnosis or taking insulin or anti-diabetic pills or HbA1c ≥ 6.5 %. [b]Systolic blood pressure (SBP) ≥ 140 mm Hg or diastolic blood pressure (DBP) ≥ 90 mm Hg, self-reported physician diagnosis, or currently taking antihypertensive drugs were hypertensive patients. [c]A total Patient Health Questionnaire (PHQ-9) score of ≥ 10. [d]Self-report of general health condition. [e]Self-reported physician diagnosis.

Supplementary Table II. The baseline characteristics of participants by epilepsy status

Characteristics	**Total (*n* = 11910)**	**Yes (*n* = 93)**	**No (*n* = 11817)**	***p*-value**
OBS (continuous)	20.3 ± 7.1	16.7 ± 8.1	20.4 ± 7.1	*< 0.001*
Quartiles of OBS, (%)				*< 0.001*
Q1	20.7	41.1	20.6	
Q2	23.1	17.5	23.2	
Q3	23.9	21.1	23.9	
Q4	32.2	20.3	32.3	
Age (years)	47.1 ± 17.0	46.1 ± 17.3	47.1 ± 17.0	0.557
Age (years), (%)				0.773
20-39	37.6	38.4	37.6	
40-59	36.4	38.8	36.3	
60-80	26.0	22.8	26.0	
Gender, (%)				0.286
Male	50.7	56.3	50.6	
Female	49.3	43.7	49.4	
Race/ethnicity, (%)				0.556
Hispanic	15.2	13.4	15.2	
Non-Hispanic white	65.1	70.2	65.1	
Non-Hispanic black	10.5	11.8	10.5	
Non-Hispanic Asian	5.5	1.9	5.5	
Other races	3.7	2.6	3.7	
Education level, (%)				*0.002*
More than high school	64.5	46.7	64.7	

High school or equivalent	23.6	34.1	23.5	
Less than high school	11.9	19.2	11.8	
Marital status, (%)				*< 0.001*
Married/living with partner	62.8	42.4	63.0	
Never married	19.7	38.2	19.5	
divorced/separated/ widowed	17.5	19.4	17.5	
PIR, (%)				*0.001*
< 1.3	19.6	32.5	19.5	
1.3-1.8	8.5	10.6	8.5	
> 1.8	64.6	45.1	64.8	
Not recorded	7.3	11.8	7.3	
Diabetes, (%)				0.062
Yes	12.5	19.0	12.4	
No	87.5	81.0	87.6	
Hypertension, (%)				*0.048*
Yes	38.7	48.9	38.6	
No	61.3	51.1	61.4	
Depression, (%)				*< 0.001*
Yes	8.2	13.8	8.2	
No	90.9	72.6	91.0	
Not recorded	0.9	13.6	0.8	
General health condition, (%)				*< 0.001*
Excellent	9.9	5.1	10.0	
Very good/good	72.1	58.0	72.2	

Fair/poor	17.5	36.9	17.3	
Not recorded	0.5		0.5	
Sleep disorders, (%)				0.050
Yes	29.8	39.3	29.7	
No	70.2	60.7	70.3	

Mean ± SD for continuous variables: the *p*-value was calculated by the weighted linear regression model. (%) for categorical variables: the *p*-value was calculated by the weighted chi-square test. PIR: poverty income ratio; OBS: oxidative balance score.