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Associations of oxidative balance score and cognition in US older adults: A cross-sectional study of National Health and Nutrition Examination Survey (NHANES) 2011 to 2014

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Abstract

Background: Oxidative stress is linked to cognitive decline in the elderly. Diet, as a key energy source, affects brain function and serves as a modifiable risk factor for cognitive decline.

Objective: This study investigates the relationship between the Oxidative Balance Score (OBS), which reflects diet and lifestyle impact on oxidative stress, and cognitive function in older adults.

Methods: This study utilized data from the National Health and Nutrition Examination Survey (NHANES) from 2011–2014, including 2716 participants aged 60 and older. Cognitive outcomes measured were the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word Learning test, Animal Fluency test, and Digit Symbol Substitution test. Linear regression models were used to assess the relationship between the OBS and cognitive performance, with stratification and sensitivity analyses conducted to explore these associations further.

Results: Among 2716 participants, higher dietary OBS scores were linked to better cognitive test performance after adjusting for confounders. For example, the highest OBS quartile had a 4.35-point increase in CERAD immediate recall compared to the lowest quartile (OR: 4.35, 95% CI: 2.14–8.84, $p = 0.001$). Subgroup analyses showed this positive association across age groups and genders, though it was stronger among non-Hispanic white participants compared to other racial groups.

Conclusions: Our findings indicate a positive correlation between OBS and cognitive function in older adults, suggesting that an antioxidant-rich diet and lifestyle may help prevent cognitive decline in this population. However, since this study is cross-sectional, further prospective research is needed to confirm these results.

Keywords

Alzheimer's disease, cognitive function, national health and nutrition examination survey (NHANES), older adults, oxidative balance score

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Introduction

Cognitive function includes mental processes such as learning, attention, memory, and decision-making. Research in the United States shows that about one-third of people aged 65 and older have dementia or mild cognitive impairment (MCI).[1] MCI is a syndrome where cognitive decline exceeds what is expected for a person's age and education level.[2] As the population ages, cognitive impairment and dementia have become major healthcare and public health challenges. Currently, apart from some newly approved Alzheimer's drugs, there are no effective treatments to alter the course of dementia.[3] Recent studies have found that healthy lifestyle choices, like regular exercise, a balanced diet, and active social engagement, can help slow cognitive decline.[4,5] Therefore, modifying diet and other controllable risk factors to develop prevention strategies is crucial for preventing or delaying cognitive impairment and dementia.

Oxidative stress is crucial in neurodegenerative diseases, often involving abnormal protein aggregation that produces reactive oxygen species (ROS) and causes mitochondrial dysfunction.[6] Aging increases free radicals, worsening oxidative stress and damaging cells, particularly neurons, leading to cognitive decline.[7] Antioxidants are essential in combating oxidative stress. They neutralize free radicals, chelate metal ions, activate antioxidant systems, and protect biomolecules, thus preventing cognitive decline.[8,9] Increasing dietary antioxidants is a simple, cost-effective way to support cognitive health throughout life. Optimizing diet to boost antioxidant intake is vital for maintaining brain health. Over the past few decades,[10–12] however, many studies differ in their methods of collecting dietary intake data. More importantly, dietary components, including antioxidants, often work synergistically, making it limited to measuring individual components alone.[13] Additionally, lifestyle factors such as smoking, alcohol consumption, and physical activity also affect inflammation and oxidative stress in the body.[14,15]

The Oxidative Balance Score (OBS) is a novel method of assessing antioxidant and oxidant levels using a scoring system with 20 dietary and lifestyle components. It offers a comprehensive measure of the overall balance between pro-oxidants and antioxidants. Higher OBS typically indicates antioxidant predominance. Previous research links OBS negatively to conditions like osteoarthritis, metabolic diseases, and cardiovascular diseases.[16–18] Lifestyle components such as weight management, a balanced diet, and regular exercise are known antioxidants, contributing to a higher OBS and reduced diabetes risk.[19] However, no study has explored the OBS relationship with cognitive function in older adults. Thus, I conducted a cross-sectional study using 2011–2014 National Health and Nutrition Examination Survey (NHANES) data to explore this potential association.

Methods

Source of data and study population

NHANES, a cross-sectional survey, evaluates the health and nutrition status of the US population. Using a stratified multistage probability design, it selects a representative sample. NHANES collects demographic data, dietary intake, physical exams, and lab tests by trained personnel. Additional details on NHANES design and procedures are available elsewhere. This study utilized data from the 2011–2014 NHANES cycles.

This study examines individuals aged 60 and older from two survey cycles spanning 2011 to 2014. Exclusion criteria were applied, which included: 1) participants under 60 years old (n = 16,299); 2) missing OBS data (n = 564); 3) incomplete cognitive function test data (n = 352); 4) duplicate surveys. Following the selection process outlined in Figure 1, our study comprised 2716 participants.

Ethics approval and consent to participate

The study utilized anonymized NHANES data and adhered to ethical guidelines outlined in the Declaration of Helsinki. Approval was obtained from the Ethics Review Board of the National Center for Health Statistics, and participants provided written informed consent.

Assessment of OBS (exposure)

OBS was introduced by Zhang et al. and has since gained widespread validation and adoption in numerous previous research.[20] It comprises 16 dietary and 4 lifestyle components. Dietary OBS involves fiber, carotene, riboflavin, niacin, vitamin B6, total folate, vitamin B12, vitamin C, vitamin E, calcium, magnesium, zinc, copper, selenium, total fat, and iron. Lifestyle OBS includes BMI, physical activity, alcohol consumption, and smoking status. These factors can be classified as pro-oxidants (such as total fat, iron, alcohol intake, BMI, and smoking) and antioxidants (the other 15 components).

Average data from both the in-person dietary interview on the first day at the Mobile Examination Center and the telephone-based dietary interview on the second day were utilized for analysis. Additionally, the combined amount of α-carotene and β-carotene was referred to as total carotene in this study. The components of OBS are scored based on gender with scores ranging from 0 to 2 for antioxidants, with 0 being the lowest and 2 the highest, while for pro-oxidants, the scoring is the opposite. OBS is calculated by summing the scores of these 20 components, with higher OBS indicating higher antioxidant exposure levels. Additionally, in this study, OBS was further categorized by quartiles, with the lowest quartile serving as the reference group in weighted linear regression models.

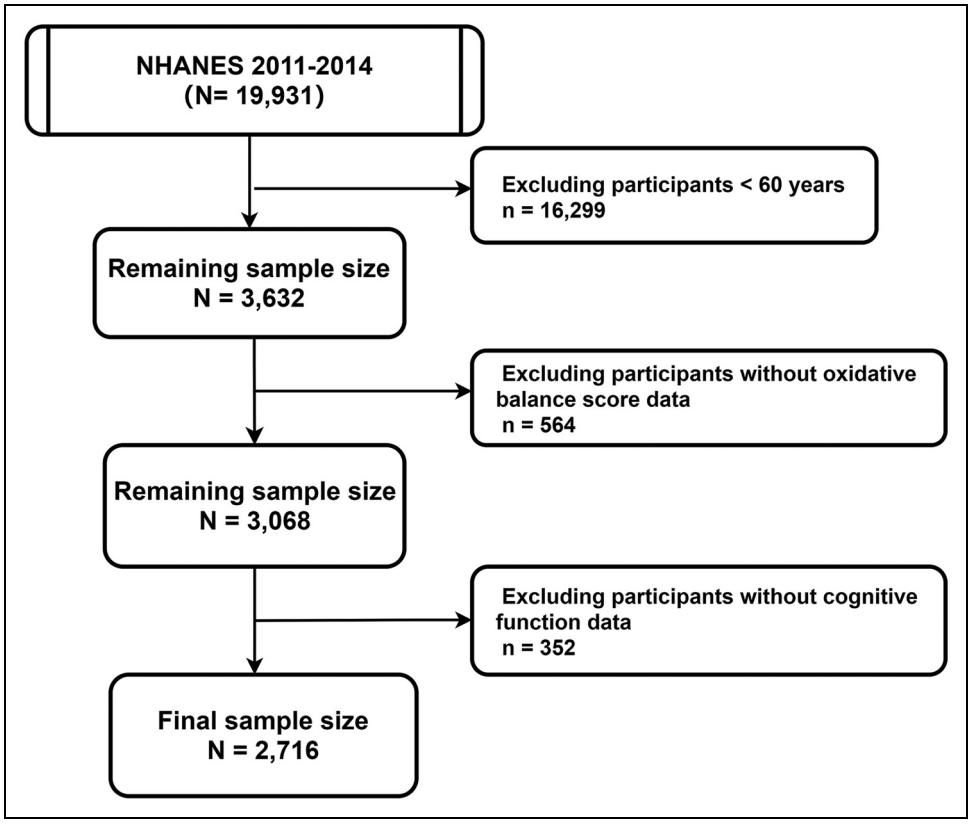

Figure 1. Participant screening process.

For specific components included in OBS, refer to Supplemental Table 1.

Cognitive outcomes

In the NHANES surveys conducted between 2011 and 2014, participants aged 60 and above underwent three cognitive assessments. These tests comprised the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word Learning subset, evaluating immediate and delayed learning of new verbal information (memory); the animal fluency (AF) test, examining categorical verbal fluency (executive function); and the Digit Symbol Substitution Test (DSST), assessing processing speed, sustained attention, and working memory.[21]

In the CERAD modules, participants underwent three rounds of learning trials followed by a delayed recall session. They were tasked with recalling as many words as possible immediately after hearing a list of 10 unrelated words. The delayed recall session occurred around 8–10 min after the initial learning trials. Scores for immediate recall (CERAD-IR) ranged from 0 to 30, while scores for delayed recall (CERAD-DR) ranged from 0 to 10. During the AF test, participants were given one minute to list as many animals as they could, earning a point for each named animal. In the DSST test, participants matched symbols to numbers within a set time limit, with scores ranging from 0 to 133.

Covariates

The study considered various factors, including age, gender, race/ethnicity, income status (measured by poverty-to-income ratio, PIR), body mass index (BMI), education level, smoking and alcohol habits, presence of diabetes mellitus, hypertension, stroke, cardiovascular disease, physical activity, and total cholesterol levels. Racial categories included Mexican Americans, non-Hispanic Blacks, non-Hispanic Whites, other Hispanics, and individuals of other races.

Income status was evaluated using the PIR, which indicates income level and potential eligibility for federal nutrition programs like the Supplemental Nutrition Assistance Program (SNAP), with a PIR of 130% suggesting potential eligibility.[22,23] The study categorized PIR into three groups: < 1.30, 1.30–3.5, and > 3.5. Subjects' education level was categorized as high school or below and above high school. BMI categories included underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5 to < 25 kg/m^2), overweight (BMI 25 to < 30 kg/m^2), and obese (BMI ≥ 30 kg/m^2). Participants' smoking status was classified into three groups: current smokers (those who smoked at least 100 cigarettes in their lifetime and currently smoke), former

Table 1. Participant characteristics by oxidative balance score status, NHANES 2011 to 2014 (n = 2716).

Characteristic	Total Individuals	Oxidative balance score status					
		Overall, N[a] = 2716 (100%)[b]	Q1, N = 742 (21%)[b]	Q2, N = 659 (23%)[b]	Q3, N = 682 (28%)[b]	Q4, N = 633 (28%)[b]	p[c]
Age (y), Median (Mean, SD)	2716	68 (69, 7)	68 (69, 7)	68 (69, 7)	68 (69, 7)	68 (69, 7)	0.3
Age group, n (%)	2716						0.3
60-69 y	1373	1373 (51%)	375 (51%)	321 (49%)	343 (50%)	334 (53%)	
70–79 y	750	750 (28%)	201 (27%)	185 (28%)	196 (29%)	168 (27%)	
80 + y	593	593 (21%)	166 (22%)	153 (23%)	143 (21%)	131 (20%)	
Gender, n (%)	2716						0.04
Female	1380	1380 (51%)	321 (43%)	325 (49%)	365 (53%)	369 (58%)	
Male	1336	1336 (49%)	421 (57%)	334 (51%)	317 (47%)	264 (42%)	
Race, n (%)	2716						<0.001
Mexican American	233	233 (9%)	66 (9%)	54 (8%)	62 (9%)	51 (8%)	
Other Hispanic	274	274 (10%)	84 (11%)	72 (11%)	66 (10%)	52 (8%)	
Non-Hispanic White	1332	1332 (49%)	277 (37%)	318 (48%)	379 (56%)	358 (57%)	
Non-Hispanic Black	645	645 (24%)	252 (34%)	170 (26%)	121 (18%)	102 (16%)	
Other races	232	232 (8%)	63 (8%)	45 (7%)	54 (7%)	70 (11%)	
Education level, n (%)	2716						<0.001
<=High school	675	675 (25%)	275 (37%)	171 (26%)	137 (20%)	92 (15%)	
>High school	2039	2039 (75%)	466 (63%)	487 (74%)	545 (80%)	541 (85%)	
Missing data	2	2 (<0.1%)	1 (<0.1%)	1 (<0.1%)	0 (0%)	0 (0%)	
Ratio of family income to poverty, Median (Mean, SD)	2716	3.12 (3.14, 1.57)	2.19 (2.56, 1.56)	2.72 (2.94, 1.51)	3.58 (3.35, 1.56)	3.91 (3.54, 1.50)	<0.001
Ratio of family income to poverty, n (%)	2716						<0.001
PIR < 1.30	734	734 (27%)	272 (37%)	190 (29%)	155 (23%)	117 (18%)	
PIR: 1.30–3.5	967	967 (36%)	268 (36%)	249 (38%)	237 (35%)	213 (34%)	
PIR > 3.5	807	807 (30%)	144 (19%)	164 (25%)	241 (35%)	258 (41%)	
Missing data	208	208 (7%)	58 (8%)	56 (8%)	49 (7%)	45 (7%)	
Body Mass Index, Median (Mean, SD)	2716	28 (29, 6)	29 (30, 7)	29 (30, 6)	29 (30, 6)	27 (27, 5)	<0.001
Body Mass Index group, n (%)	2716						<0.001
Underweight (<18.5)	38	38 (1%)	11 (1%)	7 (1%)	7 (1%)	13 (2%)	
Normal (18.5 to <25)	681	681 (25%)	160 (22%)	145 (22%)	167 (24%)	209 (33%)	
Overweight (25 to <30)	939	939 (35%)	248 (33%)	231 (35%)	239 (35%)	221 (35%)	
Obese (30 or greater)	1023	1023 (38%)	302 (41%)	270 (41%)	265 (39%)	186 (29%)	
Missing data	35	35 (1%)	21 (3%)	6 (<0.1%)	4 (<0.1%)	4 (<0.1%)	
Smoking status, n (%)	2716						<0.001
Current	340	340 (13%)	157 (21%)	81 (12%)	58 (9%)	44 (7%)	
Former	1046	1046 (39%)	265 (36%)	261 (40%)	285 (42%)	235 (37%)	
Non-smoker	1330	1330 (48%)	320 (43%)	317 (48%)	339 (49%)	354 (56%)	

(continued)

Table 1. Continued.

Characteristic	Total Individuals	Oxidative balance score status					
		Overall, N[a] = 2716 (100%)[b]	Q1, N = 742 (21%)[b]	Q2, N = 659 (23%)[b]	Q3, N = 682 (28%)[b]	Q4, N = 633 (28%)[b]	p[c]
Alcohol consumption status, n (%)	2716						0.2
Non-drinker	842	842 (31%)	245 (33%)	212 (32%)	205 (30%)	180 (28%)	
1–5 drinks/month	1310	1310 (48%)	358 (48%)	317 (48%)	332 (49%)	303 (48%)	
5–10 drinks/month	120	120 (5%)	29 (4%)	33 (5%)	25 (4%)	33 (5%)	
10 + drinks/month	423	423 (16%)	102 (14%)	92 (14%)	116 (17%)	113 (19%)	
Missing data	21	21 (<0.1%)	8 (<0.1%)	5 (<0.1%)	4 (<0.1%)	4 (<0.1%)	
Diabetes group, n (%)	2716						<0.001
Yes	804	804 (30%)	278 (37%)	203 (31%)	201 (29%)	122 (19%)	
No	1912	1912 (70%)	464 (63%)	456 (69%)	481 (71%)	511 (81%)	
Hypertension group, n (%)	2716						0.005
Yes	1693	1693 (62%)	502 (68%)	404 (61%)	434 (60%)	353 (56%)	
No	1018	1018 (38%)	237 (32%)	255 (39%)	247 (40%)	279 (44%)	
Missing data	5	5 (<0.1%)	3 (<0.1%)	0 (0%)	1 (<0.1%)	1 (<0.1%)	
Cardiovascular disease, n (%)	2716						0.07
Yes	239	239 (9%)	74 (10%)	62 (9%)	64 (9%)	39 (6%)	
No	2473	2473 (91%)	667 (90%)	595 (91%)	617 (91%)	594 (94%)	
Missing data	4	4 (<0.1%)	1 (<0.1%)	2 (<0.1%)	1 (<0.1%)	0 (0%)	
Stroke group, n (%)	2716						0.037
Yes	187	187 (7%)	69 (9%)	40 (7%)	38 (6%)	40 (6%)	
No	2524	2524 (93%)	673 (91%)	617 (93%)	644 (94%)	590 (94%)	
Missing data	5	5 (<0.1%)	0 (0%)	2 (<0.1%)	0 (0%)	2 (<0.1%)	
Oxidative balance score, Median (Mean, SD)	2716	21 (20, 8)	9 (8, 4)	17 (17, 2)	22 (22, 2)	29 (29, 2)	<0.001
CERAD: Total Score of immediate recall (3 Recall trials), Median (Mean, SD)	2716	20.0 (19.8, 4.4)	19.0 (18.5, 4.7)	20.0 (19.4, 4.3)	20.0 (19.9, 4.2)	21.0 (21.1, 4.2)	<0.001
CERAD: Delayed Recall Score, Median (Mean, SD)	2716	6.00 (6.27, 2.27)	6.00 (5.69, 2.36)	6.00 (6.09, 2.21)	7.00 (6.36, 2.30)	7.00 (6.78, 2.12)	<0.001
Animal Fluency: Total Score, Median (Mean, SD)	2716	18.0 (18.2, 5.7)	16.0 (16.2, 5.3)	17.0 (17.7, 5.6)	18.0 (18.6, 5.5)	20.0 (19.8, 5.7)	<0.001
Digit Symbol: Score, Median (Mean, SD)	2716	53 (52, 17)	47 (45, 17)	51 (51, 16)	54 (55, 16)	58 (57, 15)	<0.001

[a]N not Missing (unweighted).
[b]Median (IQR) for continuous; n (%) for categorical.
[c]Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction.

smokers (those who smoked at least 100 cigarettes in their lifetime but currently do not smoke), and never smokers (those who either never smoked or smoked fewer than 100 cigarettes in their lifetime). Participants' alcohol consumption was assessed using a questionnaire, with categories including non-drinkers, those consuming 1–5 drinks per month, 5–10 drinks per month, and those consuming 10 or more drinks per month. Cardiovascular disease (CVD) in this study comprises coronary heart disease, heart failure, and angina. The diagnostic criteria for diabetes included physician-diagnosed diabetes, a glycosylated hemoglobin (HbA1c) level above 6.5%, and a fasting blood glucose (FBG) level of ≥7.0 mmol/L. The presence of any of these three conditions signified a diabetes diagnosis.

Statistical analysis

Given the complex sampling method employed, the study utilized weighted statistical analysis. Continuous variables were represented as mean (SD), while categorical variables were expressed as frequency (percentage). Baseline characteristics were compared using chi-square tests for categorical variables and t-tests or one-way analysis of variance for continuous variables. Categorical data were summarized using counts and percentages [n (%)], with comparisons conducted using the Rao-Scott chi-square test. Statistical analyses were carried out using SPSS (version 23.0) and R (version 4.1.3) software.

Participants' characteristics were described using OBS quartiles, with means for continuous variables and proportions for categorical variables. Weighted linear regression models analyzed the link between OBS and cognitive function, with results shown as adjusted odds ratios (ORs) and 95% confidence intervals (CIs). Cognitive test outcomes were the dependent variables, and OBS was included as both a continuous variable and quartiles, using the lowest quartile as the reference. Model 1 adjusted for gender and age; Model 2 also adjusted for race, education, and PIR; and Model 3 further adjusted for BMI, alcohol use, smoking, hypertension, diabetes, stroke, cholesterol levels, cardiovascular disease, and physical activity. Variance inflation factors assessed multicollinearity among covariates. Subgroup analyses by age, gender, race, and BMI evaluated the OBS impact on cognitive function in different groups. Missing covariate values were handled with multiple imputations. A p-value < 0.05 was considered statistically significant.

Results

Demographics

The baseline characteristics of 2716 participants are shown in Table 1. Participants were divided into OBS quartiles. Except for age, cardiovascular disease, and alcohol consumption, significant differences were found across quartiles for PIR, gender, race, education level, total cholesterol, diabetes, hypertension, and stroke (all $p < 0.05$). As OBS quartiles increased, participants tended to be wealthier, with higher proportions of women, non-Hispanic whites, and higher education levels. They also had lower BMIs, were more likely to be single, scored higher on the four cognitive function tests, and had lower rates of diabetes and hypertension. Notably, higher OBS levels corresponded to higher scores on all four cognitive tests, including CERAD immediate and delayed recall, animal fluency, and digit symbol tests.

Association between oxidative balance score and cognitive function

The linear regression models for CERAD immediate recall, delayed recall, animal fluency, and digit symbol scores, as shown in Table 2, exhibit a consistent pattern of results. Higher OBS values, whether as continuous or categorical variables, correlate with increased scores across all three tests. In Model 3, after adjusting for covariates including age and gender, OBS exhibits a positive correlation with CERAD immediate recall scores (OR = 1.07; 95% CI [1.03, 1.10]; $p = 0.001$). When OBS is divided into quartiles and adjusted for potential confounders, individuals in the highest quartile score 4.35 points higher on CERAD immediate recall compared to the lowest quartile (OR = 4.35; 95% CI [2.14, 8.84]; $p = 0.001$).

Similar results are observed in Model 3, where OBS is positively associated with CERAD delayed recall scores (OR = 1.03; 95% CI [1.01, 1.05]; $p = 0.002$), animal fluency scores (OR = 1.09; 95% CI [1.04, 1.13]; $p < 0.001$), and digit symbol scores (OR = 1.21; 95% CI [1.08, 1.35]; $p = 0.003$). After categorizing OBS into quartiles and adjusting for potential confounders, individuals in the highest OBS quartile score 1.9 points higher on CERAD delayed recall (OR = 1.9; 95% CI [1.32, 2.74]; $p = 0.003$), 5.81 points higher on animal fluency (OR = 5.81; 95% CI [2.63, 12.9]; $p < 0.001$), and 60.8 points higher on digit symbol scores (OR = 60.8; 95% CI [5.63, 656]; $p = 0.004$) compared to those in the lowest quartile.

Subgroup analyses for CERAD immediate recall score

The subgroup analysis stratified participants by age, gender, and race to assess the relationship between OBS and the results of three cognitive function tests. The goal was to determine the consistency of this relationship in the general population and identify any potential demographic differences.

The results for the CERAD immediate recall score showed a positive correlation with OBS across different age groups. In the 60–69 age group, the OR was 1.05 (95% CI [1.01, 1.09], $p = 0.027$); in the 70–79 age group,

Table 2. Linear regression models for associations oxidative balance score with cognitive tests score in NHANES 2011 to 2014.

Cognitive Tests Score Group	Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
CERAD: Total Score of immediate recall (3 Recall trials)	Oxidative balance score	1.11 (1.08–1.14)	<0.001	1.08 (1.05–1.11)	<0.001	1.07 (1.03–1.10)	0.001
	Oxidative balance score, quartile						
	Q1	Ref		Ref		Ref	
	Q2	2.17 (1.49–3.16)	<0.001	1.5 (0.91–2.48)	0.11	1.37 (0.78–2.39)	0.2
	Q3	3.12 (1.51–6.43)	0.003	1.74 (0.81–3.71)	0.15	1.55 (0.68–3.50)	0.3
	Q4	9.86 (5.78–16.8)	<0.001	5.19 (2.88–9.34)	<0.001	4.35 (2.14–8.84)	0.001
CERAD: Delayed Recall Score	Oxidative balance score	1.05 (1.03–1.06)	<0.001	1.03 (1.02–1.05)	<0.001	1.03 (1.01–1.05)	0.002
	Oxidative balance score, quartile						
	Q1	Ref		Ref		Ref	
	Q2	1.42 (1.16–1.72)	0.001	1.23 (0.96–1.57)	0.092	1.17 (0.90–1.51)	0.2
	Q3	1.72 (1.18–2.52)	0.007	1.34 (0.88–2.03)	0.2	1.3 (0.82–2.06)	0.2
	Q4	2.58 (1.92–3.45)	<0.001	1.96 (1.39–2.76)	<0.001	1.9 (1.32–2.74)	0.003
Animal Fluency: Total Score	Oxidative balance score	1.18 (1.13–1.23)	<0.001	1.11 (1.07–1.16)	<0.001	1.09 (1.04–1.13)	<0.001
	Oxidative balance score, quartile						
	Q1	Ref		Ref		Ref	
	Q2	4.19 (2.08–8.44)	<0.001	2.49 (1.21–5.14)	0.016	2.17 (1.01–4.67)	0.048
	Q3	9.46 (4.48–20.0)	<0.001	3.32 (1.59–6.93)	0.003	2.95 (1.43–6.11)	0.008
	Q4	31 (16.1–59.4)	<0.001	9.4 (4.47–19.8)	<0.001	5.81 (2.63–12.9)	<0.001
Digit Symbol: Score	Oxidative balance score	1.7 (1.50–1.92)	<0.001	1.3 (1.17–1.44)	<0.001	1.21 (1.08–1.35)	0.003
	Oxidative balance score, quartile						
	Q1	Ref		Ref		Ref	
	Q2	225 (21.1–2403)	<0.001	15.7 (1.73–143)	0.017	11.6 (1.26–107)	0.034
	Q3	6144 (717–52,642)	<0.001	73.2 (8.12–659)	<0.001	38.7 (4.10–366)	0.005
	Q4	68,774 (5983–790,601)	<0.001	248 (25.1–2459)	<0.001	60.8 (5.63–656)	0.004

OR: odds ratio, CI: confidence interval; Model 1 was adjusted for age and gender; Model 2, adjusted for age, gender, race, education, and the ratio of family income to poverty; Model 3 was adjusted for age, gender, race, education, the ratio of family income to poverty, BMI, alcohol consumption status, smoking status, hypertension, diabetes, stroke, cardiovascular disease, and physical activity.

the OR was 1.09 (95% CI [1.04, 1.15], p = 0.002); and in the 80 + age group, the OR was 1.1 (95% CI [1.02, 1.17], p = 0.013). Compared to the lowest quartile, individuals in the highest OBS quartile scored higher on the CERAD immediate recall by 2.85 points in the 60–69 age group (OR = 2.85, 95% CI [1.25, 6.52], p = 0.002); by 6.93 points in the 70–79 age group (OR = 6.93, 95% CI [2.32, 20.7], p = 0.002); and by 7.81 points in the 80 + age group (OR = 7.81, 95% CI [1.54, 39.7], p = 0.018).

Gender stratification analysis also revealed a positive correlation. For females, the OR was 1.06 (95% CI [1.02, 1.11], p = 0.004), and for males, the OR was 1.07 (95% CI [1.02, 1.13], p = 0.016). Compared to the lowest quartile, females in the highest OBS quartile scored 1.07 points higher on the CERAD immediate recall (OR = 3.14, 95% CI [1.40, 7.04], p = 0.01), while males scored 6.07 points higher (OR = 6.07, 95% CI [1.81, 20.4], p = 0.008). However, when stratified by race, this positive correlation was significant only among non-Hispanic white participants (OR = 1.08, 95% CI [1.04, 1.12], p < 0.001), with no significant correlation observed in other racial groups (Table 3).

Subgroup analyses for CERAD delayed recall score

Subgroup analysis for the CERAD delayed recall scores showed a positive correlation between OBS and CERAD delayed recall scores across different age groups. In the 60–69 age group, the OR was 1.03 (95% CI [1.00, 1.05], p = 0.038); in the 70–79 age group, the OR was 1.03 (95% CI [1.00, 1.06], p = 0.015); and in the 80 + age group, the OR was 1.05 (95% CI [1.01, 1.09], p = 0.019). Compared to the lowest quartile, individuals in the highest OBS quartile scored 1.66 points higher on the CERAD delayed recall in the 60–69 age group (OR = 1.66, 95% CI [1.03, 2.68], p = 0.039); 1.7 points higher in the 70–79 age group (OR = 1.7, 95% CI [1.11, 3.71], p = 0.03); and 3.02 points higher in the 80 + age group (OR = 3.02, 95% CI [1.32, 6.88], p = 0.014).

Gender stratification analysis showed a similar positive correlation only among female participants. For females, the OR was 1.04 (95% CI [1.01, 1.06], p = 0.004). Compared to the lowest quartile, females in the highest OBS quartile scored 2.01 points higher on the CERAD

Table 3. Subgroup analysis of the association between oxidative balance score and the total score of immediate recall of CERAD test.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
Age subgroup	60–69 y	Oxidative balance score	1.1 (1.06–1.15)	<0.001	1.06 (1.02–1.10)	0.002	1.05 (1.01–1.09)	0.027
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.66 (0.89–3.10)	0.1	1.14 (0.54–2.41)	0.7	1.03 (0.47–2.26)	>0.9
		Q3	2.52 (0.97–6.58)	0.058	1.38 (0.52–3.61)	0.5	1.27 (0.46–3.48)	0.6
		Q4	8.39 (4.02–17.5)	<0.001	3.67 (1.79–7.51)	0.001	2.85 (1.25–6.52)	0.018
	70–79 y	Oxidative balance score	1.11 (1.06–1.17)	<0.001	1.09 (1.04–1.15)	0.001	1.09 (1.04–1.15)	0.002
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	2.77 (1.22–6.29)	0.017	1.54 (0.59–4.01)	0.4	1.53 (0.56–4.21)	0.4
		Q3	4.23 (1.22–14.6)	0.024	2.63 (0.77–8.98)	0.12	2.63 (0.81–8.60)	0.1
		Q4	10.9 (3.96–30.3)	<0.001	7.18 (2.42–21.3)	0.001	6.93 (2.32–20.7)	0.002
	80 + y	Oxidative balance score	1.14 (1.06–1.22)	<0.001	1.11 (1.04–1.19)	0.004	1.1 (1.02–1.17)	0.013
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	3.84 (1.31–11.2)	0.016	3.66 (1.10–12.2)	0.036	2.98 (0.87–10.2)	0.077
		Q3	6.25 (2.37–16.5)	<0.001	3.72 (1.19–11.6)	0.026	3.01 (0.95–9.58)	0.06
		Q4	14.9 (2.92–75.6)	0.002	9.5 (1.85–48.8)	0.009	7.81 (1.54–39.7)	0.018
Gender subgroup	Female	Oxidative balance score	1.11 (1.07–1.15)	<0.001	1.08 (1.04–1.12)	<0.001	1.06 (1.02–1.11)	0.004
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.19 (0.60–2.37)	0.6	0.84 (0.37–1.89)	0.7	0.82 (0.35–1.89)	0.6
		Q3	2.45 (0.95–6.33)	0.063	1.42 (0.55–3.68)	0.5	1.25 (0.47–3.30)	0.6
		Q4	6.64 (3.38–13.1)	<0.001	3.72 (1.74–7.96)	0.002	3.14 (1.40–7.04)	0.01
	Male	Oxidative balance score	1.12 (1.06–1.17)	<0.001	1.08 (1.03–1.13)	0.002	1.07 (1.02–1.13)	0.016
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	3.93 (1.83–8.41)	<0.001	2.69 (1.15–6.31)	0.025	2.23 (0.85–5.84)	0.092
		Q3	3.74 (1.38–10.1)	0.011	2.02 (0.77–5.35)	0.15	1.87 (0.63–5.58)	0.2
		Q4	14.5 (5.26–39.8)	<0.001	7.21 (2.57–20.2)	<0.001	6.07 (1.81–20.4)	0.008
Race subgroup	Mexican American	Oxidative balance score	1.11 (1.02–1.20)	0.02	1.06 (0.98–1.15)	0.13	1.03 (0.98–1.12)	0.2
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	2.91 (0.54–15.7)	0.2	3.75 (0.56–25.1)	0.14	2.62 (0.54–21.15)	0.16
		Q3	5.85 (1.08–31.7)	0.042	4.01 (1.11–14.4)	0.037	3.47 (0.89–18.76)	0.25
		Q4	5.36 (0.81–35.2)	0.075	2.06 (0.23–18.3)	0.5	0.88 (0.14–15.67)	0.16
	Other Hispanic	Oxidative balance score	1.01 (0.92–1.10)	>0.9	0.97 (0.90–1.05)	0.4	0.96 (0.89–1.04)	0.3
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	3.18 (0.63–16.0)	0.15	2.56 (0.36–18.2)	0.3	2.03 (0.23–17.9)	0.4
		Q3	2.04 (0.30–13.8)	0.4	1.02 (0.19–5.54)	>0.9	1.15 (0.14–9.21)	0.9
		Q4	0.73 (0.13–4.07)	0.7	0.31 (0.06–1.68)	0.2	0.25 (0.04–1.58)	0.11

(continued)

Table 3. Continued.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
	Non-Hispanic White	Oxidative balance score	1.12 (1.08–1.16)	<0.001	1.09 (1.05–1.12)	<0.001	1.08 (1.04–1.12)	<0.001
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.82 (1.09–3.03)	0.024	1.26 (0.63–2.51)	0.5	1.25 (0.61–2.55)	0.5
		Q3	2.89 (1.17–7.17)	0.023	1.55 (0.62–3.85)	0.3	1.52 (0.62–3.75)	0.3
		Q4	11.5 (6.01–22.0)	<0.001	6.08 (3.07–12.0)	<0.001	5.95 (2.76–12.8)	<0.001
	Non-Hispanic Black	Oxidative balance score	1.09 (1.03–1.15)	0.003	1.05 (1.00–1.11)	0.068	1.05 (0.99–1.12)	0.089
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	3.06 (0.89–10.6)	0.075	2.14 (0.60–7.56)	0.2	1.77 (0.46–6.87)	0.4
		Q3	5.16 (1.82–14.7)	0.003	3.6 (1.15–11.3)	0.03	3.76 (1.12–12.6)	0.035
		Q4	3.52 (1.10–11.3)	0.035	1.57 (0.47–5.24)	0.4	1.53 (0.44–5.34)	0.5
	Other races	Oxidative balance score	1.09 (1.02–1.16)	0.011	1.07 (1.0–1.15)	0.068	1.07 (0.99–1.17)	0.085
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	4.47 (0.38–52.8)	0.2	4.73 (0.31–71.7)	0.2	5.15 (0.31–85.9)	0.2
		Q3	6.54 (1.29–33.3)	0.026	4.87 (0.87–27.1)	0.068	5.29 (0.62–44.8)	0.1
		Q4	9.95 (2.20–45.1)	0.005	6.39 (1.15–35.6)	0.036	7.98 (0.84–75.8)	0.063

OR: odds ratio, CI: confidence interval; Model 1 was adjusted for age and gender; Model 2, adjusted for age, gender, race, education, and the ratio of family income to poverty; Model 3 was adjusted for age, gender, race, education, the ratio of family income to poverty, BMI, alcohol consumption status, smoking status, hypertension, diabetes, stroke, cardiovascular disease, and physical activity.

delayed recall (OR = 2.01, 95% CI [1.27, 3.18], p = 0.007). However, in the race stratification analysis, a positive correlation between OBS and CERAD delayed recall scores was found across all racial groups except for Mexican Americans (Table 4).

Subgroup analyses for animal fluency score

Subgroup analysis for animal fluency test scores showed a positive correlation between OBS and animal fluency scores across all age groups except the 70–79 age group. In the 60–69 age group, the OR was 1.11 (95% CI [1.05, 1.17], p = 0.001); in the 80 + age group, the OR was 1.11 (95% CI [1.00, 1.23], p = 0.042). Compared to the lowest quartile, individuals in the highest OBS quartile scored 8.43 points higher on the animal fluency test in the 60–69 age group (OR = 8.43, 95% CI [3.29, 21.6], p < 0.001); and 8.19 points higher in the 80 + age group (OR = 8.19, 95% CI [1.05, 70.4], p = 0.045).

Gender stratification analysis showed similar positive correlations. For females, the OR was 1.09 (95% CI [1.03, 1.16], p = 0.008), and for males, the OR was 1.09 (95% CI [1.02, 1.16], p = 0.014). Compared to the lowest quartile, females in the highest OBS quartile scored 5.64 points higher on the animal fluency test (OR = 5.64, 95% CI [1.71, 18.6], p = 0.009); males scored 6.38 points higher (OR = 6.38, 95% CI [2.09, 19.5], p = 0.004). However, in the race stratification analysis, a positive correlation between OBS and animal fluency scores was found in Mexican Americans, non-Hispanic whites, and non-Hispanic blacks, but not in other Hispanics and other races (Table 5).

Subgroup analyses for digit symbol score

Subgroup analysis for digit symbol test scores showed a positive correlation between OBS and digit symbol scores in all age groups except those 80 and older. In the 60–69 age group, the OR was 1.18 (95% CI [1.03, 1.35], p = 0.024); in the 70–79 age group, the OR was 1.29 (95% CI [1.08, 1.54], p = 0.008). Compared to the lowest quartile, individuals in the highest OBS quartile scored 29.9 points higher in the 60–69 age group (OR = 29.9, 95% CI [1.69, 528], p = 0.025); and 169 points higher in the 70–79 age group (OR = 169, 95% CI [3.33, 8562], p = 0.015).

Gender stratification also showed positive correlations. For females, the OR was 1.32 (95% CI [1.16, 1.50], p < 0.001), and for males, the OR was 1.11 (95% CI [1.08, 1.25], p = 0.044). Compared to the lowest quartile, females in the highest OBS quartile scored 268 points

Table 4. Subgroup analysis of the association between oxidative balance score and the delayed recall score of the CERAD test.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
Age subgroup	60–69 y	Oxidative balance score	1.04 (1.02–1.06)	<0.001	1.03 (1.01–1.05)	0.01	1.03 (1.00–1.05)	0.038
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.3 (0.93–1.83)	0.12	1.1 (0.76–1.59)	0.6	1.04 (0.72–1.50)	0.8
		Q3	1.6 (1.04–2.48)	0.035	1.29 (0.81–2.04)	0.3	1.31 (0.80–2.13)	0.2
		Q4	2.37 (1.61–3.49)	<0.001	1.73 (1.15–2.59)	0.01	1.66 (1.03–2.68)	0.039
	70–79 y	Oxidative balance score	1.04 (1.01–1.07)	0.012	1.03 (1.00–1.06)	0.08	1.03 (1.00–1.06)	0.015
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.35 (0.73–2.51)	0.3	1.09 (0.58–2.03)	0.8	1.05 (0.55–2.03)	0.9
		Q3	2 (0.93–4.30)	0.075	1.51 (0.69–3.32)	0.3	1.44 (0.64–3.26)	0.3
		Q4	2.27 (1.15–4.46)	0.02	1.79 (1.09–3.59)	0.016	1.7 (1.11–3.71)	0.03
	80 + y	Oxidative balance score	1.06 (1.03–1.10)	<0.001	1.05 (1.02–1.08)	0.005	1.05 (1.01–1.09)	0.019
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	2.04 (1.18–3.56)	0.013	2.1 (1.13–3.90)	0.021	1.9 (0.96–3.79)	0.064
		Q3	2.01 (1.22–3.31)	0.008	1.56 (0.84–2.91)	0.15	1.41 (0.68–2.92)	0.3
		Q4	3.98 (1.97–8.05)	<0.001	3.31 (1.57–6.97)	0.003	3.02 (1.32–6.88)	0.014
Gender subgroup	Female	Oxidative balance score	1.05 (1.04–1.07)	<0.001	1.04 (1.02–1.06)	<0.001	1.04 (1.01–1.06)	0.004
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.26 (0.87–1.82)	0.2	1.07 (0.68–1.68)	0.8	1.04 (0.64–1.68)	0.9
		Q3	1.64 (0.99–2.75)	0.056	1.30 (0.74–2.30)	0.3	1.24 (0.68–2.29)	0.4
		Q4	2.81 (2.02–3.91)	<0.001	2.19 (1.43–3.37)	0.001	2.01 (1.27–3.18)	0.007
	Male	Oxidative balance score	1.04 (1.01–1.07)	0.008	1.02 (0.99–1.05)	0.11	1.03 (0.99–1.06)	0.11
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.61 (1.19–2.16)	0.003	1.44 (1.03–2.03)	0.036	1.33 (0.91–1.94)	0.13
		Q3	1.81 (1.12–2.91)	0.017	1.38 (0.84–2.28)	0.2	1.35 (0.77–2.37)	0.3
		Q4	2.27 (1.29–4.01)	0.006	1.71 (0.92–3.18)	0.084	1.72 (0.88–3.38)	0.1
Race subgroup	Mexican American	Oxidative balance score	1.06 (1.01–1.11)	0.02	1.04 (0.99–1.08)	0.11	1.02 (0.98–1.07)	0.2
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	2.55 (1.08–6.01)	0.036	2.62 (0.98–7.04)	0.054	2.1 (0.78–3.47)	0.3
		Q3	1.86 (0.64–5.36)	0.2	1.34 (0.51–3.56)	0.5	1.19 (0.82–3.18)	0.4
		Q4	3.58 (1.30–9.82)	0.019	2.08 (0.80–5.44)	0.11	1.31 (0.92–3.43)	0.16
	Other Hispanic	Oxidative balance score	1.05 (1.02–1.09)	0.006	1.04 (1.01–1.07)	0.02	1.04 (1.01–1.06)	0.024
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.79 (0.79–4.05)	0.2	1.77 (0.70–4.49)	0.2	1.72 (0.69–4.30)	0.2
		Q3	2.2 (1.03–4.68)	0.043	1.78 (0.87–3.64)	0.11	1.93 (0.81–4.58)	0.11
		Q4	2.54 (1.26–5.13)	0.012	1.83 (1.01–3.62)	0.046	1.62 (1.02–3.19)	0.037
	Non-Hispanic White	Oxidative balance score	1.04 (1.02–1.06)	<0.001	1.03 (1.01–1.05)	0.002	1.03 (1.01–1.05)	0.001
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.25 (0.97–1.62)	0.081	1.1 (0.79–1.53)	0.5	1.09 (0.80–1.49)	0.6
		Q3	1.65 (1.01–2.69)	0.045	1.28 (0.76–2.14)	0.3	1.32 (0.78–2.21)	0.3
		Q4	2.43 (1.66–3.55)	<0.001	1.88 (1.27–2.79)	0.003	1.99 (1.35–2.92)	0.002

(continued)

Table 4. Continued.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
	Non-Hispanic Black	Oxidative balance score	1.05 (1.03–1.08)	<0.001	1.03 (1.01–1.06)	0.009	1.03 (1.01–1.06)	0.013
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	1.51 (0.83–2.74)	0.2	1.2 (0.69–2.06)	0.5	1.11 (0.61–2.00)	0.7
		Q3	1.91 (1.15–3.16)	0.015	1.43 (0.80–2.55)	0.2	1.48 (0.83–2.64)	0.2
		Q4	2.62 (1.42–4.82)	0.003	1.77 (1.02–3.23)	0.04	1.8 (1.05–3.42)	0.047
	Other races	Oxidative balance score	1.07 (1.03–1.11)	0.003	1.05 (1.01–1.10)	0.021	1.05 (1.00–1.11)	0.048
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	3.09 (1.01–9.44)	0.049	2.86 (0.85–9.61)	0.084	2.88 (0.84–9.86)	0.076
		Q3	2.09 (1.05–4.17)	0.037	1.7 (0.86–3.36)	0.12	1.95 (0.76–5.01)	0.12
		Q4	4.98 (1.77–14.0)	0.004	3.74 (1.27–11.0)	0.02	3.49 (1.01–12.1)	0.049

OR: odds ratio; CI: confidence interval; Model 1 was adjusted for age and gender; Model 2, adjusted for age, gender, race, education, and the ratio of family income to poverty; Model 3 was adjusted for age, gender, race, education, the ratio of family income to poverty, BMI, alcohol consumption status, smoking status, hypertension, diabetes, stroke, cardiovascular disease, and physical activity.

higher (OR = 268, 95% CI [14.8, 4863], p = 0.001); males scored 12.7 points higher (OR = 12.7, 95% CI [1.90, 180], p = 0.048). Race stratification analysis showed a positive correlation between OBS and digit symbol test scores across all racial groups (Table 6).

Discussion

This study utilized data from two waves of NHANES (2011–2014) to assess the cross-sectional relationship between OBS and cognitive function in elderly Americans. Our findings indicate that higher OBS is associated with better performance in memory, language, and executive function tests. Subgroup analyses revealed that this positive association between OBS and cognitive function is consistent across different age groups and genders. However, the positive relationship between OBS and cognitive function tests was not uniformly observed across different racial groups.

OBS, derived from dietary and lifestyle factors, estimates individual oxidative stress levels and serves as a comprehensive measure of oxidative and antioxidative balance. Although influenced by external exposures like diet and lifestyle, various studies have validated OBS's reliability by linking it to inflammation markers, oxidative stress indicators (f2-isoprostanes), and γ-glutamyl transferase.[24,25] Furthermore, research has shown a connection between OBS and oxidative stress, including its mediating role between OBS and depressive symptoms.[26] Initially, OBS included only vitamin C, β-carotene, and iron but has since expanded to include more factors related to oxidative stress. Vitamin E intake, for example, can mitigate Alzheimer's-related oxidative stress, delaying cognitive decline. Oxidative stress, triggered by substances like amyloid-β, damages lipids, proteins, and tau proteins, harming synapses and neurons.[27] Studies suggest that boosting vitamin E intake could counteract oxidative stress, improving cognition and memory. Moreover, combining vitamin E with other antioxidants or anti-inflammatory agents may enhance its effectiveness.[28,29] Seleno-proteins in the central nervous system, dependent on selenium, guard against ROS-induced damage, crucial for preserving cognitive function and preventing neurological disorders.[30] Magnesium is vital for regulating NMDA receptors, oxidative stress, and neuroinflammation. NMDA receptors, crucial for developmental plasticity and memory, are affected by magnesium deficiency, leading to neuronal overexcitation and cell death.[31] Additionally, magnesium deficiency boosts the release of substance P and inflammatory mediators, exacerbating cognitive decline and dementia by interacting with amyloid-β proteins in the brain.[32] Our study, using NHANES data and accounting for gender, age, and racial differences, found that higher OBS may provide antioxidative benefits and is positively linked to cognitive function.

We use the OBS as a comprehensive measure of an individual's oxidative balance. OBS includes not only dietary components but also lifestyle factors such as physical activity and alcohol consumption. Higher OBS scores may indicate that participants consume more antioxidant-rich foods and follow a healthier lifestyle. Such foods include fruits, vegetables, and whole grains, rich in vitamins C, E, and other antioxidant phytochemicals. Although this study did not analyze specific dietary components in detail, previous research has shown that plant-based dietary patterns, such as the Mediterranean diet, are typically associated with higher OBS scores.[33] This suggests that diets rich in antioxidants may play a key role in maintaining oxidative balance and supporting cognitive health. Physical exercise is

Table 5. Subgroup analysis of the association between oxidative balance score and the total score of animal fluency test.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
Age subgroup	60–69 y	Oxidative balance score	1.22 (1.16–1.28)	<0.001	1.14 (1.09–1.21)	<0.001	1.11 (1.05–1.17)	0.001
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	6.37 (2.16–18.8)	0.002	3.86 (1.31–11.4)	0.017	3.26 (1.16–9.21)	0.029
		Q3	16.7 (6.16–45.3)	<0.001	6.25 (2.27–17.2)	0.001	5.92 (1.99–17.6)	0.004
		Q4	63.3 (31.3–128)	<0.001	16.1 (7.28–35.8)	<0.001	8.43 (3.29–21.6)	<0.001
	70–79 y	Oxidative balance score	1.11 (1.04–1.19)	0.002	1.04 (0.97–1.12)	0.2	1.03 (0.96–1.11)	0.4
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	2.08 (0.50–8.72)	0.3	0.93 (0.24–3.67)	>0.9	0.82 (0.18–3.73)	0.8
		Q3	4.73 (1.20–18.6)	0.028	1.26 (0.32–4.99)	0.7	1.06 (0.28–4.10)	>0.9
		Q4	8.43 (2.41–29.5)	0.002	2.31 (0.53–10.0)	0.3	2.13 (0.50–9.01)	0.3
	80 + y	Oxidative balance score	1.18 (1.09–1.28)	<0.001	1.13 (1.03–1.24)	0.01	1.11 (1.00–1.23)	0.042
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	4.71 (1.36–16.3)	0.016	3.83 (1.21–12.1)	0.025	3.21 (0.79–13.0)	0.092
		Q3	10.1 (2.48–40.7)	0.002	4.21 (1.17–15.2)	0.03	2.87 (0.60–13.7)	0.2
		Q4	28.5 (5.51–147)	<0.001	14.3 (2.19–92.7)	0.008	8.19 (1.05–70.4)	0.045
Gender subgroup	Female	Oxidative balance score	1.17 (1.11–1.23)	<0.001	1.11 (1.06–1.18)	<0.001	1.09 (1.03–1.16)	0.008
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	3.36 (1.04–10.9)	0.044	2.35 (0.72–7.65)	0.15	2.11 (0.69–6.45)	0.2
		Q3	7.21 (2.45–21.2)	<0.001	3.27 (1.20–8.89)	0.023	2.38 (0.82–6.91)	0.1
		Q4	23.8 (8.73–64.7)	<0.001	9.01 (3.22–25.2)	<0.001	5.64 (1.71–18.6)	0.009
	Male	Oxidative balance score	1.19 (1.11–1.27)	<0.001	1.11 (1.04–1.19)	0.003	1.09 (1.02–1.16)	0.014
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	5.1 (1.49–17.5)	0.011	2.88 (1.03–8.01)	0.043	2.36 (0.83–6.68)	0.1
		Q3	12.2 (3.77–39.7)	<0.001	3.34 (1.02–11.0)	0.047	3.81 (1.09–13.3)	0.038
		Q4	40 (12.7–126)	<0.001	10.6v	<0.001	6.38 (2.09–19.5)	0.004
Race subgroup	Mexican American	Oxidative balance score	1.21 (1.10–1.33)	<0.001	1.17 (1.08–1.26)	0.002	1.12 (1.09–1.24)	0.004
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	0.83 (0.20–3.48)	0.8	0.63 (0.13–3.06)	0.5	0.58 (0.34–3.01)	0.6
		Q3	7.01 (0.65–75.4)	0.1	4.51 (0.63–32.5)	0.11	4.43 (0.67–27.8)	0.15
		Q4	64.8 (4.60–915)	0.006	30.1 (2.83–320)	0.011	9.8 (2.78- 765)	0.023
	Other Hispanic	Oxidative balance score	1.09 (1.02–1.18)	0.018	1.06 (0.96–1.16)	0.2	1.05 (0.95–1.17)	0.3
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	13.1 (3.20–53.7)	0.001	10.6 (1.55–73.2)	0.02	10.2 (1.18–88.9)	0.04
		Q3	4.38 (0.83–23.0)	0.078	2.05 (0.36–11.6)	0.4	2.62 (0.25–27.3)	0.3
		Q4	5.72 (1.06–31.0)	0.044	2.46 (0.24–25.1)	0.4	1.98 (0.10–37.7)	0.6

(continued)

Table 5. Continued.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
	Non-Hispanic White	Oxidative balance score	1.18 (1.12–1.24)	<0.001	1.13 (1.07–1.19)	<0.001	1.1 (1.05–1.16)	<0.001
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	4.43 (1.90–10.3)	0.001	3.48 (1.49–8.12)	0.005	3.12 (1.29–7.53)	0.015
		Q3	9.04 (3.43–23.8)	<0.001	4.15 (1.68–10.2)	0.003	3.79 (1.60–9.00)	0.005
		Q4	30.4 (12.6–73.2)	<0.001	12.4 (4.74–32.5)	<0.001	7.51 (2.92–19.3)	<0.001
	Non-Hispanic Black	Oxidative balance score	1.15 (1.09–1.22)	<0.001	1.11 (1.05–1.17)	0.001	1.12 (1.04–1.19)	0.004
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	2.8 (0.99–7.95)	0.052	1.73 (0.58–5.18)	0.3	1.83 (0.59–5.69)	0.3
		Q3	7.44 (2.11–26.2)	0.003	4.71 (1.23–18.0)	0.025	6.01 (1.50–24.1)	0.016
		Q4	14.6 (4.00–53.0)	<0.001	6.54 (2.02–21.2)	0.003	7.12 (1.88–27.0)	0.008
	Other races	Oxidative balance score	1.03 (0.89–1.18)	0.7	1	>0.9	1.07 (0.94–1.22)	0.3
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	0.05 (0.00–1.29)	0.069	0.04 (0.00–1.28)	0.066	0.07 (0.00–1.49)	0.073
		Q3	0.7 (0.15–3.29)	0.6	0.35 (0.07–1.79)	0.2	0.46 (0.03–7.58)	0.5
		Q4	1.5 (0.08–28.0)	0.8	1.05 (0.04–27.9)	>0.9	2.94 (0.09–95.6)	0.4

OR: odds ratio; CI: confidence interval; Model 1 was adjusted for age and gender; Model 2, adjusted for age, gender, race, education, and the ratio of family income to poverty; Model 3 was adjusted for age, gender, race, education, the ratio of family income to poverty, BMI, alcohol consumption status, smoking status, hypertension, diabetes, stroke, cardiovascular disease, and physical activity.

significantly associated with memory formation and consolidation.[34] Meta-analyses indicate that aerobic exercise notably enhances overall cognitive ability and memory in individuals with MCI and may offer protective effects against cognitive decline.[35,36] Exercise improves hippocampal function, neurogenesis, synaptic plasticity, and cerebral blood flow regulation in older adults while reducing cardiovascular risks and pro-inflammatory activity.[37] High-intensity aerobic exercise has been shown to improve executive function in MCI patients. Numerous studies suggest that modifiable lifestyle factors, such as physical activity and diet, significantly contribute to cognitive health, helping to stabilize or improve cognitive decline.[4,38,39] Additionally, physical activity can mitigate or delay the progression of risk factors like obesity, diabetes, and hypertension, enhancing cognitive function in older adults.[5,40] Therefore, the most effective strategy to improve and protect cognitive function in older adults is to combine regular physical activity with an appropriate antioxidant diet.

Oxidative stress is caused by free radicals interacting with cellular antioxidants. Pro-oxidants like ROS and malondialdehyde enhance oxidative stress and lead to cell death, while antioxidants like superoxide dismutase and glutathione peroxidase inhibit oxidative stress and offer neuroprotection.[41] Prolonged oxidative stress and free radical exposure damage cellular DNA, lipids, and proteins. The brain, rich in mitochondria and unsaturated fats but with low antioxidant capacity, is particularly susceptible to oxidative stress.[42] Studies show increased leukocyte apoptosis in Parkinson's disease patients, correlated with striatal dopamine neuron loss, indicating that systemic oxidative stress may play a key role in cognitive impairment.[43,44] Aging increases blood-brain barrier permeability, triggering inflammation. Astrocytes and microglia, usually inactive, release neuroinflammatory molecules when stimulated, and chronic inflammation can impair neurogenesis and contribute to neurodegenerative diseases.[45] Oxidative stress is closely tied to inflammation. Peripheral leukocyte apoptosis and the infiltration of adhesion molecules link systemic oxidative stress with neuroinflammation. Free radicals, ROS, and reactive nitrogen species activate key inflammation pathways, such as NF-κB and MAPK.[46] ROS can trigger the NLRP3 inflammasome, interact with NF-κB signaling, and activate the MAPK pathway, increasing the production of inflammatory factors and mediators, exacerbating neuroinflammation and brain damage, and impairing cognitive function.[47,48] Studies indicate that antioxidants like carotenoids and vitamin E can neutralize free radicals and reduce inflammation, potentially protecting cognitive function.[27,49] Our study shows that individuals in the highest OBS quartile score significantly higher on three cognitive function tests than those in the lowest quartile. Higher

Table 6. Subgroup analysis of the association between oxidative balance score and the score of digit symbol test.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
Age subgroup	60–69 y	Oxidative balance score	1.69 (1.47–1.95)	<0.001	1.24 (1.06–1.45)	0.009	1.18 (1.03–1.35)	0.024
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	162 (4.65–5637)	0.007	15.8 (0.66–379)	0.086	14.2 (0.45–444)	0.12
		Q3	17,316 (694–431,849)	<0.001	224 (6.98–7175)	0.004	141 (5.11–3870)	0.007
		Q4	53,914 (3389–857,573)	<0.001	95.5 (3.82–2389)	0.008	29.9 (1.69–528)	0.025
	70–79 y	Oxidative balance score	1.77 (1.49–2.10)	<0.001	1.39 (1.17–1.65)	<0.001	1.29 (1.08–1.54)	0.008
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	385 (12.3–12,049)	0.001	7.25 (0.31–167)	0.2	10.0 (0.32–310)	0.2
		Q3	9241 (311–274,213)	<0.001	49.6 (1.35–1821)	0.035	40.9 (1.14–1470)	0.043
		Q4	103,755 (2546–4,228,447)	<0.001	589 (13.6–25,538)	0.002	169 (3.33–8562)	0.015
	80 + y	Oxidative balance score	1.70 (1.28–2.26)	<0.001	1.35 (1.08–1.69)	0.012	1.22 (0.95–1.58)	0.11
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	620 (1.45–265,086)	0.038	121 (0.70–20,689)	0.066	51.9 (0.26–10,331)	0.13
		Q3	2926 (15.0–571,407)	0.004	88.2 (1.13–6908)	0.045	14.5 (0.26–824)	0.2
		Q4	193,985 (424–88,765,183)	<0.001	1642 (8.94–301,730)	0.008	181 (0.58–56,160)	0.071
Gender subgroup	Female	Oxidative balance score	1.85 (1.62–2.11)	<0.001	1.44 (1.28–1.61)	<0.001	1.32 (1.16–1.50)	<0.001
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	288 (13.2–6282)	<0.001	19.6 (1.22–315)	0.037	13.7 (0.75–252)	0.073
		Q3	12,520 (607–258,272)	<0.001	218 (14.2–3327)	<0.001	62.0 (4.08–943)	0.007
		Q4	312,796 (18,022–5,429,003)	<0.001	1539 (116–20,394)	<0.001	268 (14.8–4863)	0.001
	Male	Oxidative balance score	1.55 (1.33–1.80)	<0.001	1.17 (1.03–1.33)	0.015	1.11 (1.08–1.25)	0.044
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	190 (6.37–5670)	0.004	16.7 (1.45–192)	0.026	12.2 (1.13–131)	0.041
		Q3	3017 (272–33,493)	<0.001	25.0 (2.24–279)	0.011	28.4 (2.00–402)	0.018
		Q4	11,830 (468–299,305)	<0.001	39.6 (1.99–787)	0.018	12.7 (1.90–180)	0.048
Race subgroup	Mexican American	Oxidative balance score	1.73 (1.31–2.27)	0.001	1.31 (1.05–1.64)	0.024	1.21 (1.02–1.56)	0.034
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	5.20 (0.03–966)	0.5	1.05 (0.01–132)	>0.9	0.41 (0.11–113)	0.8
		Q3	29.9 (0.04–24,091)	0.3	1.83 (0.02–135)	0.8	0.78 (0.45- 108)	0.5
		Q4	90,123 (405–20,039,173)	0.001	70.0 (1.12–6827)	0.004	11.5 (1.56- 5043)	0.003

(continued)

Table 6. Continued.

Subgroup		Exposure	Model 1 [OR (95% CI)]	p	Model 2 [OR (95% CI)]	p	Model 3 [OR (95% CI)]	p
	Other Hispanic	Oxidative balance score	1.67 (1.27–2.20)	<0.001	1.29 (1.04–1.59)	0.022	1.31 (1.05–1.65)	0.025
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	760 (11.0–52,400)	0.004	50.1 (0.65–3862)	0.074	117 (0.46–30,156)	0.078
		Q3	14,835 (96.3–2,284,691)	<0.001	71.1 (0.60–8368)	0.076	838 (3.64–192,487)	0.024
		Q4	17,024 (35.8–8,094,954)	0.004	51.7 (0.19–14,082)	0.2	30.9 (4.06–17,241)	0.02
	Non-Hispanic White	Oxidative balance score	1.57 (1.38–1.80)	<0.001	1.30 (1.14–1.49)	<0.001	1.22 (1.08–1.39)	0.004
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	114 (5.32–2423)	0.004	24.6 (1.13–535)	0.042	24.6 (1.43–423)	0.03
		Q3	2480 (150–40,867)	<0.001	116 (5.65–2370)	0.003	78.8 (4.78–1297)	0.005
		Q4	20,142 (1213–334,338)	<0.001	388 (22.7–6648)	<0.001	124 (8.69–1755)	0.002
	Non-Hispanic Black	Oxidative balance score	1.75 (1.49–2.06)	<0.001	1.39 (1.18–1.64)	<0.001	1.39 (1.16–1.66)	0.002
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	181 (2.61–12,553)	0.018	13.4 (0.24–756)	0.2	8.30 (0.10–703)	0.3
		Q3	4088 (55.2–302,655)	<0.001	221 (3.14–15,603)	0.015	215 (3.53–13,095)	0.016
		Q4	22,536 (453–1,122,358)	<0.001	182 (5.14–6418)	0.006	181 (3.60–9113)	0.014
	Other races	Oxidative balance score	1.52 (1.18–1.94)	0.002	1.31 (1.06–1.64)	0.017	1.40 (1.09–1.80)	0.016
		Oxidative balance score, quartile						
		Q1	Ref		Ref		Ref	
		Q2	0.95 (0.00–365)	>0.9	0.11 (0.00–31.0)	0.4	0.21 (0.00–128)	0.5
		Q3	144 (1.33–15,603)	0.039	2.83 (0.02–352)	0.7	17.2 (0.03–8708)	0.3
		Q4	3267 (15.8–675,995)	0.005	289 (1.54–54,379)	0.036	486 (1.61–384,155)	0.042

OR: odds ratio: CI: confidence interval; Model 1 was adjusted for age and gender; Model 2, adjusted for age, gender, race, education, and the ratio of family income to poverty; Model 3 was adjusted for age, gender, race, education, the ratio of family income to poverty, BMI, alcohol consumption status, smoking status, hypertension, diabetes, stroke, cardiovascular disease, and physical activity.

OBS is associated with better cognitive test scores. This finding aligns with previous epidemiological evidence, supporting a significant link between oxidative stress and cognitive function.[50,51]

The study finds that elderly individuals from minority ethnic groups are at higher risk of dementia and Alzheimer's disease compared to non-Hispanic white individuals.[52] Ethnicity-based analysis reveals a stronger link between cognitive test scores and OBS among white participants, particularly in learning, memory, executive function, and sustained memory. It is important to note that these results may be influenced by the significant differences in sample sizes across ethnic groups in this study. Specifically, there were 1332 non-Hispanic white participants and 645 non-Hispanic black participants, while the number of participants from other ethnicities, such as Mexican American and other Hispanic groups, was less than 300. Due to the small sample sizes, findings for certain ethnic subgroups may show greater variability, which could affect the stability and representativeness of the results. Therefore, these differences should be interpreted with caution, and future studies should aim to include larger and more diverse ethnic groups to validate these findings. Interestingly, OBS is positively correlated with digit symbol test scores across all ethnicities, suggesting universal benefits for sustained memory and working abilities. Gender-specific analysis shows a stronger impact of OBS on cognitive performance among females, especially in learning, memory, executive function, and sustained memory, while male participants generally align with females except for delayed recall in the CERAD test. OBS has the most significant impact on females and the 60 to 69 age group in the age-stratified analysis. Although limited by sample size in other age groups and minority ethnicities, further research is warranted to explore the relationship between OBS and cognitive function. Despite variations in the strength of these associations across different population characteristics, even moderately effective interventions can help protect cognitive function or delay cognitive impairment onset, significantly reducing the growing economic and societal burden associated with these conditions. Additionally, dietary interventions are relatively inexpensive and have no side effects.

This study boasts several strengths. Firstly, it's pioneering in exploring the link between OBS and cognitive function among older adults. Secondly, its sample represents the broader U.S. population and maintains rigorous data collection protocols. Thirdly, its ample sample size ensures robust statistical power for subgroup analyses. Nevertheless, several limitations should be considered. First, relying on self-reported data for cardiovascular conditions such as coronary heart disease, heart attacks, and strokes could lead to reporting biases. Second, the cross-sectional design limits the ability to infer causality. Additionally, due to the limited sample size, we could not separately assess the contributions of dietary OBS and lifestyle OBS, restricting our ability to evaluate their distinct effects on cognitive function. Future research should include larger sample sizes to address this issue and examine these components independently. Moreover, large-scale prospective cohort studies and randomized controlled trials are recommended to validate our findings.

Conclusions

Our study reveals the association between OBS and cognitive function in elderly Americans, highlighting the importance of antioxidant-rich diets and lifestyle modifications in preventing cognitive decline. The results show that OBS is positively correlated with cognitive performance across various domains, with particularly strong effects observed among non-Hispanic white individuals, females, and those aged 60 to 69, suggesting potential benefits in these high-risk groups. These findings underscore the value of targeted dietary and lifestyle interventions. However, differences in sample sizes, especially among ethnic groups, may affect the stability and generalizability of these results, indicating the need for future studies with larger and more balanced samples to validate these conclusions.

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Statements and declarations

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Data availability

The datasets utilized in this study can be accessed from the NHANES repository at https://www.cdc.gov/nchs/nhanes/. The Raw data supporting the findings of this article are included within the dataset.

Supplemental material

Supplemental material for this article is available online.

References

1. Manly JJ, Jones RN, Langa KM, et al. Estimating the prevalence of dementia and mild cognitive impairment in the US: the 2016 health and retirement study harmonized cognitive assessment protocol project. *JAMA Neurol* 2022; 79: 1242–1249.
2. Lee K, Choi K-M, Park S, et al. Selection of the optimal channel configuration for implementing wearable EEG devices for the diagnosis of mild cognitive impairment. *Alzheimers Res Ther* 2022; 14: 170.
3. U.S. Food and Drug Administration. FDA grants accelerated approval for Alzheimer's drug. 2021. https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug (accessed 7 June 2021).
4. Phillips C. Lifestyle modulators of neuroplasticity: how physical activity, mental engagement, and diet promote cognitive health during aging. *Neural Plast* 2017; 2017: 3589271.
5. Dominguez LJ, Veronese N, Vernuccio L, et al. Nutrition, physical activity, and other lifestyle factors in the prevention of cognitive decline and dementia. *Nutrients* 2021; 13: 4080.
6. Halliwell B and Gutteridge JMC. *Free radicals in biology and medicine, 5th edition*. New York: Oxford University Press, USA, 2015.
7. Tan BL, Norhaizan ME, Liew W-P-P, et al. Antioxidant and oxidative stress: a mutual interplay in age-related diseases. *Front Pharmacol* 2018; 9: 402374.
8. Nooyens AC, Milder IE, Van Gelder BM, et al. Diet and cognitive decline at middle age: the role of antioxidants. *Br J Nutr* 2015; 113: 1410–1417.
9. Singh A, Kukreti R, Saso L, et al. Oxidative stress: a key modulator in neurodegenerative diseases. *Molecules* 2019; 24: 1583.
10. Ozawa H, Miyazawa T and Miyazawa T. Effects of dietary food components on cognitive functions in older adults. *Nutrients* 2021; 13: 2804.
11. Tan BL and Norhaizan ME. Effect of high-fat diets on oxidative stress, cellular inflammatory response and cognitive function. *Nutrients* 2019; 11: 2579.
12. Scarmeas N, Anastasiou CA and Yannakoulia M. Nutrition and prevention of cognitive impairment. *Lancet Neurol* 2018; 17: 1006–1015.
13. Maxwell SR, Dietrich T and Chapple IL. Prediction of serum total antioxidant activity from the concentration of individual serum antioxidants. *Clin Chim Acta* 2006; 372: 188–194.
14. Barreiro E, Peinado VI, Galdiz JB, et al. Cigarette smoke–induced oxidative stress: a role in chronic obstructive pulmonary disease skeletal muscle dysfunction. *Am J Respir Crit Care Med* 2010; 182: 477–488.
15. Arazi H, Eghbali E and Suzuki K. Creatine supplementation, physical exercise and oxidative stress markers: a review of the mechanisms and effectiveness. *Nutrients* 2021; 13: 869.
16. Demirer B, Yardımcı H and Basmaz SE. Inflammation level in type 2 diabetes is associated with dietary advanced glycation end products, Mediterranean diet adherence and oxidative balance score: a pathway analysis. *J Diabetes Complications* 2023; 37: 108354.
17. Lee J-H, Joo YB, Han M, et al. Relationship between oxidative balance score and quality of life in patients with osteoarthritis: data from the Korea National Health and Nutrition Examination Survey (2014–2015). *Medicine* 2019; 98: e16355.
18. Wu C, Ren C, Song Y, et al. Gender-specific effects of oxidative balance score on the prevalence of diabetes in the US population from NHANES. *Front Endocrinol (Lausanne)* 2023; 14: 1148417.
19. Kwon Y-J, Park H-M and Lee J-H. Inverse association between oxidative balance score and incident type 2 diabetes mellitus. *Nutrients* 2023; 15: 2497.
20. Zhang W, Peng S-F, Chen L, et al. Association between the oxidative balance score and telomere length from the national health and nutrition examination survey 1999–2002. *Oxid Med Cell Longev* 2022; 2022: 1345071.
21. Brody DJ, Kramarow EA, Taylor CA, et al. Cognitive performance in adults aged 60 and over: National Health and Nutrition Examination survey, 2011–2014. *Natl Health Stat Report* 2019; (126): 1–23.
22. Ogden CL, Carroll MD, Fakhouri TH, et al. Prevalence of obesity among youths by household income and education level of head of household - United States 2011–2014. *MMWR Morb Mortal Wkly Rep* 2018; 67: 186–189.
23. Bailey RL, Akabas SR, Paxson EE, et al. Total usual intake of shortfall nutrients varies with poverty among US adults. *J Nutr Educ Behav* 2017; 49: 639–646.e633.
24. Kong SYJ, Bostick RM, Flanders WD, et al. Oxidative balance score, colorectal adenoma, and markers of oxidative stress and inflammation. *Cancer Epidemiol Biomarkers Prev* 2014; 23: 545–554.
25. Cho A-R, Kwon Y-J, Lim H-J, et al. Oxidative balance score and serum γ-glutamyltransferase level among Korean adults: a nationwide population-based study. *Eur J Nutr* 2018; 57: 1237–1244.
26. Li H, Song L, Cen M, et al. Oxidative balance scores and depressive symptoms: mediating effects of oxidative stress and inflammatory factors. *J Affect Disord* 2023; 334: 205–212.
27. Gugliandolo A, Bramanti P and Mazzon E. Role of vitamin E in the treatment of Alzheimer's disease: evidence from animal models. *Int J Mol Sci* 2017; 18: 2504.
28. Boyd-Kimball D, Sultana R, Mohmmad-Abdul H, et al. Rodent Abeta(1–42) exhibits oxidative stress properties similar to those of human Abeta(1–42): implications for proposed mechanisms of toxicity. *J Alzheimers Dis* 2004; 6: 515–525.
29. Rota C, Rimbach G, Minihane AM, et al. Dietary vitamin E modulates differential gene expression in the rat hippocampus: potential implications for its neuroprotective properties. *Nutr Neurosci* 2005; 8: 21–29.

30. Zhou J, Zhang W, Cao Z, et al. Association of selenium levels with neurodegenerative disease: a systemic review and meta-analysis. *Nutrients* 2023; 15: 3706.
31. Olivares D, Deshpande VK, Shi Y, et al. N-methyl D-aspartate (NMDA) receptor antagonists and memantine treatment for Alzheimer's disease, vascular dementia and Parkinson's disease. *Curr Alzheimer Res* 2012; 9: 746–758.
32. Yu X, Guan PP, Zhu D, et al. Magnesium ions inhibit the expression of tumor necrosis factor α and the activity of γ-secretase in a β-amyloid protein-dependent mechanism in APP/PS1 transgenic mice. *Front Mol Neurosci* 2018; 11: 172.
33. Tapsell LC, Neale EP, Satija A, et al. Foods, nutrients, and dietary patterns: interconnections and implications for dietary guidelines. *Adv Nutr* 2016; 7: 445–454.
34. Fernandes J, Soares JCK, do Amaral Baliego LGZ, et al. A single bout of resistance exercise improves memory consolidation and increases the expression of synaptic proteins in the hippocampus. *Hippocampus* 2016; 26: 1096–1103.
35. Zheng G, Xia R, Zhou W, et al. Aerobic exercise ameliorates cognitive function in older adults with mild cognitive impairment: a systematic review and meta-analysis of randomised controlled trials. *Br J Sports Med* 2016; 50: 1443–1450.
36. Dieckelmann M, González-González AI, Banzer W, et al. Effectiveness of exercise interventions to improve long-term outcomes in people living with mild cognitive impairment: a systematic review and meta-analysis. *Sci Rep* 2023; 13: 18074.
37. Augusto-Oliveira M, Arrifano GP, Leal-Nazaré CG, et al. Exercise reshapes the brain: molecular, cellular, and structural changes associated with cognitive improvements. *Mol Neurobiol* 2023; 60: 6950–6974.
38. Leyland LA, Spencer B, Beale N, et al. The effect of cycling on cognitive function and well-being in older adults. *PLoS One* 2019; 14: e0211779.
39. Sewell KR, Erickson KI, Rainey-Smith SR, et al. Relationships between physical activity, sleep and cognitive function: a narrative review. *Neurosci Biobehav Rev* 2021; 130: 369–378.
40. Xiu S, Liao Q, Sun L, et al. Risk factors for cognitive impairment in older people with diabetes: a community-based study. *Ther Adv Endocrinol Metab* 2019; 10: 2042018819836640.
41. Marrocco I, Altieri F and Peluso I. Measurement and clinical significance of biomarkers of oxidative stress in humans. *Oxid Med Cell Longev* 2017; 2017: 6501046.
42. Jurcau A. Insights into the pathogenesis of neurodegenerative diseases: focus on mitochondrial dysfunction and oxidative stress. *Int J Mol Sci* 2021; 22: 11847.
43. Bennett S, Grant MM and Aldred S. Oxidative stress in vascular dementia and Alzheimer's disease: a common pathology. *J Alzheimers Dis* 2009; 17: 245–257.
44. Li H, Knight WC and Xu J. Striatal oxidative damages and neuroinflammation correlate with progression and survival of Lewy body and Alzheimer diseases. *Neural Regen Res* 2022; 17: 867–874.
45. Knox EG, Aburto MR, Clarke G, et al. The blood-brain barrier in aging and neurodegeneration. *Mol Psychiatry* 2022; 27: 2659–2673.
46. Morgan MJ and Liu Z-g. Crosstalk of reactive oxygen species and NF-κB signaling. *Cell Res* 2011; 21: 103–115.
47. Alva R, Mirza M, Baiton A, et al. Oxygen toxicity: cellular mechanisms in normobaric hyperoxia. *Cell Biol Toxicol* 2023; 39: 111–143.
48. Wu A-G, Zhou X-G, Qiao G, et al. Targeting microglial autophagic degradation in NLRP3 inflammasome-mediated neurodegenerative diseases. *Ageing Res Rev* 2021; 65: 101202.
49. Christensen K, Gleason CE and Mares JA. Dietary carotenoids and cognitive function among US adults, NHANES 2011–2014. *Nutr Neurosci* 2020; 23: 554–562.
50. Fan Z, Yang C, Qu X, et al. Association of oxidative stress on cognitive function: a bidirectional Mendelian randomisation study. *Mol Neurobiol* 2024. Epub ahead of print 16 May 2024. DOI: 10.1007/s12035-024-04231-3.
51. Hoyos CM, Stephen C, Turner A, et al. Brain oxidative stress and cognitive function in older adults with diabetes and prediabetes who are at risk for dementia. *Diabetes Res Clin Pract* 2022; 184: 109178.
52. Mehta KM and Yeo GW. Systematic review of dementia prevalence and incidence in United States race/ethnic populations. *Alzheimers Dement* 2017; 13: 72–83.