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Associations between exposure to brominated flame retardants with cognitive function in U.S. older adults: A cross-sectional study of NHANES from 2011 to 2012

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ABSTRACT

Background: Brominated flame retardants (BFRs) are commonly used in electronic products, clothing, and furniture to reduce their flammability. They are related to reproductive system dysfunction, liver dysfunction, and fetal development disorders. However, few studies have investigated the relationship between exposure to BFRs mixtures and cognitive impairment in the general population aged 60 and above.

Methods: Total 348 adults aged 60 years or older who had serum BFRs measured and four cognitive tests were enrolled in this study. Use multiple linear regression weighted models and stratified analysis to determine the causal relationship between BFRs and cognitive function in the elderly.

Results: Multiple linear regression weighted models indicate a negative correlation between BFRs and cognitive function in the elderly. Result display a negative correlation between PBDE99 and animal fluency testing (β:- 1.1,95%CI:-2.0,-0.12,P = 0.032).

Conclusions: Our study provides new clues to the association of BFRs with cognitive function.

1. Introduction

The WHO released a report in 2014 indicating that 3.7 million premature deaths globally were attributable to ambient air pollution [1].A cohort study from 2010 to 2018 (N = 7042) showed that long-term exposure of middle-aged people to ambient air pollution would affect cognitive function. The air pollution caused by BFRs is a component of air pollution, which may be related to the occurrence or development of cognitive impairment.Based on the population-based representative data, we find that some BFRs remained high in human serum even after they were withdrawn from the US market for many years [2].

BFRs have for a long time been used to decrease flammability of a variety of products in houses and homes, for instance electronic devices, electric cables and home textiles [3]. According to the incorporations into polymers, BFRs can be divided into brominated monomers, reactive and additive agents. The polybrominated diphenyl ethers (PBDEs) and 2,2′,4,4′,5,5′-hexabromobiphenyl (PBB153) are reactive BFRs, and considered to be with a higher risk [4]. BFRs are not chemically bound to the flame-retarded material, so they can enter the environment from volatilization, leaching, or degradation of BFRs-containing products. PBDEs are generally persistent in the environment and have been measured in aquatic sediments, house dust, and aquatic and terrestrial animals [5].

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Abbreviations

BMI	Body mass index
BFRs	Brominated flame retardants
CERAD	Consortium to establish a registry for Alzheimer's disease
AFT	Animal Fluency Test
DSST	Digit symbol substitution test
NHANES	National health and nutrition examination survey
SD	Standard deviation
PBDEs	Polybrominated diphenyl ethers
PBB153	2,2′,4,4′,5,5′-hexabromobiphenyl
LOD	Lower limits of detection
POPs	Persistent organic pollutants

PBDEs have been shown to bio accumulate in fish. Humans may be exposed though the diet, including breast feeding, and by contact with BFRs-treated products and contaminated house dust [6].Therefore, humans will continually to be exposed to BFRs through diet, breastfeeding, drinking water, and product use. Several epidemiological studies have shown that exposures to BFRs were positively associated with serious diseases or disorders in neurology system, reproductive system, thyroid function, liver function, fetal development and birth [7–10].

Aging is a physiological event dependent on multiple pathways that are linked to lifespan and processes leading to cognitive decline. This process represents the major risk factor for aging-related diseases such as Alzheimer's disease, Parkinson's disease, and ischemic stroke. The incidence of all these pathologies increases exponentially with age [11]. cognitive health has become an important public health issue for America's aging population [12]. The process from cognitive decline to dementia is continuous and irreversible, and there is no effective treatment for dementia so far, the therapeutic value of drugs currently used is limited. Thus, developing measures to reduce risk for low cognitive performance as well as treatments of diagnosed dementia occupy a high priority in society [13].

Multiple studies have shown that BFRs have an impact on the neural development of infants and young children [14–17].Less is known about the effects of BFRs on the cognitive function, especially for the elderly.

We conducted a cross-sectional study using nationally representative data from the NHANES database (2011–2012) to analyze the correlation between serum BFRs and cognitive function in adults aged 60 and above, providing more comprehensive population-based epidemiological evidence for the role of cognitive functional toxicology and providing information for the prevention and control of dementia.

2. Methods

2.1. Study design

The NHANES is a program designed to assess the health and nutritional status of adults and children in the US. The NHANES recruits approximately 5000 people each year, uses a complex, multi-stage, probability sampling design, and has sampled certain populations that may be at greater health risks. The NHANES interviews include demographic, socioeconomic, dietary, and health-related questions. The examinations consist of medical, dental, and physiological measurements, as well as laboratory tests administered by highly trained medical personnel [18]. This national cross-sectional study measured serum BFRs concentrations from participants in the NHANES 2001–2016.NHANES has a survey cycle every two years, except for data collected from 2017 to March 2020. Data collected from 2019 to March 2020 were combined with data from the NHANES 2017–2018 cycle to form a nationally representative sample of NHANES 2017–March 2020 pre-pandemic data.In 2005–2006, a weighted pooled-sample design was implemented to facilitate pooling samples before making analytical measurements for specific environmental chemicals. Pooling samples allowed for larger sample volumes, which resulted in lower limits of detection (LOD) and reduced the number of measurements and costs. The data files involved were linked using the unique survey participant identifier (i.e., SEQN and SAMPLEID).

2.2. Study population

Participants (N = 9756) from the NHANES 2011–2012 were recruited for this serum BFRs and cognitive function association analysis. We included adults aged 60 years and older who had completed measurements of all serum BFRs and filled four cognitive function test questionnaires. We excluded participants with missing data on covariates, pregnant females, and persons diagnosed with cancers.Finally, a total of 348 adults were included in the analyses (Fig. 1).All participants' data collection procedures and research protocols were approved by the National Center for Health Statistics Research Ethics Review Board.

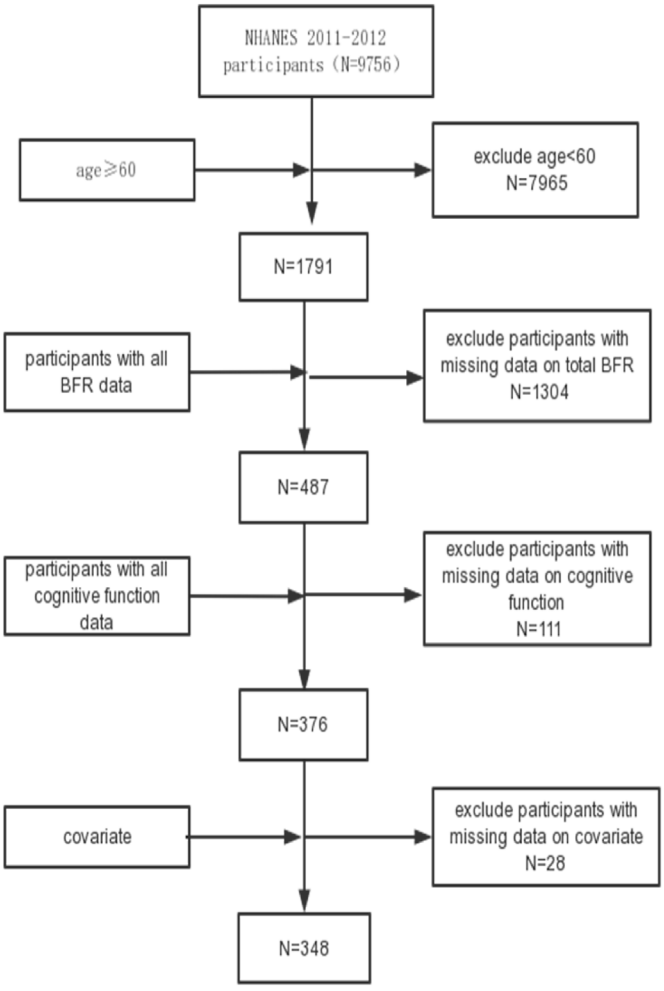

Fig. 1. Flow chart of enrolled participants.

2.3. Cognitive performance assessment

Cognitive functioning has been measured periodically in NHANES surveys, either during the household interview or as a component in the Mobile Examination Center and cognitive tests were performed among participants aged 60 years or older. In 2011–2012, a series of assessments in NHANES were re-introduced, including: 1) word learning and recall modules from the Consortium to Establish a Registry for Alzheimer's disease (CERAD); 2) the Animal Fluency test; and 3) the Digit Symbol Substitution test (DSST) [19]. These tests, which have been used in large screenings, epidemiological and clinical studies [20,21], evaluate working memory, language, processing speed and executive functioning in older adults. Participants were asked for consent to audio-record the administration for quality control purposes. In addition, review of the audio-recordings of assessments were evaluated for consistency of interviewer instructions and to determine test score accuracy. Approximately 10% of recorded interviews were independently reviewed over the course of the data collection cycles.Edits were made to ensure the completeness, consistency, and analytic usefulness of the data. When available, extensive review of the recorded interviews were conducted to clarify inconsistent responses, to evaluate the quality of the data, and to finalize the data set [22].

The CERAD test consisted of three consecutive learning trials as well as a delayed recall, which were designed to assess immediate and delayed learning ability for new verbal information. In the learning trials, participants were organized to read aloud 10 unrelated words when they were presented one at a time. Immediately following the introduction of the words, participants recalled as words as possible. The delayed word recall was completed after the Animal Fluency and DSST tests. The score on each trial ranged from 0 to 10, and the total score of the CERAD test was the sum of three learning trials and a delayed recall trial. As a component of executive function, the Animal Fluency test examined categorical verbal fluency, participants were called upon to name as many animals as possible in 1 min. The score was the sum of the number of correct answers. The DSST, a performance module from the Wechsler Adult Intelligence Scale, was used to assess processing speed, sustained attention and working memory. The exercise was performed using a piece of paper with a key at the top pairing numbers with nine symbols. Participants had 2 min to copy the corresponding symbols from the 133 boxes that held adjacent numbers. The score, ranging from 0 to 133, was the sum for the number of correct matches.

Currently, there is no gold standard of cutoff point for the CERAD, Animal Fluency and DSST tests to identify low cognitive performance. Therefore, we used the 25th percentile of the score, the lowest quartile, as the cutoff point, which is consistent with the methods used in the published literature. For each dimension, participants were divided into two groups: the low cognitive performance group, with people who scored lower than the corresponding cutoff values, and the rest, who were assigned to the normal cognitive performance group [22].

2.4. Measurement of serum BFRs and exposure to BFRs

Serum samples from NHANES 2011–2012 were stored frozen before analysis. Eleven polybrominated diphenyl ethers (PBDEs) and PBB-153 were measured in serum through the use of automated liquid/liquid extraction and subsequent sample clean-up. Final determination of target analytes was performed by isotope dilution gas chromatography high-resolution mass spectrometry GC/IDHRMS [23]. However, in this study, we only considered PBB-153 and eight PBDEs whose detection rate of >50% or all quartile are different, i.e.Decabromodiphenyl ether (PBDE209), 2,4,4-Tribromodiphenyl ether(PBDE28),2,2,4,4-Tetrabromodipheny lether(PBDE47), 2,2,3,4,4-Tentabromodiphenyl ether(PBDE85), 2,2,4,4,5-Pentabromodiphenylether PBDE99), 2,2,4,4,6-Pentab romodiphenyl ether (PBDE100), 2,2,4,4,5,5-Hexabromodiphenyl ether, 2,2,4,4,5,6-Hexabromodiphenyl ether (PBDE154), and 2,2,4,4,5,5-Hexabromobiphenyl (PBB153).

2.5. Other variables

Information on sex, age, race, education, smoking status, alcohol consumption, diabetes, Hypertension, stroke,and Body mass index (BMI) was collected by self-reported questionnaire and examination survey. Race was self-reported, allowing for multiple categories as Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other races. The education level is divided into high school and below, and above high school.In the study, smoking was defined as having at least 100 cigarettes in a lifetime, and alcohol consumption was defined as having at least 12 alcoholic beverages a year.Body mass index (BMI) was calculated by dividing the weight in kilograms by height in meters squared,BMI can be divided into four categories, too light:<18.5 kg/m^2,normal: 18.5 to <25 kg/m^2, overweight: 25 to <30 kg/m^2, obese: ≥30 kg/m^2. Hypertension is the average of the first three blood pressure measurements using MEC. Systolic blood pressure<140 and diastolic blood pressure<90 are considered not hypertension, while others are considered hypertension.History of diabetes or stroke was defined as self-reported physician diagnosis of diabetes or stroke.

2.6. Statistical analysis

Data analyses were conducted using SPSS (v. 26.0; IBM Corp., Armonk, NY, USA) and R software (v. 4.1.2; R Foundation for Statistical Computing, Vienna, Austria) using the NHANES 2011–2012 BFRs analyses sample weights. The distribution of serum BFRs was right-skewed, and medians and interquartile ranges were used to represent the distribution of serum BFRs in demographic characteristics. We used multiple linear regression models evaluate the relationship between cognitive function and BFRs, which is consistent with the methods used in the published literature [24].To correct for the skewed distribution, serum BFRs concentrations were included in the analysis after common log conversion; participants cognitive test scores were included in the form of raw data. Given the well-acknowledged age difference in cognitive function and serum BFRs concentration, we conducted the layered linear regression analysis in three age stages(60–70,70-80,≥80) to explore the potential association modification by age. Table 1 shows that there are significant differences ($p < 0.05$) in the distribution of age, gender, race, education level, and alcohol consumption among all participants in CERAD test, animal mobility test, and DSST. For the elderly, BMI and stroke are very important influencing factors, so in the linear regression model, the adjustment model adjusted these covariates.

The Kolmogorov–Smirnov normality test was adopted to test the normality of continuous variables, and we described normally distributed variables with mean ± standard deviation (SD) and non-normally distributed variables with median (interquartile range). Student's t-test was used to compare the mean levels between the low cognitive performance group and the normal cognitive performance group if the variable was normally distributed. The Mann–Whitney *U* test was adopted if the variable was not normally distributed. Chi-square tests were chosen to compare the percentages of categorical variables between the different groups. Confidence intervals were set at 95%. The statistical

Table 1
Characteristics of the study population, National Health and Nutrition Examination Survey (NHANES) 2011−2012(N = 348).

	CERAD delayed recall			AFT			DSST			CERAD recall		
	Normal Cognitive Performance	Low Cognitive Performance	P	Normal Cognitive Performance	Low Cognitive Performance	P	Normal Cognitive Performance	Low Cognitive Performance	P	Normal Cognitive Performance	Low Cognitive Performance	P
age	68.35(0.40)	72.75(0.85)	<0.001	68.56(0.43)	72.82(1.06)	<0.001	68.71(0.50)	73.78(1.27)	0.002	68.56(0.42)	73.59(0.75)	<0.0001
gender(%)			<0.001			0.3			0.35			0.17
male	112(38.56)	65(63.55)		127(46.90)	50(36.11)		123(43.82)	54(49.88)		114(42.40)	63(55.54)	
female	136(61.44)	35(36.45)		119(53.10)	52(63.89)		137(56.18)	34(50.12)		144(57.60)	27(44.46)	
race(%)			0.24			0.01			<0.001			0.004
Mexican American	11(1.48)	8(3.70)		12(1.63)	7(3.57)		13(1.66)	6(4.21)		11(1.43)	8(4.85)	
Other Hispanic	25(3.19)	15(6.73)		27(3.43)	13(6.51)		20(2.43)	20(13.82)		24(2.87)	16(9.71)	
Non-Hispanic White	109(83.26)	45(78.88)		121(85.79)	33(68.16)		131(86.10)	23(58.75)		120(84.41)	34(71.60)	
Non-Hispanic Black	77(8.70)	24(7.75)		62(6.24)	39(17.13)		68(6.79)	33(18.50)		80(8.42)	21(8.70)	
Other Races	26(3.37)	8(2.94)		24(2.91)	10(4.63)		28(3.02)	6(4.72)		23(2.87)	11(5.13)	
education(%)			0.02			0.03			0.13			0.01
High school and below	71(21.45)	45(39.81)		72(21.14)	44(44.69)		72(23.40)	44(41.22)		75(21.76)	41(45.85)	
Above high school	177(78.55)	55(60.19)		174(78.86)	58(55.31)		188(76.60)	44(58.78)		183(78.24)	49(54.15)	
smoke(%)			0.15			0.59			0.39			0.57
Yes	136(51.49)	56(61.69)		136(53.13)	56(57.34)		140(52.75)	52(61.44)		146(54.68)	46(50.76)	
No	112(48.51)	44(38.31)		110(46.87)	46(42.66)		120(47.25)	36(38.56)		112(45.32)	44(49.24)	
drink(%)			<0.001			0.24			0.43			0.65
Yes	169(70.43)	75(84.76)		178(76.46)	66(64.16)		186(74.53)	58(70.48)		181(73.51)	63(76.04)	
No	79(29.57)	25(15.24)		68(23.54)	36(35.84)		74(25.47)	30(29.52)		77(26.49)	27(23.96)	
Hypertension(%)			0.78			0.26			0.89			0.54
Yes	52(21.47)	27(24.68)		49(20.73)	30(28.20)		54(21.91)	25(24.37)		57(21.91)	22(23.91)	
No	196(78.53)	73(75.32)		197(85.96)	72(71.80)		206(78.10)	63(75.63)		201(78.08)	68(76.08)	
diabetes(%)			0.89			0.13			0.39			0.63
Yes	58(19.12)	21(17.95)		48(16.58)	31(27.61)		51(17.52)	28(26.69)		52(18.84)	27(18.80)	
No	190(80.88)	79(82.05)		198(83.42)	71(72.39)		209(82.48)	60(73.31)		206(2.65)	63(81.20)	
stroke(%)			0.69			0.09			0.81			0.73
Yes	11(2.20)	3(1.42)		7(1.85)	7(2.61)		10(1.99)	4(2.12)		10(1.82)	4(2.92)	
No	237(97.80)	97(98.58)		239(98.15)	95(97.39)		250(98.02)	84(97.88)		248(98.19)	86(97.08)	
BMI(kg/m2)(%)			0.12			0.37			0.71			0.2
<18.5	4(3.32)	1(2.15)		4(3.15)	1(2.58)		4(2.92)	1(3.69)		4(3.03)	1(3.04)	
18.5−25.0	61(23.86)	40(41.00)		69(25.61)	32(37.64)		74(27.17)	27(33.44)		68(25.02)	33(42.54)	
25.0−30.0	90(38.89)	33(33.20)		93(40.35)	30(26.40)		95(39.17)	28(27.47)		90(38.37)	33(33.35)	
≥30	93(33.93)	26(23.65)		80(30.90)	39(33.38)		87(30.74)	32(35.40)		96(33.58)	23(21.08)	
PBB153	16.78(12.77,33.32)	22.06(15.59,36.61)	0.4	17.98(12.77,29.66)	21.79(15.36,40.41)	0.33	17.98(12.77,30.57)	24.28(14.98,39.61)	0.26	17.98(12.77,30.57)	23.11(15.70,57.22)	0.24
PBDE209	17.52(11.47,19.32)	16.32(10.51,23.80)	0.59	17.79(11.47,21.31)	11.47(10.16,26.43)	0.25	16.32(11.13,19.32)	14.95(10.45,26.43)	0.81	17.62(11.47,19.32)	12.97(10.16,26.43)	0.35
PBDE28	6.98(5.44,10.03)	7.70(5.51,10.59)	0.37	7.21(5.51,10.03)	7.58(5.26,10.59)	0.87	6.98(5.30,10.03)	7.60(5.63,10.59)	0.17	7.21(5.26,10.03)	7.58(5.80, 8.45)	0.14
PBDE47	117.80(88.33,224.70)	117.80(88.33,214.00)	0.69	114.90(88.33,224.70)	130.50(88.33, 214.00)	0.59	114.90(84.85,224.70)	130.50(97.13, 214.00)	0.36	116.90(84.85, 224.70)	120.70(91.52, 183.60)	0.96
PBDE85	1.95(1.38,4.75)	1.94(1.33,4.43)	0.63	1.94(1.38,4.75)	2.20(1.63,4.60)	0.35	1.94(1.37,4.75)	2.20(1.63,4.88)	0.37	1.94(1.38,4.75)	1.98(1.43,3.05)	0.73
PBDE99	23.20(14.49,40.94)	19.44(14.26,40.94)	0.96	19.67(14.26,40.94)	24.89(14.49,50.28)	0.13	19.44(14.26,40.94)	24.89(14.75,48.32)	0.41	19.67(14.19,43.80)	23.20(14.49,40.94)	0.47
PBDE100	22.95(16.40,42.46)	22.95(16.40,39.00)	0.54	22.95(16.40,42.46)	22.95(16.40,39.00)	0.93	22.95(16.40,42.46)	22.95(17.93,43.31)	0.78	22.95(16.40,42.46)	22.95(16.40,26.48)	0.4
PBDE153	48.52(29.59,74.37)	50.88(27.45,80.96)	0.96	48.52(28.32,80.96)	50.09(28.32,72.86)	0.61	48.52(28.32,80.96)	50.88(27.67,72.86)	0.98	48.52(28.32,80.96)	45.84(27.64,70.76)	0.78
PBDE154	2.00(1.24,3.52)	2.00(1.37,3.85)	0.86	2.00(1.24,3.52)	2.05(1.47,4.37)	0.28	2.00(1.24,3.52)	2.05(1.46,4.37)	0.63	2.00(1.24,4.18)	2.05(1.46,2.72)	0.86

significance level was set at $\alpha = 0.05$ using two-sided tests.

3. Results

3.1. Participant characteristics

Of all the participants, there were significant differences ($p < 0.05$) between individuals with low cognitive performance and normal cognitive performance in the distribution of age, gender, race,educational level, drinking status among the CERAD test, Animal Fluency test and DSST (Table 1).As can be seen in the tables, compared to individuals with normal cognitive abilities, those with low cognitive abilities are more likely to be male, non black, lower educated, and alcohol drinkers.The detection rates and the distribution of all BFRs were shown in Table 2. Specifically, eleven serum BFRs were detectable in >50% of all participants, whereas the detection rates of PBDE66 were <50%.It can be seen from the table that the minimum and minimum quartile of PBDE17 and PBDE183 are equal, so they are not included in the study.Finally, 9 BFRs were included in the study(i.e., PBB153, PBDE209, PBDE28, PBDE47, PBDE85, PBDE99, PBDE100, PBDE153, PBDE154).

3.2. Association between BFRs with cognitive function

Fig. 2 shows the use of β Coefficients and 95% CI were used to evaluate multiple linear regression analysis of BFRs and cognitive function test scores. In unadjusted and adjusted models, some BFRs were found to have a negative correlation with cognitive test scores ($P < 0.05$). As can be seen from the table, in the adjusted model, PBDE99 is negatively correlated with AFT detection (β:- 1.1; 95% CI: -2.0, −0.12), PBB153, PBDE28, PBDE47, PBDE85, PBDE99, PBDE154 were negatively correlated with DSST detection.

3.3. Stratification analysis

Table 3 shows the adoption of β Multiple linear regression analysis of BFRs and cognitive function test scores under age stratification evaluated by coefficients and 95% CI. Model 1 is an unadjusted model, while Model 2 adjusts for covariates such as age, gender, education level, BMI, and stroke. In the unadjusted models, in the age range of 60–70 years, the correlation between PBDE99 and AFT scores is statistically significant (β:- 1.7; 95% CI: -3.4, −0.01); in the age range of 70–80 years, the correlation between PBDE209 and CERAD recall scores is statistically significant (β:- 2.2; 95% CI: -3.8, −0.60); at the age range of 80 years and above, the correlation between PBDE154 and AFT scores is statistically significant (β:- 1.3; 95% CI: -2.4, −0. 08). In the adjustment model, in the age range of 60–70 years, the correlation between PBDE154 and AFT scores is statistically significant (β:- 2; 95% CI: -3.9, −0.15) and the correlation between PBDE99 and DSST scores is statistically significant (β:- 6.2; 95% CI: -11, −1.4).

In age stratification, the comprehensive impact of partial BFRs on cognitive function in the elderly is statistically significant.We also evaluated the relationship between BFRs exposure and cognitive ability, assessing potential differences by gender between males and females, respectively (Supplementary Table S1). For women, in the unadjusted model, the correlation between PBDE47 and AFT scores is statistically significant (β:- 1.5; 95% CI: -2.9, −0.16) and the correlation between PBDE85 and DSST scores is statistically significant (β:- 4.7; 95% CI: -9, −0.35). For women, in the adjusted model, there was no statistical significance($P > 0.05$). For males, neither the adjusted model nor the unadjusted model has statistical significance($P > 0.05$).

4. Discussion

In this study, we aim to use multiple linear regression analysis to analyze the causal relationship between BFRs and cognitive function in the elderly. We observed a negative correlation between the exposure of BFRs and cognitive function test scores. The results of age stratification analysis indicate that the cognitive function of elderly people aged 60 to 70 is more likely to be affected by BFRs. In summary, these findings indicate that exposure to BFRs has adverse effects on cognitive function in elderly people.

Research has shown that human health is impacted by BFRs that have thyrotoxicity, neurotoxicity, and reproductive developmental toxicity. BFRs could disrupt thyroid homeostasis, including competing with thyroid hormones for binding to thyroid transport proteins, promoting thyroid hormone metabolism in the liver and brain, and altering thyroid hormone receptor activity [25].More studies have also reported higher concentrations of BFRs in paediatric versus adult serum and can most likely be attributed to breastfeeding and dust ingestion from mouthing behaviours and playing closer to ground level [15]. Furthermore, the continuing growth and maturation of young children's immune and neurological systems make them especially vulnerable to the adverse effects of environmental exposures [26].Multiple studies have shown that prenatal exposure of BFRs by pregnant women can have adverse effects on the early neural development of the fetus, and fetuses born to pregnant women who consume more BFRs have decreased cognitive abilities such as language and execution [27–29].However, there is no research on whether BFRs have adverse effects on cognitive function in the elderly.

To investigate the association between BFRs and cognitive function in the elderly, we employed 348 Americans aged 60 and above who had all BFRs data from NHANES from 2011 to 2012. To our knowledge, this is the first study to evaluate the association between serum BFRs and cognitive function in elderly

Table 2
Distribution of exposure biomarkers (N = 348), NHANES, 2011–2012.

	Mean	Min	25th	Median	75th	Max	Total detection frequency
PBB153	36.96158333	1.273	13.86	21.79	40.41	218.5	100
PBDE17	1.379787356	1.273	1.273	1.273	1.273	5.575	100
PBDE209	20.41904885	4.455	10.62	16.07	21.76	143.5	100
PBDE28	8.007491379	1.838	5.19775	7.207	9.975	26.04	100
PBDE47	154.3473851	34.74	84.85	121.1	198.1	645.5	100
PBDE85	3.172506897	0.7071	1.344	2.091	4.43	19.12	98.28
PBDE99	34.76485345	5.989	14.49	23.2	40.94	229.6	100
PBDE100	32.09749138	6.139	16.4	22.95	38.94	140.6	100
PBDE66	1.577241379	1.556	1.556	1.556	1.556	2.612	2.01
PBDE153	73.87479885	11.85	27.67	45.37	72.86	794	100
PBDE154	3.175876149	0.7071	1.4475	1.996	3.85	19.54	91.67
PBDE183	1.660227011	0.8485	0.8485	1.355	1.806	8.391	100

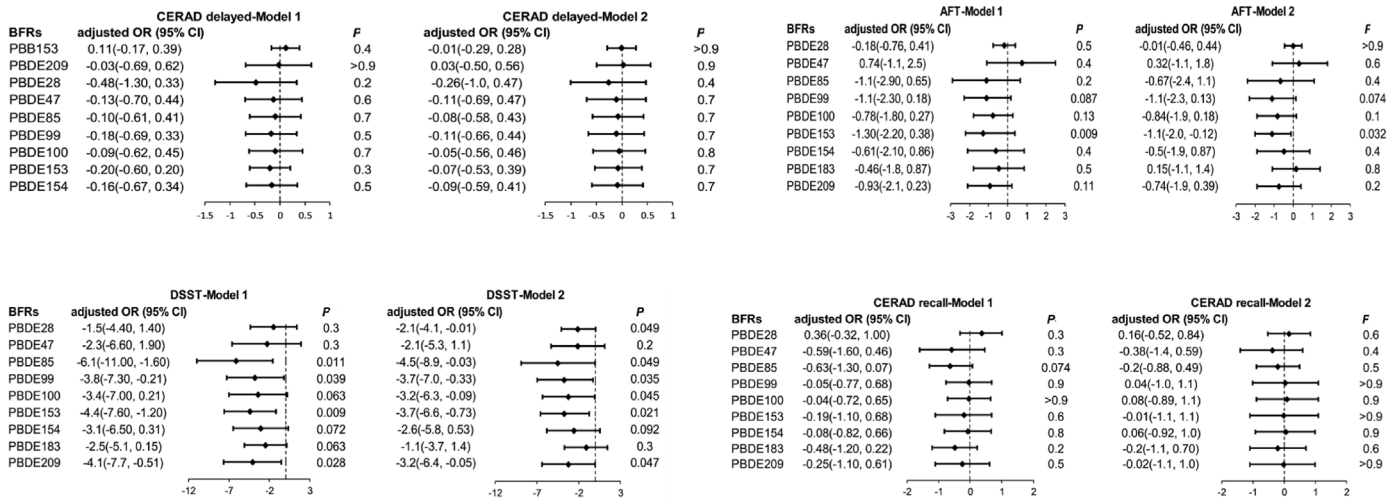

Fig. 2. Association between BFRs and cognitive performance in adults≥60 years old from NHANES 2011–2012 (N = 348)
*Model 1 is an unadjusted model, while Model 2 adjusts for covariates such as age, gender, education level, BMI, and stroke.

individuals.This study shows that in a multiple linear regression model, PBDE99 is negatively correlated with AFT and DSST test scores, while PBB153, PBDE28, PBDE47, PBDE85, PBDE99, PBDE154 are negatively correlated with DSST test scores. The lower the score on a cognitive test, the more likely it is to have cognitive impairment. In age stratification, the comprehensive impact of partial BFRs on cognitive function in the elderly is statistically significant. For women, there was no statistical significance in the adjusted model. For males, neither the adjusted model nor the unadjusted model has statistical significance. This suggests that women may be more likely to experience a decrease in cognitive function after consuming BFRs. However, the study population is relatively small.Further validation is needed.

The mechanism by which BFRs cause diseases is not fully understood.Currently, experimental studies have confirmed that BFRs can may have impaired the cell's ability to make immunological synapses and present antigens, down-regulating the expression of HLA-DR and CD209 antigens,and then affect the function of macrophages [30].Other animal studies have shown that exposure to BFRs will reduce the level of sex hormones, induce oxidative damage, and have reproductive toxicity [31].In another animal study, scholars showed that BFRs were related to nephrotoxicity at the gene level, and further confirmed the developmental toxicity and reproductive toxicity of BFRs [32].BFRs belong to persistent organic pollutants (POPs). Studies have found that maternal exposure to POP mixtures during pregnancy and weaning can lead to changes in gene expression in the hippocampus of offspring, which are related to brain function and learning and memory deficits in mouse offspring tested in the Barnes maze [33,34].In existing studies, only infants and young children are mentioned regarding the mechanism of the impact of BFRs on cognitive function, and there is no research on the mechanism of BFRs on cognitive function in the elderly. However, previous studies have found that even at the age of 90, the human brain still develops [35]. The developing brain undergoes complex and specific developmental processes, such as the proliferation of neural stem cells (NSCs), commitment of neuronal and glial progenitor cells, followed by migration (occurring after 8 postconceptional weeks, PCW), differentiation into various neuronal and glial subtypes, synaptogenesis (starting after 12–13 PCW), pruning (occurring after birth), myelination (taking place after 24 PCW), networking and terminal functional neuronal and glial maturation [36].And BFRs have been confirmed to have neurodevelopmental toxicity [37].This study provides population evidence on the relationship between BFRs and cognitive function in the elderly, but the disadvantage is that the number of subjects included in the study is small and further research is needed to confirm.The world's population structure is showing an aging trend, and it is urgent to pay attention to the health of the elderly. Reducing the risk of cognitive impairment in the elderly is an important way to maintain social stability and development. Therefore, we need to find more measures to control cognitive diseases such as Alzheimer's disease. The significance of this study is to confirm the impact of BFRs on cognitive decline in elderly people, providing a new way to control the occurrence of dementia.

5. Conclusions

In conclusion, this study observed negative effects of BFRs exposure on the occurrence of cognitive function among older adults across the United States.Age on 60–70 years are potential high-risk individuals. In results, most β are negative numbers, indicating a negative correlation, meaning that the more BFRs consumed the lower the cognitive function level. This study suggests that exposure of BFRs can lead to lower scores in animal fluency and numerical symbol tests, both of which are cognitive tests for evaluating language and executive function in older adults. Although these results suggest that reducing the exposure of BFRs may be a way to alleviate age-related cognitive decline and reduce the risk of dementia, large-scale prospective studies are still needed to further elucidate the impact and mechanism of BFRs on cognitive ability in elderly people.

Ethical approval and to participate

Ethical approval was obtained from the NCHS Ethics Review Board (ERB) (Protocol #2011-17). All individuals volunteered to participate in the study and provided informed written consent for participation and follow up.

Consent for publication

N/A.

Table 3
Age stratification analysis of the association between BFRs and cognitive function in adults≥60 years old from NHANES 2011–2012 (N = 348).

	CERAD delayed recall				AFT				DSST				CERAD recall			
60–70	Model1	P	Model2	P	Model1	P	Model2	P	Model1	P	Model2	P	Model1	P	Model2	P
PBB153	0.12(-0.40, 0.64)	0.6	0.03(-0.56, 0.61)	>0.9	−0.39(-1.2, 0.40)	0.3	−0.12(-0.78, 0.55)	0.7	−2.2(-6.1, 1.8)	0.3	−3.6(-7.3, 0.18)	0.06	0.04(-0.84, 0.91)	>0.9	−0.1(-1.0, 0.81)	0.8
PBDE209	0.26(-0.78, 1.3)	0.6	0.72(-0.20, 1.6)	0.11	0.59(-0.80, 2.0)	0.4	0.03(-1.9, 2.0)	>0.9	0.04(-7.1, 7.2)	>0.9	2.2(-5.5, 9.9)	0.5	0.83(-0.88, 2.5)	0.3	1.5(-0.39, 3.4)	0.1
PBDE28	−0.65(-1.7, 0.40)	0.2	−0.24(-1.2, 0.74)	0.6	−1.4(-3.9, 1.1)	0.3	−1.9(-4.8, 0.92)	0.2	−6.6(-14, 0.65)	0.071	−4.9(-12, 1.8)	0.13	−0.78(-1.9, 0.38)	0.2	−0.18(-1.4, 1.0)	0.7
PBDE47	−0.44(-1.3, 0.46)	0.3	−0.15(-1.0, 0.68)	0.7	−1.6(-3.7, 0.45)	0.12	−2.1(-4.3, 0.09)	0.058	−6.3(-12, −0.46)	0.036	−5.2(-10, −0.02)	0.049	−0.37(-1.3, 0.53)	0.4	0.08(-0.88, 1.0)	0.9
PBDE85	−0.33(-1.1, 0.43)	0.4	−0.07(-0.76, 0.62)	0.8	−1.1(-2.7, 0.46)	0.15	−1.69(-3.5, 0.19)	0.073	−5.3(-11, 0.23)	0.059	−4.3(-9.0, 0.33)	0.065	−0.27(-1.0, 0.48)	0.5	0.16(-0.63, 0.95)	0.7
PBDE99	−0.41(-1.2, 0.38)	0.3	−0.12(-0.90, 0.66)	0.7	−1.7(-3.4, −0.01)	0.048	−2.2(-4.1, −0.26)	0.03	−7.5(-13, −2.1)	0.01	−6.2(-11, −1.4)	0.017	−0.39(-1.3, 0.55)	0.4	0.07(-0.93, 1.1)	0.9
PBDE100	−0.26(-1.1, 0.62)	0.5	0.01(-0.77, 0.79)	>0.9	−1.5(-3.4, 0.46)	0.12	−1.9(-4.1, 0.22)	0.073	−5(-11, 0.60)	0.077	−3.8(-8.8, 1.2)	0.12	−0.15(-1.0, 0.69)	0.7	0.29(-0.50, 1.1)	0.4
PBDE153	−0.33(-1.3, 0.62)	0.5	0.14(-0.82, 1.1)	0.7	−1.2(-3.1, 0.73)	0.2	−2.1(-4.6, 0.50)	0.1	−4.6(-12, 2.5)	0.2	−2.4(-9.2, 4.3)	0.4	−0.59(-1.8, 0.66)	0.3	0.04(-1.3, 1.4)	>0.9
PBDE154	−0.3(-1.1, 0.52)	0.5	−0.01(-0.78, 0.76)	>0.9	−1.5(-3.0, 0.06)	0.058	−2(-3.9, −0.15)	0.037	−6.3(-12, −0.44)	0.037	−5(-10, 0.20)	0.058	−0.23(-1.1, 0.65)	0.6	0.24(-0.60, 1.1)	0.5
70–80																
PBB153	0.13(-0.70, 1.0)	0.7	−0.02(-0.90, 0.85)	>0.9	0.15(-0.86, 1.2)	0.8	0.39(-0.74, 1.5)	0.4	−0.8(-3.7, 2.1)	0.6	−0.82(-4.7, 3.0)	0.6	0.89(-0.67, 2.4)	0.2	0.69(-1.0, 2.4)	0.4
PBDE209	−0.51(-1.4, 0.38)	0.2	−0.53(-1.7, 0.63)	0.3	1.2(-1.4, 3.8)	0.3	0.78(-2.7, 4.3)	0.6	−3.6(-9.0, 1.8)	0.2	−2.7(-9.9, 4.5)	0.4	−2.2(-3.8, −0.60)	0.011	−1.8(-3.7, 0.00)	0.05
PBDE28	−0.25(-2.2, 1.7)	0.8	−0.45(-2.3, 1.4)	0.6	1.2(-2.8, 5.1)	0.5	1.8(-3.0, 6.7)	0.4	−2.4(-11, 6.3)	0.6	−2.7(-12, 7.1)	0.5	0.14(-2.6, 2.9)	>0.9	−0.12(-2.7, 2.5)	>0.9
PBDE47	−0.04(-1.0, 1.0)	>0.9	−0.25(-1.4, 0.89)	0.6	0.49(-2.5, 3.5)	0.7	1.1(-2.7, 4.9)	0.5	0.14(-5.6, 5.8)	>0.9	−0.48(-7.8, 6.8)	0.9	0.17(-1.8, 2.2)	0.9	−0.1(-2.1, 1.9)	>0.9
PBDE85	−0.07(-1.1, 0.93)	0.9	−0.26(-1.4, 0.89)	0.6	0.41(-2.2, 3.1)	0.7	0.88(-2.6, 4.4)	0.6	−0.47(-6.1, 5.1)	0.9	−0.86(-8.0, 6.3)	0.8	0.11(-1.6, 1.8)	0.9	0(-1.8, 1.8)	>0.9
PBDE99	−0.02(-0.77, 0.72)	>0.9	−0.2(-1.1, 0.75)	0.6	0.01(-2.4, 2.4)	>0.9	0.63(-2.5, 3.8)	0.6	0.49(-4.3, 5.3)	0.8	−0.04(-6.2, 6.2)	>0.9	0.15(-1.4, 1.7)	0.8	−0.07(-1.7, 1.6)	>0.9
PBDE100	0(-0.84, 0.85)	>0.9	−0.22(-1.2, 0.76)	0.6	1.4(-1.0, 3.8)	0.2	1.8(-1.3, 4.8)	0.2	0.16(-4.0, 4.4)	>0.9	0.15(-5.7, 6.0)	>0.9	−0.09(-1.6, 1.4)	>0.9	−0.21(-1.9, 1.5)	0.8
PBDE153	0.05(-0.48, 0.58)	0.8	−0.18(-0.88, 0.51)	0.5	1.1(-0.32, 2.6)	0.12	1.7(-0.10, 3.4)	0.061	1.5(-0.55, 3.7)	0.14	1.3(-2.4, 4.9)	0.4	0.11(-1.0, 1.2)	0.8	−0.15(-1.3, 1.0)	0.8
PBDE154	−0.07(-0.83, 0.70)	0.9	−0.27(-1.2, 0.66)	0.5	0.72(-1.8, 3.2)	0.5	1.2(-1.9, 4.3)	0.4	−0.09(-4.5, 4.4)	>0.9	−0.09(-6.1, 5.9)	>0.9	−0.21(-1.7, 1.2)	0.8	−0.32(-1.9, 1.3)	0.6
≥80																
PBB153	0.08(-1.1, 1.3)	0.9	0.64(-1.3, 2.6)	0.3	−1.4(-3.3, 0.46)	0.12	−1.8(-5.9, 2.4)	0.2	−1.3(-6.0, 3.4)	0.6	−0.8(-13, 11)	0.8	−0.38(-2.3, 1.5)	0.7	−0.01(-3.5, 3.5)	>0.9
PBDE209	0.16(-0.68, 1.0)	0.7	−0.13(-2.1,1.9)	0.8	−0.79(-3.1, 1.5)	0.4	−0.8(-6.3, 4.7)	0.6	−5.2(-9.3, −1.0)	0.021	−4.5(-16, 7.1)	0.2	0.04(-2.0, 2.1)	>0.9	−0.09(-4.2, 4.0)	>0.9
PBDE28	0.9(-2.1, 3.9)	0.5	0.61(-4.5, 5.7)	0.7	−2.4(-5.8, 1.1)	0.2	−2.9(-9.4, 3.6)	0.2	−2.3(-13, 8.2)	0.6	−2.5(-20, 15)	0.6	0.63(-5.7, 7.0)	0.8	−0.08(-10, 10)	>0.9
PBDE47	0.55(-1.6, 2.7)	0.6	0.35(-3.4, 4.1)	0.7	−2(-3.7, −0.30)	0.026	−2.4(-6.3, 1.5)	0.11	−2.8(-8.3, 2.7)	0.3	−2.7(-14, 8.7)	0.4	0.38(-4.2, 5.0)	0.9	−0.04(-8.2, 8.1)	>0.9
PBDE85	0.34(-1.2, 1.9)	0.6	0.15(-2.7, 3.0)	0.8	−1.6(-2.6, −0.52)	0.009	−1.9(-4.6, 0.90)	0.1	−3(-6.2, 0.17)	0.061	−2.6(-11, 5.4)	0.3	0.13(-3.4, 3.7)	>0.9	−0.13(-6.6, 6.3)	>0.9
PBDE99	0.32(-1.2, 1.9)	0.6	0.09(-2.8, 3.0)	>0.9	−1.6(-2.6, −0.56)	0.007	−2(-4.7, 0.69)	0.085	−2.9(-6.3, 0.54)	0.088	−2.8(-11, 5.7)	0.3	0.25(-3.2, 3.7)	0.9	−0.15(-6.3, 6.0)	>0.9
PBDE100	0.5(-1.3, 2.3)	0.5	0.22(-3.0, 3.5)	0.8	−1.3(-3.0, 0.37)	0.11	−1.6(-6.4, 3.1)	0.3	−1.5(-6.8, 3.9)	0.5	−1.1(-13, 10)	0.7	0.61(-3.9, 5.1)	0.8	0.2(-7.9, 8.2)	>0.9
PBDE153	0.26(-0.83, 1.4)	0.6	0.06(-2.1, 2.2)	>0.9	−0.88(-2.5, 0.76)	0.3	−1(-5.8, 3.8)	0.5	−0.9(-5.9, 4.1)	0.7	0.17(-12, 12)	>0.9	0.11(-2.8, 3.0)	>0.9	−0.05(-5.9, 5.8)	>0.9
PBDE154	0.3(-1.0, 1.6)	0.6	0.08(-2.5, 2.6)	>0.9	−1.3(-2.4, −0.08)	0.039	−1.6(-4.7, 1.5)	0.2	−2.3(-5.4, 0.93)	0.14	−2.1(-9.9, 5.7)	0.4	0.31(-2.9, 3.5)	0.8	−0.02(-6.0, 6.0)	>0.9

*Model 1 is an unadjusted model, while Model 2 adjusts for covariates such as age, gender, education level, BMI, and stroke.

Availability of supporting data

N/A.

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Authors' contributions

RX H: Conceptualization, Writing – original draft manuscript, funding acquisition; JJ Y: Formal statistical analysis; LH X, CJ B, V M,HMH Z and D S I check out to extract data; V M,HMH Z and D S I

also participated in discussions on analytical methods and polishing articles. RX H critically reviewed the manuscript for important intellectual content, and critically revised the manuscript. RX H is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.emcon.2023.100259.

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