RESEARCH



Association between age at first birth and cognitive function in women 60 years and older: the 2011–2014 cross-sectional National Health and Nutrition Examination Survey (NHANES) study

Jia-nan Zhao^{1†}, Linqi Deng^{1†}, Chunyu Sun^{2†} and Muhui Lin^{1*}

Abstract

Background Cognitive function is a fundamental capacity essential for maintaining independence and performing complex tasks in daily life. Cognitive abilities gradually decline with age, potentially leading to dementia. Evidence suggests that female reproductive factors may influence cognitive function in later life through various mechanisms. However, the relationship between age at first birth (AFB) and cognitive function requires further investigation.

Methods This study utilizes data from the 2011–2014 National Health and Nutrition Examination Survey (NHANES), including 1,057 female participants. AFB data are obtained from reproductive health questionnaire. Cognitive function is assessed using the CERAD Word Learning Test, Animal Fluency Test, and Digit Symbol Substitution Test. Multiple linear regression, smoothed curve fitting, threshold analyses, and subgroup analyses are conducted to evaluate the association between AFB and cognitive function.

Results AFB is significantly and positively associated with cognitive function after adjusting for covariates. Women with $AFB \ge 20$ years exhibit a 34% lower prevalence of cognitive impairment and significantly higher cognitive test scores compared to those with AFB < 20 years. A nonlinear relationship is observed, with the positive effect of increasing AFB on cognitive function being more pronounced before age 21. The association between AFB and cognitive function is stronger among individuals without a history of stroke and those with moderate to high levels of waist-to-height ratio (WHtR) and weight-adjusted waist index (WWI).

Conclusion Later AFB is associated with a reduced prevalence of cognitive impairment and improved cognitive outcomes, particularly when the first birth occurs after age 21. Considering WHtR and WWI may further optimize the protective effects of AFB on cognitive health. These findings underscore the importance of reproductive timing for long-term cognitive health.

Keywords Age at first birth, Female reproductive factors, Cognitive impairment, Cognitive function, NHANES

[†]Jia-nan Zhao, Linqi Deng and Chunyu Sun contributed equally to this work.

*Correspondence: Muhui Lin IclImh@126.com Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Background

Cognitive function encompasses a range of mental processes and abilities including information processing, thinking, learning and memory. It forms the basis for maintaining independence in daily activities, as well as a core competency necessary for adapting to the environment and performing complex tasks. Therefore, cognitive health is essential for overall well-being and significantly influences quality of life. Previous research indicates that cognitive abilities gradually decline with aging [1]. Declining cognitive abilities eventually impair daily functioning, potentially progressing to dementia. Globally, dementia affects over 55 million individuals, with approximately 10 million new cases diagnosed annually [2]. Currently, the exact causes of dementia remain unclear, and there is no cure. In advanced stages, dementia patients experience a complete loss of self-care ability, placing significant burdens on families and society. Therefore, identifying factors that may influence cognitive function is of paramount importance. A study of age-related endophenotypes in advanced maternal age points to a correlation between age at last reproduction and cognitive function [3]. This suggests that female reproductive age may influence cognitive function in later life through a variety of mechanisms, and that there may be a complex biological link between female reproductive factors and cognitive function.

An increasing body of research suggests that female reproductive factors are closely associated with women's health. A study by Zuo et al. indicates that women who give birth for the first time at age 18 or older have a lower prevalence of depression compared to those whose first birth occurs before age 18 [4]. Furthermore, other studies demonstrate associations between female reproductive factors and various diseases, including cardiovascular disease, metabolic syndrome, and non-alcoholic fatty liver disease [5–7]. Nevertheless, studies exploring the association between AFB and cognitive function are still scarce, and the connections between AFB and specific cognitive domains have yet to be clarified.

Therefore, this study employs a cross-sectional design using data from the 2011–2014 NHANES to investigate

the relationship between a key milestone in the female reproductive cycle—age at first birth(AFB)—and cognitive function, including its specific domains.

Methods

Study design and data sources

The National Health and Nutrition Examination Survey (NHANES), conducted by the National Center for Health Statistics (NCHS), is a comprehensive, long-term health survey providing demographic data, physical examinations, laboratory tests, and questionnaire responses. It serves as a valuable resource for medical research. This study utilizes data from the 2011-2014 NHANES to explore the association between age at first birth and cognitive function in women aged 60 years and older. Of the initial sample of 19,931 participants, 16,299 individuals under the age of 60 are excluded, along with 698 participants lacking complete cognitive function questionnaire data, 1,813 missing AFB information, and 64 missing covariate data on BMI, waist circumference (WC), diabetes and alcohol consumption. Ultimately, 1,057 women aged 60 years and older are included in the analysis (Fig. 1). All NHANES protocols receive approval from the NCHS Ethics Review Board, and informed consent is collected from participants during recruitment. Further information can be found on the NHANES official website (https://www.cdc.gov/nchs/nhanes/index.htm).

Age at first birth

Information on age at first birth is obtained from the reproductive health questionnaire. Notably, AFB refers specifically to the age at first live birth excluding miscarriages or stillbirths. In the NHANES database, 20 years is used as the threshold to differentiate adolescent and adult [8–10]. Accordingly, participants are categorized into two groups: those with an AFB of less than 20 years and those with an AFB of 20 years or older.

Cognitive function

Cognitive function in individuals aged 60 and older is evaluated in NHANES through three standardized tests: the Consortium to Establish a Registry for Alzheimer's Disease Word Learning subtest (CERAD-WL), the Animal Fluency Test (AFT), and the Digit Symbol

⁽See figure on next page.)

Fig. 1 Flow chart. Presents a flowchart illustrating the screening process for the final study sample drawn from the 2011–2014 National Health and Nutrition Examination Survey (NHANES). The initial dataset comprises 19,931 participants. Of these, 16,299 participants who are younger than 60 years are excluded. Among the remaining 3,632 participants aged 60 years or older, 698 are excluded due to incomplete cognitive function data. Subsequently, 1,813 participants lacking information on age at first birth (AFB) are further excluded. Lastly, 64 participants with missing data on key covariates, including BMI, waist circumference (WC), alcohol consumption, hypertension, or diabetes, are excluded. After this screening process, the final eligible study sample consists of 1,057 participants

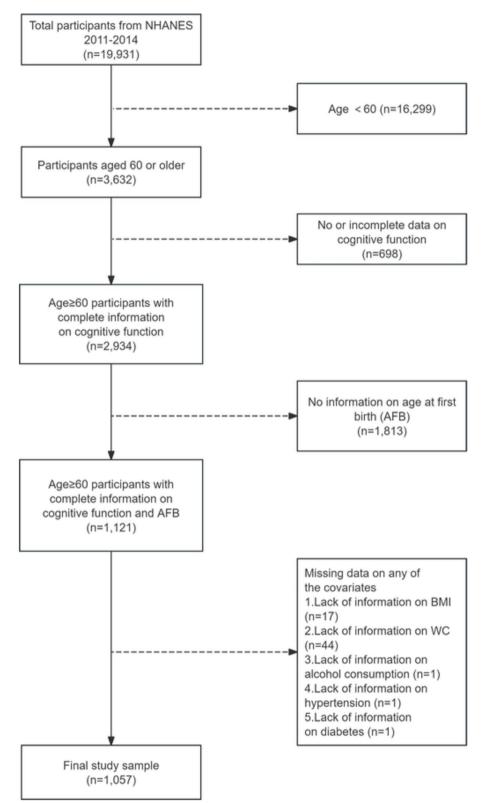


Fig. 1 (See legend on previous page.)

Substitution Test (DSST). These assessments are administered either during in-home interviews or at mobile examination centers.

The CERAD-WL assesses both immediate and delayed memory for newly acquired verbal information. Previous studies demonstrate that the CERAD-WL is an effective tool for screening for cognitive impairment [11, 12]. The test includes three sequential learning trials and a delayed recall session (DRT). In the learning trials, participants read aloud a list of 10 unrelated words and immediately attempt to recall as many as they can. Delayed recall is conducted approximately 8–10 min, following the completion of other cognitive tasks. The CERAD-WL score is determined by adding the number of words recalled during the three learning trials and the delayed recall phase, with a maximum possible score of 40.

The AFT is mainly used to evaluate categorical verbal fluency, which is an essential aspect of executive function [13]. Research indicates that AFT scores are effective in distinguishing between individuals with normal cognitive function, those with mild cognitive impairment, and those with more severe cognitive deficits, such as Alzheimer's disease [14–16]. In the test, participants are asked to name as many animals as they can in one minute, earning one point for each correct answer.

The DSST, part of the Wechsler Adult Intelligence Scale (WAIS III), assesses processing speed, sustained attention, and working memory. It has been widely employed in large-scale screening, epidemiological studies, and clinical research [17–19]. During the test, participants are presented with nine symbols, each paired with a corresponding number. They are required to match as many symbols with their corresponding numbers as possible within two minutes. The participant's score is determined by the total number of correct matches.

Overall cognitive function

To compare cognitive abilities across individuals, z-scores are calculated for each cognitive test. The z-scores is computed using the formula: $z = (x - m) / \sigma$ where x denotes the individual's raw score, m represents the population mean, and is the population standard deviation. The overall cognitive function score is derived by summing the z-scores of the CERAD-WL, AFT, and DSST, providing a composite measure of global cognitive function (CF). Cognitive impairment is characterized by a composite cognitive score that is one standard deviation below the population mean [20–23].

Covariates

Based on previous literature [24–27], potential confounding factors that might influence the association between AFB and cognitive function are adjusted for. These covariates encompass demographic factors such as age, race, education level, and marital status, as well as health and lifestyle elements including BMI, smoking status, alcohol consumption, and engagement in moderate recreational activities. In addition, common health conditions such as hypertension, diabetes, and stroke are also considered. It is important to note that although BMI is widely used as an indicator of obesity and associated health risks, it has inherent limitations. For example, BMI does not distinguish between muscle mass and fat mass, nor does it reflect the distribution of adipose tissue [28–30]. Given these limitations, two additional indices— WHtR and WWI-are incorporated to better capture the accumulation of abdominal and visceral fat. These indices are calculated as follows: WHtR=WC (cm) / height (cm), and WWI = WC (cm) / square root of Weight (KG).

Participants are categorized into three age groups: 60–69, 70–79, and \geq 80 years. Race is classified as Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other. Educational attainment is divided into five levels: less than 9th grade, 9th-11th grade, high school graduate/GED or equivalent, some college or an AA degree, and college graduate or above. Marital status is categorized as married, widowed, divorced, separated, never married, or living with a partner. BMI is grouped into underweight (<18.5), normal $(\geq 18.5, <25)$, overweight $(\geq 25, <30)$, and obese (≥ 30) . WHtR and WWI are categorized into quartiles. Alcohol consumption is defined as "yes" or "no" depending on whether participants consumed at least 12 alcoholic beverages in the past year. Smoking status is similarly classified as "yes" or "no" based on whether participants have smoked at least 100 cigarettes in their lifetime. Hypertension, diabetes, and stroke status are determined based on whether a physician has informed the participant of these conditions, diabetes is further categorized as "yes", "no", or "borderline". Engagement in moderate physical activity which defined as activities such as brisk walking, cycling, swimming, or golfing for at least 10 consecutive minutes is also recorded as "yes" or "no". Additional information about the covariates is available on the official NHANES website (https://www.cdc.gov/nchs/nhanes/index.htm).

Statistical analysis

To explore the relationship between AFB and cognitive function, this study initially uses chi-square tests and t-tests to compare the demographic characteristics of participants. Continuous variables are reported as means with standard deviations, while categorical variables are represented as percentages. Subsequently, three multiple linear regression models are then developed to clarify the relationship between AFB and cognitive function, with adjustments made for potential confounding factors. Model 1 is unadjusted, Model 2 adjusts for age and race, and Model 3 further adjusts for age, race, education level, marital status, BMI, smoking status, alcohol consumption, engagement in moderate physical activity, hypertension, diabetes, and stroke. Additionally, AFB, originally considered as a continuous variable, is converted into a categorical variable based on adulthood status for trend analysis to evaluate its potential association with cognitive function. Cognitive scores are also converted into categorical variables, and multiple logistic regression is performed to further explore the relationship between AFB and cognitive function. To compare the impact of different obesity indicators, BMI in Model 3 is replaced with WHtR and WWI, respectively, to evaluate differences in the association between AFB and cognitive function when different obesity measures are used as covariates. In terms of analytical methods, generalized sum model and smooth fitting curves are used to visualize the nonlinear relationship between AFB and cognitive function, and threshold analysis is conducted to identify inflection points. In addition, stratified analyses and interaction tests are performed to compare differences among subgroups, with a *p*-value of < 0.05 considered statistically significant. All statistical analyses are conducted using R version 4.3.3 and Empowerstats version 2.0.

Results

Baseline characterization

Participants are divided into two groups based on adulthood status at first birth: the AFB < 20 years group (31.98%) and the AFB \geq 20 years group (68.02%). Table 1 presents the differences in demographic characteristics and health status between these groups (Table 1).

In terms of age, the mean age in the AFB<20 years group is 68.48 ± 6.45 years, significantly lower than 70.22 ± 6.89 years in the AFB \geq 20 years group (p < 0.001). Although non-Hispanic Whites constitute a large proportion in both groups, significant differences in racial composition are observed (p < 0.001). Regarding education, despite a high proportion of participants with some college or an AA degree in both groups, overall educational levels differ significantly (p < 0.001). Similarly, marital status differs significantly between groups, even though both are predominantly composed of married individuals (p < 0.001). Concerning health indicators, the AFB < 20 group exhibits a significantly higher BMI (30.53 ± 6.63) compared to the AFB \geq 20 group (29.16 ± 6.60, *p* = 0.003), and the WHtR is also notably higher in the AFB<20 group (0.64 ± 0.08 vs. 0.63 ± 0.09 , p = 0.016). In addition, the proportion of smokers is higher in the AFB < 20 group (p < 0.001), whereas a greater proportion of participants in the AFB \geq 20 group engage in moderate physical activity (p = 0.019). Significant differences are also observed in the prevalence of hypertension and diabetes: the AFB < 20 group shows a hypertension prevalence of 71.30% compared to 63.84% in the AFB ≥ 20 group (p=0.017), and the diabetes prevalence is 28.40% in the AFB < 20 group, which is significantly higher than 18.78% in the AFB ≥ 20 group (p=0.001). No significant differences are observed between the two groups for WWI, alcohol consumption, or stroke.

Regarding cognitive function, the proportion of cognitive impairment is 20.71% in the AFB < 20 group, which is significantly higher than the 13.77% observed in the AFB \geq 20 group (p = 0.004). In specific cognitive tests, scores in the AFB \geq 20 group are significantly higher than those in the AFB < 20 group. Furthermore, the composite cognitive function score for the AFB \geq 20 group is 0.34 ± 2.42, which is significantly higher than the -0.49 ± 2.22 observed in the AFB < 20 group (p < 0.001). These results further indicate that a later AFB may be associated with better cognitive performance.

Association of AFB with cognitive function

To assess the relationship between AFB and the prevalence of cognitive impairment, the overall cognitive function score is dichotomized into a binary variable. In the unadjusted model, participants with AFB \geq 20 years exhibit a 39% lower prevalence of cognitive impairment compared to those with AFB < 20 years [0.61 (0.44,0.86)]. After full adjustment, the prevalence of cognitive impairment in the AFB \geq 20 years group remains 34% lower compared to the AFB < 20 years group [0.66 (0.44,0.99)] (Table 2).

To further clarify the relationship between AFB and specific cognitive domains, as well as overall cognitive function scores, multiple linear regression analyses are conducted to explore the relationships between AFB and CERAD-WL, DRT, AFT, DSST, and CF. A strong positive correlation is observed between AFB and cognitive performance across all models, including unadjusted, partially adjusted, and fully adjusted models. In the unadjusted model, AFB as a continuous variable shows positive correlations with CERAD-WL [0.03 (0.02,0.05)], DRT [0.03 (0.02,0.04)] · AFT [0.04 (0.02,0.05)], DSST [0.05 (0.03,0.06)] and CF [0.11 (0.08,0.15)]. These positive associations persist in the fully adjusted model, with CERAD-WL [0.02 (0.01,0.04)], DRT [0.02 (0.01,0.03)], AFT [0.03 (0.01,0.04)], DSST [0.02 (0.01,0.04)] and CF [0.07 (0.04,0.10)] all demonstrating significant positive relationships. When AFB is categorized, further analyses reveal a robust association between AFB and cognitive function. In the fully adjusted model, participants in the AFB \geq 20 years group outperform those in the AFB < 20 years group across all cognitive measures, including CERAD-WL [0.22 (0.09,0.34)], DRT

Characteristics	AFB<20 n=338(31.98%)	AFB > = 20 n = 719(68.02%)	<i>P</i> -value
Age	68.48±6.45	70.22±6.89	< 0.001
Race			< 0.001
Mexican American	40 (11.83%)	63 (8.76%)	
Other Hispanic	45 (13.31%)	78 (10.85%)	
Non-Hispanic White	128 (37.87%)	397 (55.22%)	
Non-Hispanic Black	112 (33.14%)	110 (15.30%)	
Other Race—Including Multi-Racial	13 (3.85%)	71 (9.87%)	
Education			< 0.001
Less than 9th grade	55 (16.27%)	59 (8.21%)	
9-11th grade	91 (26.92%)	84 (11.68%)	
High school graduate/GED or equivalent	82 (24.26%)	180 (25.03%)	
Some college or AA degree	93 (27.51%)	240 (33.38%)	
College graduate or above	17 (5.03%)	156 (21.70%)	
Marital			< 0.001
Married	118 (34.91%)	368 (51.18%)	
Widowed	115 (34.02%)	204 (28.37%)	
Divorced	69 (20.41%)	101 (14.05%)	
Separated	13 (3.85%)	19 (2.64%)	
Never married	15 (4.44%)	17 (2.36%)	
Living with partner	8 (2.37%)	10 (1.39%)	
BMI	30.53±6.63	29.16±6.60	0.003
WHtR	0.64 ± 0.08	0.63 ± 0.09	0.016
WWI	11.64±0.69	11.64±0.72	0.857
Smoke			< 0.001
Yes	159 (47.04%)	242 (33.66%)	
No	179 (52.96%)	477 (66.34%)	
Drink			0.499
Yes	173 (51.18%)	384 (53.41%)	
No	165 (48.82%)	335 (46.59%)	
Hypertension			0.017
Yes	241 (71.30%)	459 (63.84%)	
No	97 (28.70%)	260 (36.16%)	
Diabetes			0.001
Yes	96 (28.40%)	135 (18.78%)	
No	225 (66.57%)	554 (77.05%)	
Borderline	17 (5.03%)	30 (4.17%)	
Stroke			0.762
Yes	23 (6.80%)	44 (6.12%)	
No	315 (93.20%)	675 (93.88%)	
Moderate Recreational Activities			0.019
Yes	110 (32.54%)	288 (40.06%)	
No	228 (67.46%)	431 (59.94%)	
Cognitive Impairment			0.004
Yes	70 (20.71%)	99 (13.77%)	
No	268 (79.29%)	620 (86.23%)	
CERAD-WL	25.04±6.11	26.52 ± 6.51	< 0.001
DRT	5.99±2.17	6.37±2.29	0.004
AFT	15.63±4.81	17.01±5.43	< 0.001
DSST	43.62±16.62	49.70±16.99	< 0.001
CF	-0.49±2.22	0.34 ± 2.42	< 0.001

The baseline characteristics of women aged 60 years and older are categorized into two groups based on age at first birth (AFB): AFB < 20 years and AFB \geq 20 years. These characteristics include age, race, education level, marital status, BMI, WHtR, WWI, smoking, alcohol use, engagement in moderate recreational activities, hypertension, diabetes, stroke, and cognitive impairment. Additionally, *p*-values are provided for each characteristic to indicate the statistical significance of differences between the two groups

Table 2 Association between AFB and cognitive impairment

Crude Model (Model 1)	
Continuous	0.92 (0.88, 0.96) < 0.001
Categories	
< 20	Reference
>=20	0.61 (0.44, 0.86) 0.004
Partly adjusted Model (Model 2)	
Continuous	0.93 (0.89, 0.98) 0.004
Categories	
< 20	Reference
>=20	0.60 (0.41, 0.88) 0.009
Fully adjusted Model (Model 3)	
Continuous	0.94 (0.90, 0.99) 0.022
Categories	
< 20	Reference
>=20	0.66 (0.44, 0.99) 0.042

The association between AFB and cognitive impairment is described, including odds ratios (ORs) and 95% confidence intervals (Cls) for unadjusted (Model 1), partially adjusted (Model 2), and fully adjusted (Model 3) models. *P*-values are also provided to indicate the statistical significance of the findings

[0.14 (0.01,0.26)], AFT [0.20 (0.07,0.32)], DSST [0.25 (0.14,0.36)] and CF [0.66 (0.39,0.94)] (Table 3).

Due to the inherent limitations of BMI in measuring obesity, WHtR and WWI are used as alternative covariates in Model 3. These indices more accurately reflect abdominal obesity and visceral fat accumulation compared with BMI. By comparing the relationship between AFB and cognitive function after adjusting for different obesity indicators, a more precise evaluation of the association between AFB and cognitive function is achieved. Table 4 displays the associations between AFB and cognitive function across three models. The results indicate that when BMI is replaced with either WHtR or WWI, the association between AFB and cognitive function remains essentially unchanged. In other words, regardless of whether BMI, WHtR, or WWI is used as a covariate, a later AFB is consistently associated with better cognitive performance and a lower prevalence of cognitive impairment.

Nonlinear relationship between AFB and cognitive function

This study finds a positive association between AFB and cognitive function using multiple linear regression analysis. However, the model assumes a linear relationship between the independent and dependent variables. Therefore, to further investigate whether a nonlinear association exists between AFB and CF, this study employs a smoothing curve fitting method to explore potential nonlinear trends and assess the presence of threshold effects.

The results of the threshold effect analysis reveal significant nonlinear relationships between AFB and DSST as well as AFB and CF (LLR < 0.001, LLR = 0.024) (Table 5). Specifically, when AFB is below 22 years, the positive association between AFB and DSST is more pronounced, while beyond 22 years, further increases in AFB have a negligible effect on DSST (Fig. 2D). Similarly, for CF, a positive trend is observed as AFB increases up to 21 years, but after 21 years, the influence of AFB on overall cognitive function diminishes (Fig. 2E). These findings suggest that an earlier AFB may have a greater impact on women's cognitive function, while the effect of AFB becomes less significant for those whose first birth occurs after the ages of 21 or 22. Specifically, cognitive processing speed, attention, memory, coordination, and overall cognitive ability are less influenced by AFB in women whose first birth occurs at a later age. Additionally, linear relationships are observed between AFB and CERAD-WL, DRT and AFT (Fig. $2A \times B$ and C). These findings provide new perspectives for understanding the complexity of the effects of AFB on women's cognitive function and highlight that the timing of childbirth may have varying effects on cognitive function at different stages of life.

Subgroup analysis

To assess whether the relationship between AFB and cognitive function remains consistent across various populations, this study conducts a stratified analysis base on variables including age, race, marital status, engagement in moderate physical activity, alcohol consumption, smoking status, hypertension, diabetes, stroke, BMI, WHtR, and WWI. Interaction tests are performed to evaluate potential variations in the relationship between AFB and cognitive function across subgroups. The results indicate that, among individuals with a history of stroke, the association between AFB and CERAD-WL is not statistically significant [-0.05 (-0.13, 0.02)], whereas among participants without a history of stroke, each unit increase in AFB is associated with a 0.03 point increase in the standardized CERAD-WL score [0.03 (0.01, 0.04)]. This finding suggests heterogeneity in the relationship between AFB and verbal learning and memory across stroke status (P for interaction = 0.04). No significant differences are observed in the association between AFB and various cognitive domains or overall cognitive function across different BMI levels. However, when stratifying by WHtR, significant differences in the association emerge. In the Q1 (≥ 0.566) and Q2 $(>0.566, \le 0.624)$ groups, the relationship between AFB and cognitive function is not significant, whereas in the Q3 (>0.624, \leq 0.687) and Q4 (>0.687) groups, a significant positive association is observed, particularly for DSST and CF. Further interaction tests reveal significant

AFB	CERAD-WL β(95% CI) <i>p</i> -value	DRT β(95% CI) <i>p</i> -value	AFT β(95% CI) <i>p</i> -value	DSST β(95% CI) <i>p</i> -value	CF β(95% CI) <i>p</i> -value
Crude Model (Mo	odel 1)				
Continuous	0.94 (0.90, 0.99) 0.022	0.94 (0.90, 0.99) 0.022	0.94 (0.90, 0.99) 0.022	0.94 (0.90, 0.99) 0.022	0.94 (0.90, 0.99) 0.022
Categories					
< 20	Reference	Reference	Reference	Reference	Reference
>=20	0.66 (0.44, 0.99) 0.042	0.66 (0.44, 0.99) 0.042	0.66 (0.44, 0.99) 0.042	0.66 (0.44, 0.99) 0.042	0.66 (0.44, 0.99) 0.042
Partly adjusted N	lodel (Model 2)				
Continuous	0.03 (0.02, 0.04) < 0.001	0.02 (0.01, 0.04) < 0.001	0.03 (0.02, 0.04) < 0.001	0.03 (0.02, 0.04) < 0.001	0.09 (0.06, 0.12) < 0.001
Categories					
< 20	Reference	Reference	Reference	Reference	Reference
>=20	0.26 (0.14, 0.39) < 0.001	0.18 (0.06, 0.31) 0.004	0.23 (0.11, 0.35) < 0.001	0.30 (0.19, 0.41) < 0.001	0.79 (0.52, 1.07) < 0.001
Fully adjusted Mo	odel (Model 3)				
Continuous	0.02 (0.01, 0.04) < 0.001	0.02 (0.01, 0.03) 0.006	0.03 (0.01, 0.04) < 0.001	0.02 (0.01, 0.04) < 0.001	0.07 (0.04, 0.10) < 0.001
Categories					
< 20	Reference	Reference	Reference	Reference	Reference
>=20	0.22 (0.09, 0.34) < 0.001	0.14 (0.01, 0.26) 0.033	0.20 (0.07, 0.32) 0.002	0.25 (0.14, 0.36) < 0.001	0.66 (0.39, 0.94) < 0.001

Table 3 Association between AFB and cognitive scores

The associations between AFB and scores on various cognitive tests, including the CERAD-WL, DRT, AFT, DSST, and CF, are presented. The results include regression coefficients (β), 95% confidence intervals (CIs), and *p*-values for unadjusted (Model 1), partially adjusted (Model 2), and fully adjusted (Model 3) models

heterogeneity in the association between AFB and both DSST (P for interaction=0.010) and CF (P for interaction = 0.011) between the Q3 and Q4 groups. Specifically, in the Q3 group, later AFB is significantly associated with better cognitive performance, whereas in the Q4 group, although the association remains statistically significant, its magnitude is somewhat attenuated. A similar pattern is observed in the stratified analysis by WWI. For WWI, significant heterogeneity is found in the relationship between AFB and AFT (P for interaction = 0.027). In the Q1 group (\leq 11.156), no significant association is detected between AFB and AFT, however, in the Q2 $(>11.156, \le 11.658)$ and Q3 $(>11.658, \le 12.112)$ groups, a gradually stronger positive association is observed, which then weakens in the Q4 group (>12.112). Overall, the positive impact of later AFB on cognitive function is most pronounced among individuals without a history of stroke and those with higher WHtR and WWI, whereas in other subgroups, these differences are not statistically significant (Table 6).

Discussion

This study aims to evaluate the relationship between AFB and cognitive function among women aged 60 years and older. In a cross-sectional study of 1,057 participants, a significant positive association is observed between AFB and several cognitive domains as well as overall cognitive function. Further analyses reveal that the effect of AFB on different cognitive domains and overall cognitive function varies significantly among subgroups. Specifically, a linear relationship is observed between AFB and episodic memory, working memory, language fluency, cognitive flexibility, and information retrieval, indicating that later AFB is associated with stronger performance in these domains. In contrast, a nonlinear relationship is found between AFB and processing speed, sustained attention, executive function, and overall cognitive function, the positive association is significant before the age of 22 but loses statistical significance thereafter. Additionally, the association between AFB and overall cognitive function is significantly positive before 21 years and gradually weakens with increasing AFB beyond this age. Furthermore, in participants without a history of stroke, the association between AFB and verbal learning and memory is stronger, whereas in those with a history of stroke, this association is absent. In groups with higher WHtR (Q3 and Q4) and WWI (Q2, Q3, and Q4), significant associations are observed between AFB and processing speed, executive function, overall cognitive function, as well as language fluency and cognitive flexibility. In

AFB	CERAD-WL β(95% CI) <i>p</i> -value	DRT β(95% CI) <i>p</i> -value	AFT β(95% CI) <i>p</i> -value	DSST β(95% CI) <i>p</i> -value	CF β(95% CI) <i>p</i> -value	Cognitive Impairment OR(95% CI) <i>p</i> -value
BMI as covariat	es					
Continuous	0.02 (0.01, 0.04) < 0.001	0.02 (0.01, 0.03) 0.006	0.03 (0.01, 0.04) < 0.001	0.02 (0.01, 0.04) < 0.001	0.07 (0.04, 0.10) < 0.001	0.94 (0.90, 0.99)0.022
Categories						
< 20	Reference	Reference	Reference	Reference	Reference	Reference
>=20	0.22 (0.09, 0.34) < 0.001	0.14 (0.01, 0.26)0.033	0.20 (0.07, 0.32)0.002	0.25 (0.14, 0.36) < 0.001	0.66 (0.39, 0.94) < 0.001	0.66 (0.44, 0.99)0.042
WHtR as covari	ates					
Continuous	0.02 (0.01, 0.04) < 0.001	0.02 (0.01, 0.03)0.008	0.03 (0.01, 0.04) < 0.001	0.02 (0.01, 0.04) < 0.001	0.07 (0.04, 0.10) < 0.001	0.94 (0.90, 0.99)0.020
Categories						
< 20	Reference	Reference	Reference	Reference	Reference	Reference
>=20	0.22 (0.09, 0.34) < 0.001	0.14 (0.01, 0.26) 0.034	0.20 (0.08, 0.32) 0.002	0.25 (0.14, 0.36) < 0.001	0.67 (0.39, 0.94) < 0.001	0.66 (0.44, 0.98) 0.038
WWI as covaria	tes					
Continuous	0.02 (0.01, 0.04) < 0.001	0.02 (0.01, 0.03)0.007	0.03 (0.01, 0.04) < 0.001	0.02 (0.01, 0.04) < 0.001	0.07 (0.04, 0.11) < 0.001	0.94 (0.89, 0.98)0.010
Categories						
< 20	Reference	Reference	Reference	Reference	Reference	Reference
>=20	0.22 (0.10, 0.35) < 0.001	0.14 (0.02, 0.27)0.026	0.21 (0.08, 0.33)0.001	0.25 (0.14, 0.36) < 0.001	0.68 (0.41, 0.95) < 0.001	0.62 (0.41, 0.92)0.018

Table 4 Relationship between AFB and cognitive function after controlling for different obesity indic
--

This table presents the relationship between AFB and cognitive function after controlling for different obesity indicators, including BMI, WHtR, and WWI. Cognitive function is assessed using the CERAD-WL, DRT, AFT, DSST and CF. The results are reported as regression coefficients (β) with 95% confidence intervals (CIs) and corresponding *p*-values. Additionally, the association between AFB and cognitive impairment is evaluated using odds ratios (OR)

contrast, these associations are not significant in groups with lower WHtR and WWI. Overall, these findings indicate that the impact of AFB on cognitive function is domain-specific and age-dependent, suggesting that a later AFB may confer cognitive benefits in later life.

Previous studies primarily examine the effects of menopause age and length of reproductive life on cognitive function in women, revealing the potential important role of female reproductive factors in cognitive health. Evidence from research on gender differences in cognitive impairment indicates that postmenopausal women have a significantly higher risk of developing memory impairment than men. Moreover, varying levels of female reproductive factors are associated with differing degrees of increased risk for memory impairment [31]. These results suggest that female reproductive factors may partially explain gender differences in cognitive impairment. Wedatilake et al.'s study of 5,314 Norwegian women supports this hypothesis, reporting that later menopause and a longer reproductive span are linked to a lower risk of dementia. Further analysis reveals that women with later age at menopause is significantly linked to lower risks of both Alzheimer's disease and vascular dementia [32]. A study conducted in Taiwan further investigates the relationships between age at menarche, reproductive span, and the subdomains of the Mini-Mental State Examination (MMSE). It finds a negative association between age at menarche and the MMSE G2 and G5 subdomains, while no significant relationships are observed for other subdomains. Similarly reproductive span does not show significant associations with any of the MMSE subdomains [33]. These findings, aligned with our results, strengthen the evidence for an association between female reproductive factors and cognitive function.

The positive association between AFB and cognitive function may involve multiple biological mechanisms. Previous studies indicate that estrogen plays a crucial role in regulating neuroplasticity. It stimulates the growth of neural progenitor cells in the subgranular zone of the hippocampal dentate gyrus, where the generation of new neurons in the dentate gyrus is believed to support associative learning and memory functions [34, 35]. Additionally, estrogen induces morphological plasticity by increasing the number of dendritic spines [36], and enhancing synaptic junctions, thereby facilitating the dynamic regulation of neural networks [37]. This process optimizes information processing pathways and provides robust support for cognitive flexibility and adaptability. Collectively, these findings suggest that estrogen enhances and maintains cognitive function through

Tabl	e 5	Analysi	s of three	shold anc	saturation e	effects
------	-----	---------	------------	-----------	--------------	---------

Outcome	β(95% CI) <i>p</i> -value		
CERAD-WL			
Breakpoint (k)	21		
< k-segment effect 1	0.05 (0.01, 0.09) 0.022		
>k-segment effect 2	0.02 (-0.00, 0.04) 0.124		
Difference in effect between 2 and 1	-0.03 (-0.08, 0.02) 0.256		
Log likelihood ratio	0.251		
DRT			
Breakpoint (k)	17		
< k-segment effect 1	-0.04 (-0.19, 0.12) 0.646		
>k-segment effect 2	0.02 (0.01, 0.04) 0.005		
Difference in effect between 2 and 1	0.06 (-0.10, 0.21) 0.473		
Log likelihood ratio	0.468		
AFT			
Breakpoint (k)	29		
< k-segment effect 1	0.03 (0.01, 0.05) < 0.001		
>k-segment effect 2	-0.02 (-0.08, 0.05) 0.625		
Difference in effect between 2 and 1	-0.05 (-0.12, 0.03) 0.202		
Log likelihood ratio	0.197		
DSST			
Breakpoint (k)	22		
< k-segment effect 1	0.07 (0.04, 0.10) < 0.001		
>k-segment effect 2	-0.01 (-0.03, 0.02) 0.617		
Difference in effect between 2 and 1	-0.08 (-0.12, -0.03) < 0.00		
Log likelihood ratio	< 0.001		
CF			
Breakpoint (k)	21		
< k-segment effect 1	0.17 (0.08, 0.25) < 0.001		
>k-segment effect 2	0.04 (-0.01, 0.08) 0.103		
Difference in effect between 2 and 1	-0.13 (-0.24, -0.02) 0.026		
Log likelihood ratio	0.024		

Threshold and saturation effects between AFB and cognitive test scores are analyzed. The analysis includes breakpoints (k-values) for individual tests, effect sizes across different k-value bands, differences in effects, and log-likelihood ratios (LLRs)

various pathways. Based on the results of this study, it is hypothesized that a later AFB may prolong the protective effects of estrogen to some extent. Typically, estrogen levels peak during the menstrual cycle just before ovulation [38]. Earlier childbearing means that women are exposed to abrupt hormonal fluctuations at a younger age, reducing the duration of stable high estrogen exposure. In contrast, a later AFB allows women to experience more menstrual cycles before pregnancy, thus prolonging stable estrogen secretion and the period of high estrogen exposure. This extended exposure may have a positive impact on enhanced cognitive function. Furthermore, the observed threshold effect between AFB and cognitive function suggests that the effect of AFB on cognitive function differed significantly before and after a specific age point. This effect may result from changes in overall health status or physiological burdens associated with delayed childbearing, which could partially offset its cognitive benefits [39], leading to a saturation of protective effects. Therefore, reproductive decision-making at different ages should take into account the potential impacts of both age and health factors on cognitive function.

Furthermore, the study finds that the association between AFB and cognitive function varies significantly across subgroups defined by WHtR, WWI, and stroke history. WHtR and WWI are key indicators of abdominal obesity and visceral fat accumulation, which more accurately capture the impact of central obesity than BMI. Previous studies have demonstrated a significant inverse relationship between WHtR and WWI and cognitive function, with evidence of threshold effects of WWI on AFT and DSST [24, 40, 41]. Golan et al. refine the classification of visceral fat and observe that increased pancreatic and hepatic fat is associated with reduced volumes in the hippocampus and inferior frontal gyrus, indicating cognitive decline, particularly in executive decisionmaking [42]. Additional evidence suggests that obesity induces changes in brain microstructure [43], specifically, increased microglial activation in the hippocampus triggers a series of synaptic alterations, such as impaired hippocampal synaptic plasticity, reduced dendritic spine

(See figure on next page.)

Fig. 2 Nonlinear relationship between AFB and scores on different cognitive tests. This figure illustrates the relationship between age at first birth (AFB) and scores on various cognitive functioning tests. The red trend line in each graph highlights the positive correlation between AFB and cognitive test scores, while the two blue lines represent the 95% confidence intervals. Together, these graphs visually present the relationship between age at first birth and cognitive function in later life. A Displays the relationship between AFB and CERAD-WL (Word Learning Test) scores. As AFB increases, CERAD-WL scores exhibit an upward trend, suggesting that a later age at first birth is associated with better immediate and delayed memory performance. B Depicts the relationship between AFB and DRT (Delayed Recall Session) scores. DRT scores rise as AFB increases, indicating that later childbearing is associated with enhanced delayed memory. C Shows the relationship between AFB and AFT (Animal Fluency Test) scores. AFT scores also increase with higher AFB, suggesting that a later age at first birth correlates with greater categorical verbal fluency. D Illustrates the relationship between AFB and DSST (Digit Symbol Substitution Test) scores. DSST scores increase with rising AFB, but the relationship plateaus beyond a certain age. E Demonstrates the relationship between AFB and CF (Comprehensive Cognitive Function) scores. CF scores increase with AFB, but, similar to DSST, the association flattens beyond a specific age

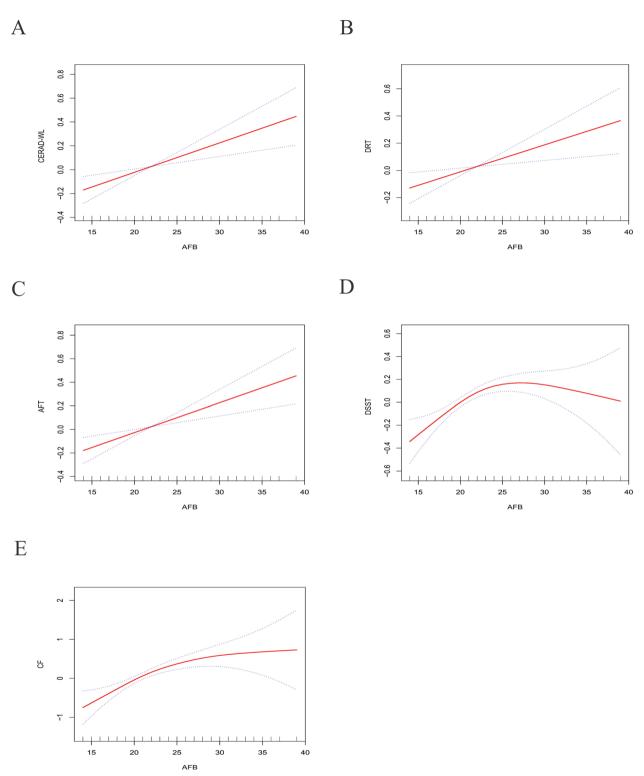


Fig. 2 (See legend on previous page.)

density, and a decreased number of excitatory synapses, all of which contribute to cognitive decline [44]. These findings indicate that abdominal obesity and visceral fat accumulation may lead to structural brain changes that adversely affect cognitive function. Moreover, research indicates that abdominal obesity, particularly visceral fat

Subgroup	CERAD-WL	DRT	AFT	DSST	CF
Age					
60–69	0.03 (0.01, 0.04)	0.02 (-0.00, 0.04)	0.04 (0.02, 0.06)	0.03 (0.01, 0.05)	0.10 (0.05, 0.14)
70–79	0.03 (-0.00, 0.06)	0.02 (-0.00, 0.05)	0.01 (-0.01, 0.04)	0.02 (-0.01, 0.04)	0.06 (-0.01, 0.12)
>=80	0.03 (-0.01, 0.07)	0.02 (-0.02, 0.06)	-0.01 (-0.05, 0.03)	0.02 (-0.02, 0.05)	0.04 (-0.05, 0.13)
P for interaction	0.976	0.929	0.072	0.490	0.380
Race					
Mexican American	0.02 (-0.02, 0.07)	0.00 (-0.04, 0.05)	0.05 (0.01, 0.09)	0.02 (-0.02, 0.06)	0.09 (-0.00, 0.19)
Other HiXspanic	-0.02 (-0.06, 0.03)	-0.01 (-0.05, 0.04)	0.01 (-0.03, 0.06)	0.01 (-0.03, 0.05)	0.01 (-0.08, 0.11)
Non-Hispanic White	0.03 (0.00, 0.05)	0.02 (-0.00, 0.04)	0.02 (0.00, 0.04)	0.02 (0.01, 0.04)	0.07 (0.03, 0.12)
Non-Hispanic Black	0.02 (-0.01, 0.05)	0.01 (-0.02, 0.04)	0.04 (0.00, 0.07)	0.02 (-0.01, 0.05)	0.08 (0.01, 0.15)
Other Race—Including Multi-Racial	0.07 (0.02, 0.12)	0.08 (0.02, 0.13)	-0.00 (-0.05, 0.05)	0.05 (0.01, 0.10)	0.12 (0.01, 0.24)
P for interaction	0.117	0.137	0.496	0.660	0.585
Marital					
Married	0.03 (0.01, 0.05)	0.03 (0.01, 0.05)	0.02 (-0.00, 0.04)	0.03 (0.01, 0.04)	0.08 (0.03, 0.12)
Widowed	0.03 (-0.00, 0.06)	0.02 (-0.01, 0.05)	0.04 (0.01, 0.06)	0.03 (0.00, 0.05)	0.09 (0.03, 0.15)
Divorced	0.02 (-0.02, 0.05)	0.00 (-0.04, 0.04)	0.07 (0.03, 0.10)	0.04 (0.01, 0.07)	0.12 (0.04, 0.20)
Separated	-0.07 (-0.20, 0.07)	-0.05 (-0.19, 0.08)	-0.07 (-0.20, 0.06)	-0.13 (-0.25, -0.02)	-0.26 (-0.55, 0.02
Never married	-0.03 (-0.21, 0.15)	0.04 (-0.14, 0.23)	-0.06 (-0.24, 0.12)	0.06 (-0.10, 0.22)	-0.03 (-0.43, 0.37
Living with partner	0.26 (-0.08, 0.60)	0.36 (0.01, 0.70)	0.02 (-0.32, 0.36)	-0.04 (-0.33, 0.26)	0.25 (-0.49, 0.99)
P for interaction	0.381	0.221	0.072	0.116	0.166
Drink					
Yes	0.04 (0.02, 0.06)	0.03 (0.01, 0.05)	0.04 (0.02, 0.06)	0.03 (0.01, 0.05)	0.10 (0.06, 0.14)
No	0.01 (-0.01, 0.03)	0.01 (-0.01, 0.03)	0.01 (-0.01, 0.03)	0.02 (0.00, 0.04)	0.04 (-0.00, 0.09)
P for interaction	0.122	0.249	0.067	0.465	0.067
Hypertension					
Yes	0.03 (0.01, 0.05)	0.02 (0.00, 0.04)	0.02 (-0.00, 0.03)	0.03 (0.01, 0.04)	0.07 (0.03, 0.11)
No	0.02 (-0.01, 0.04)	0.02 (-0.00, 0.04)	0.04 (0.02, 0.06)	0.02 (-0.00, 0.04)	0.08 (0.03, 0.13)
P for interaction	0.342	0.989	0.081	0.506	0.934
Diabetes					
Yes	0.04 (0.01, 0.08)	0.04 (0.01, 0.08)	0.03 (-0.00, 0.07)	0.03 (0.00, 0.06)	0.11 (0.03, 0.18)
No	0.02 (0.01, 0.04)	0.02 (0.00, 0.03)	0.02 (0.01, 0.04)	0.02 (0.01, 0.04)	0.07 (0.03, 0.10)
Borderline	0.06 (-0.00, 0.12)	0.03 (-0.03, 0.10)	0.06 (-0.01, 0.12)	0.05 (-0.00, 0.11)	0.17 (0.03, 0.31)
P for interaction	0.309	0.388	0.494	0.497	0.235
Smoke					
Yes	0.03 (0.01, 0.05)	0.03 (0.01, 0.05)	0.04 (0.02, 0.06)	0.03 (0.01, 0.05)	0.09 (0.05, 0.14)
No	0.02 (0.00, 0.04)	0.01 (-0.00, 0.03)	0.02 (-0.00, 0.03)	0.02 (0.00, 0.04)	0.06 (0.02, 0.10)
P for interaction	0.579	0.344	0.145	0.474	0.230
Stroke					
Yes	-0.05 (-0.13, 0.02)	-0.04 (-0.11, 0.04)	0.03 (-0.04, 0.11)	0.03 (-0.03, 0.10)	0.02 (-0.15, 0.18)
No	0.03 (0.01, 0.04)	0.02 (0.01, 0.04)	0.02 (0.01, 0.04)	0.02 (0.01, 0.04)	0.07 (0.04, 0.11)
P for interaction	0.040	0.120	0.789	0.771	0.484
Moderate Recreational Activ	ities				
Yes	0.02 (-0.01, 0.04)	0.01 (-0.01, 0.04)	0.04 (0.02, 0.07)	0.03 (0.01, 0.05)	0.09 (0.04, 0.14)
No	0.03 (0.01, 0.04)	0.02 (0.00, 0.04)	0.02 (0.00, 0.04)	0.02 (0.00, 0.03)	0.06 (0.03, 0.10)
P for interaction	0.559	0.606	0.128	0.350	0.428
BMI					
< 18.5	0.00 (-0.51, 0.51)	0.09 (-0.43, 0.60)	0.15 (-0.35, 0.65)	0.16 (-0.28, 0.60)	0.31 (-0.79, 1.42)
>=18.5,<25	0.01 (-0.02, 0.04)	0.02 (-0.01, 0.05)	0.02 (-0.01, 0.05)	0.01 (-0.01, 0.04)	0.04 (-0.02, 0.10)
>=25,<30	0.03 (0.01, 0.06)	0.03 (-0.00, 0.05)	0.03 (0.01, 0.06)	0.02 (-0.00, 0.04)	0.09 (0.03, 0.15)

Table 6 Subgroup analysis of the association between AFB and cognitive scores

Subgroup	CERAD-WL	DRT	AFT	DSST	CF
>=30	0.02 (-0.00, 0.04)	0.01 (-0.01, 0.03)	0.02 (0.00, 0.04)	0.03 (0.01, 0.05)	0.08 (0.03, 0.12)
P for interaction	0.618	0.781	0.784	0.556	0.650
WHtR					
Q1	0.02 (-0.01, 0.04)	0.02 (-0.01, 0.05)	0.01 (-0.01, 0.04)	0.01 (-0.01, 0.04)	0.04 (-0.02, 0.11)
Q2	0.02 (-0.01, 0.05)	0.01 (-0.01, 0.04)	0.00 (-0.03, 0.03)	0.00 (-0.03, 0.03)	0.02 (-0.05, 0.08)
Q3	0.06 (0.03, 0.09)	0.05 (0.01, 0.08)	0.05 (0.01, 0.08)	0.06 (0.03, 0.09)	0.16 (0.10, 0.23)
Q4	0.01 (-0.02, 0.03)	-0.01 (-0.03, 0.02)	0.04 (0.01, 0.06)	0.03 (0.00, 0.05)	0.07 (0.01, 0.13)
P for interaction	0.068	0.097	0.124	0.010	0.011
WWI					
Q1	0.02 (-0.01, 0.05)	0.02 (-0.01, 0.05)	-0.01 (-0.04, 0.02)	0.00 (-0.02, 0.03)	0.01 (-0.05, 0.08)
Q2	0.02 (-0.01, 0.05)	0.00 (-0.03, 0.03)	0.03 (0.00, 0.06)	0.01 (-0.01, 0.04)	0.07 (0.00, 0.13)
Q3	0.04 (0.01, 0.07)	0.04 (0.01, 0.07)	0.05 (0.02, 0.08)	0.04 (0.01, 0.07)	0.12 (0.06, 0.19)
Q4	0.03 (-0.00, 0.06)	0.02 (-0.01, 0.05)	0.04 (0.01, 0.07)	0.04 (0.01, 0.06)	0.10 (0.04, 0.16)
P for interaction	0.763	0.517	0.027	0.098	0.066

Table 6 (continued)

Subgroup analyses are conducted to explore the associations between AFB and cognitive test scores across subgroups stratified by age, race, marital status, smoking, alcohol use, engagement in moderate recreational activities, hypertension, diabetes, stroke, BMI, WHtR and WWI levels. The results include regression coefficients (β) and *p*-values from interaction tests for each subgroup

accumulation, is one of the core drivers of insulin resistance [45, 46]. Compared with subcutaneous fat, visceral fat is more metabolically active [47]. Visceral fat activates the sympathetic nervous system, which enhances lipolysis and leads to the release of large amounts of free fatty acids into circulation. Simultaneously, visceral fat secretes various inflammatory cytokines, including tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1), which disrupt normal insulin signaling and exacerbate systemic inflammation, ultimately resulting in insulin resistance [48-50]. Insulin resistance not only negatively affects peripheral metabolism but also damages the central nervous system. Insulin receptors are widely distributed in the brain, upon binding with insulin, they activate the PI3K/Akt/mTOR and Rac1 signaling pathways to promote dendritic spine formation and the development of excitatory synapses [51]. Moreover, the activation of insulin receptor signaling is critical for maintaining dendritic plasticity and proper synaptic function [52]. Consequently, when insulin resistance occurs, synaptic plasticity and function are compromised, leading to cognitive decline. Integrating these findings with our results, we speculate that when WHtR and WWI are in the lower quartiles (Q1, Q2), visceral fat accumulation is minimal and the overall metabolic state remains relatively healthy. In this scenario, the positive association between AFB and cognitive function may not be fully manifested due to the favorable health status of the individuals. Conversely, when WHtR and WWI are in the moderateto-high range (Q3), the onset of chronic inflammation and insulin resistance renders the positive effect of later AFB more pronounced, likely due to prolonged exposure to higher estrogen levels promoting fat redistribution, reducing visceral fat accumulation, increasing leptin secretion, and improving glucose metabolism [53–56]. Additionally, estrogen exerts antioxidative effects and directly inhibits the release of inflammatory cytokines such as TNF- α and IL-6, thereby mitigating neuronal damage and protecting cognitive function [57, 58]. However, when WHtR and WWI reach very high levels (Q4), although the positive effect of AFB on cognitive function remains significant, its strength is diminished. This attenuation may be attributed to the fact that individuals with excessive visceral fat accumulation often experience comorbidities. Elevated WHtR and WWI levels compromise the beneficial effects of AFB on cognitive function through mechanisms including neuroinflammation and insulin resistance.

This study possesses several strengths. First, the data are sourced from the nationally representative NHANES database, which provides a large sample size. This not only establishes a solid foundation for the analysis but also markedly improves the precision and reliability of the statistical results. Second, potential confounding factors are thoroughly evaluated and adjusted for, thereby reducing their influence on the findings. Additionally, subgroup analyses are performed to examine variations in the relationship between AFB and cognitive function across diverse populations. These analyses facilitate a more detailed interpretation of the results, providing scientific evidence for detecting heterogeneous effects in specific subgroups and aiding the development of targeted health intervention strategies.

Nevertheless, our study has several unavoidable limitations. First, because the data are derived from a crosssectional survey, causal inferences between AFB and cognitive function cannot be established. Future research should include larger, prospective cohort studies to clarify the causal relationship and dynamic associations between AFB and cognitive function. Second, although NHANES is a nationally representative database established by the NCHS, its data are primarily sourced from the U.S. population. Differences in cultural backgrounds and healthcare systems between the United States and other countries may limit the generalizability of our findings. Therefore, caution is warranted when extrapolating our results to broader populations. To enhance the external validity of our findings, we plan to integrate data from multicenter international cohorts in future studies. Third, due to database limitations, cognitive function is assessed using CERAD, AFT, and DSST tests. While we improve the reliability and validity of cognitive assessment by creating a composite cognitive score based on the Z-scores of these tests, the diagnostic criterion for cognitive impairment is defined as a composite score below one standard deviation from the mean. This approach differs from the more commonly used screening tools such as the MMSE and MoCA, potentially limiting the applicability of our findings to other populations. Additionally, our study focused solely on the relationship between AFB and overall cognitive function without further exploring the association between AFB and specific dementia subtypes. Finally, although multiple covariates are adjusted for, it remains challenging to entirely eliminate the influence of unmeasured confounding factors.

Conclusion

This study is based on data from the 2011–2014 NHANES database. After applying inclusion and exclusion criteria, a total of 1,057 eligible participants are included. The findings indicate that a later AFB is associated with a lower prevalence of cognitive impairment and that the relationship between AFB and cognitive function is nonlinearly positive. Controlling AFB to occur after the age of 21 may help reduce the prevalence of cognitive impairment. Moreover, the potential influence of WHtR and WWI should be considered when planning childbirth to optimize the protective effects on cognitive health.

Abbreviations

AFB	Age at first birth
NHANES	National Health and Nutrition Examination Survey
NCHS	National Center for Health Statistics
BMI	Body mass index
CERAD-WL	Consortium to Establish a Registry for Alzheimer's Disease Word
	Learning
AFT	Animal Fluency Test
DSST	Digit Symbol Substitution Test

DRT	Delayed Recall Session
CF	Cognitive Function
LLR	Log likelihood ratio
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
WHtR	Waist-to-Height Ratio
WWI	Weight-adjusted Waist Index
WC	Waist Circumference
TNF-α	Tumor Necrosis Factor-α
IL-6	Interleukin-6
MCP-1	Monocyte Chemoattractant Protein-1

Acknowledgements

We express our gratitude to the team at the National Center for Health Statistics, Centers for Disease Control and Prevention, for their efforts in planning and administering NHANES and for providing access to the NHANES datasets through their official website.

Authors' contributions

J.Z.:Designed the study, conducted data analysis, wrote the initial draft and revised the manuscript. L.D. and C.S.:Designed the study, revised and edited the initial draft. M.L.: Designed the study, analyzed the data, and revised the initial draft. All authors read and approved the final manuscript.

Funding

Not applicable.

Data availability

The data used in this study are publicly available on the NHANES official website (https://www.cdc.gov/nchs/nhanes/index.htm).

Declarations

Ethics approval and consent to participate

All NHANES protocols receive approval from the NCHS Ethics Review Board, and informed consent is collected from participants during recruitment.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Neurology, The People's Hospital of China Medical University, ShenYang 110000, China. ²Department of Oncology, The People's Hospital of China Medical University, ShenYang 110000, China.

Received: 25 November 2024 Accepted: 11 April 2025 Published online: 26 April 2025

References

- Wharton SB, Brayne C, Savva GM, Matthews FE, Forster G, Simpson J, Lace G, Ince PG, on behalf of the Medical Research Council Cognitive F, Aging S: Epidemiological Neuropathology: The MRC Cognitive Function and Aging Study Experience. J Alzheimer's Dis. 2011;25:359-372.
- 2. Dementia. https://www.who.int/news-room/fact-sheets/detail/dementia
- Barral S, Andersen SL, Perls TT, Bae H, Sebastiani P, Christensen K, Thyagarajan B, Lee J, Schupf N. Association between late maternal age and age-related endophenotypes in the Long Life Family Study. Neurosci Lett. 2022;784: 136737.
- Zuo R, Xu J, He L, Wang Y, Tang J. Associations between reproductive factors and the prevalence of depression: findings from the National Health and Nutrition Examination Survey (NHANES) 2005–2018. BMC Public Health. 2024;24(1):2761.
- Chen T, Wu J, Pan Q, Dong M. The association of female reproductive factors with history of cardiovascular disease: a large cross-sectional study. BMC Public Health. 2024;24(1):1616.

- Zuo R, Ge Y, Xu J, He L, Liu T, Wang B, Sun L, Wang S, Zhu Z, Wang Y. The association of female reproductive factors with risk of metabolic syndrome in women from NHANES 1999–2018. BMC Public Health. 2023;23(1):2306.
- Yang HH, Chen GC, Zhou MG, Xie LF, Jin YY, Chen HT, Chen ZK, Kong YH, Yuan CZ, Li ZH. Association of age at first birth and risk of non-alcoholic fatty liver disease in women: evidence from the NHANES. Hep Intl. 2023;17(2):303–12.
- Aggarwal R, Ostrominski JW, Vaduganathan M. Prevalence of Cardiovascular-Kidney-Metabolic Syndrome Stages in US Adults, 2011–2020. JAMA. 2024;331(21):1858–60.
- Luo X, Tang M, Wei X, Peng Y. Association between magnesium deficiency score and sleep quality in adults: a population-based cross-sectional study. J Affect Disord. 2024;358:105–12.
- 10 Wang Z, Wang Q, Tang F, Zhong S. Composite dietary antioxidant index and obesity among U.S. adults in NHANES 2007–2018. Scientific Reports. 2024;14(1):28102.
- 11. Karrasch M, Sinervä E, Grönholm P, Rinne J, Laine M. CERAD test performances in amnestic mild cognitive impairment and Alzheimer's disease. Acta Neurol Scand. 2005;111(3):172–9.
- 12. Sotaniemi M, Pulliainen V, Hokkanen L, Pirttilä T, Hallikainen I, Soininen H, Hänninen T. CERAD-neuropsychological battery in screening mild Alzheimer's disease. Acta Neurol Scand. 2012;125(1):16–23.
- Carone DA, Strauss E, Sherman EMS, Spreen O. A compendium of neuropsychological tests: administration, norms, and commentary. Appl Neuropsychol. 2007;14(1):62–3.
- Henry JD, Crawford JR, Phillips LH. Verbal fluency performance in dementia of the Alzheimer's type: a meta-analysis. Neuropsychologia. 2004;42(9):1212–22.
- Clark LJ, Gatz M, Zheng L, Chen YL, McCleary C, Mack WJ. Longitudinal verbal fluency in normal aging, preclinical, and prevalent Alzheimer's disease. Am J Alzheimers Dis Other Demen. 2009;24(6):461–8.
- Canning SJ, Leach L, Stuss D, Ngo L, Black SE. Diagnostic utility of abbreviated fluency measures in Alzheimer disease and vascular dementia. Neurology. 2004;62(4):556–62.
- Bienias JL, Beckett LA, Bennett DA, Wilson RS, Evans DA. Design of the Chicago Health and Aging Project (CHAP). J Alzheimers Dis. 2003;5(5):349–55.
- Plassman BL, Langa KM, Fisher GG, Heeringa SG, Weir DR, Ofstedal MB, Burke JR, Hurd MD, Potter GG, Rodgers WL, et al. Prevalence of dementia in the United States: the aging, demographics, and memory study. Neuroepidemiology. 2007;29(1–2):125–32.
- Proust-Lima C, Amieva H, Dartigues JF, Jacqmin-Gadda H. Sensitivity of four psychometric tests to measure cognitive changes in brain agingpopulation-based studies. Am J Epidemiol. 2007;165(3):344–50.
- Dong B, Yue Y, Wang Z, Sun M, Wang Y. Association between physical activity, peak expiratory flow, and cognitive function in aging: a crosssectional analysis. BMC Geriatr. 2024;24(1):460.
- Yang H, Liao Z, Zhou Y, Gao Z, Mao Y. Non-linear relationship of serum albumin-to-globulin ratio and cognitive function in American older people: a cross-sectional national health and nutrition examination survey 2011–2014 (NHANES) study. Front Public Health. 2024;12:1375379.
- Li W, Li S, Shang Y, Zhuang W, Yan G, Chen Z, et al. Associations between dietary and blood inflammatory indices and their effects on cognitive function in elderly Americans. Front Neurosci. 2023;17:1117056.
- 23. Zuo W, Yang X. A predictive model of cognitive impairment risk in older adults with hypertension. J Clin Neurosci. 2025;133:111032.
- Qiu X, Kuang J, Huang Y, Wei C, Zheng X. The association between Weight-adjusted-Waist Index (WWI) and cognitive function in older adults: a cross-sectional NHANES 2011–2014 study. BMC Public Health. 2024;24(1):2152.
- Wu J, Qiu P, Liu M, Yu W, Li M, Li Y. Physical activity patterns and cognitive function in elderly women: a cross-sectional study from NHANES 2011–2014. Front Aging Neurosci. 2024;16:1407423.
- Wu S, Wang L, Liu S, Qi J, Shi F, Zhuang H, Qian Y, Mei L, Zhang M. Relationship between domain-specific physical activity and cognitive function in older adults - findings from NHANES 2011–2014. Front Public Health. 2024;12:1390511.
- Liu X, Chen X, Chen J. Relationship between serum neurofilament light chain protein and depression: a nationwide survey and Mendelian randomization study. J Affect Disord. 2024;366:162–71.

- Rubino F, Cummings DE, Eckel RH, Cohen RV, Wilding JPH, Brown WA, Stanford FC, Batterham RL, Farooqi IS, Farpour-Lambert NJ, et al. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol. 2025;13(3):221–62.
- 29. Wu Z, Liu Y, Wang B. The relationship between weight-adjusted waist index and peripheral artery disease. Front Nutr. 2025;12:1504896.
- Zhang H, Yu M, Li L, Chen C, He Q. Obesity-related indices are associated with self-reported infertility in women: findings from the national health and nutrition examination survey. J Int Med Res. 2025;53(2):03000605251315019.
- Li J, Hao W, Fu C, Zhou C, Zhu D. Sex Differences in Memory: Do Female Reproductive Factors Explain the Differences? Front Endocrinol (Lausanne). 2022;13: 837852.
- Wedatilake Y, Myrstad C, Tom SE, Strand BH, Bergh S, Selbæk G. Female Reproductive Factors and Risk of Mild Cognitive Impairment and Dementia: The HUNT Study. J Prev Alzheimer's Dis. 2024;11(4):1063–72.
- Chou HT, Wu PY, Huang JC, Chen SC, Ho WY. Late menarche, not reproductive period, is associated with poor cognitive function in postmenopausal women in Taiwan. Int J Environ Res Public Health. 2021;18(5):2345.
- Sisti HM, Glass AL, Shors TJ. Neurogenesis and the spacing effect: learning over time enhances memory and the survival of new neurons. Learn Memory (Cold Spring Harbor, NY). 2007;14(5):368–75.
- Aimone JB, Wiles J, Gage FH. Potential role for adult neurogenesis in the encoding of time in new memories. Nat Neurosci. 2006;9(6):723–7.
- 36. Brinton RD. Estrogen-induced plasticity from cells to circuits: predictions for cognitive function. Trends Pharmacol Sci. 2009;30(4):212–22.
- Leuner B, Shors TJ. New spines, new memories. Mol Neurobiol. 2004;29(2):117–30.
- Reed BG, Carr BR. The Normal Menstrual Cycle and the Control of Ovulation. [Updated 2018 Aug 5]. In: Feingold KR, Ahmed SF, Anawalt B, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279054/.
- Raz N, Rodrigue KM. Differential aging of the brain: patterns, cognitive correlates and modifiers. Neurosci Biobehav Rev. 2006;30(6):730–48.
- Tang H, Li Q, Du C. The association between waist-to-height ratio and cognitive function in older adults. Nutr Neurosci. 2024;27(12):1405–12.
- Zhao C, Xu X, Hao C. Evidence from NHANES 2011–2014: a correlation between the weight-adjusted-waist index and cognitive abilities in the United States. Front Aging Neurosci. 2025;17:1480609.
- 42. Golan S, Boccara E, Ravona-Springer R, Inbar Y, Livny A, Yore I, Heymann A, Beeri MS. Regional abdominal adiposity and related factors are associated with brain volumes and cognitive functioning in middle-aged adults at high AD-risk. Alzheimers Dement. 2021;17(S5): e058387.
- Zhang Q, Jin K, Chen B, Liu R, Cheng S, Zhang Y, et al. Overnutrition induced cognitive impairment: insulin resistance, gut-brain axis, and neuroinflammation. Front Neurosci. 2022;16:884579.
- Cope EC, LaMarca EA, Monari PK, Olson LB, Martinez S, Zych AD, Katchur NJ, Gould E. Microglia play an active role in obesity-associated cognitive decline. J Neurosci. 2018;38(41):8889.
- Atzmon G, Yang X, Muzumdar R, Hui X, Gabriely I, Barzilai N. Differential gene expression between visceral and subcutaneous fat depots. Horm Metab Res. 2002;34:622–8.
- 46. Aggarwal M, Verma G, Wahid A, Mathew S, Roat A. Visceral fat volume is a better predictor of insulin resistance than abdominal wall fat index in patients with prediabetes and type 2 diabetes mellitus. J Assoc Physicians India. 2022;70(4):11–2.
- 47. de Mutsert R, Gast K, Widya R, de Koning E, Jazet I, Lamb H, le Cessie S, de Roos A, Smit J, Rosendaal F, et al. Associations of abdominal subcutaneous and visceral fat with insulin resistance and secretion differ between men and women: The Netherlands Epidemiology of obesity study. Metab Syndr Relat Disord. 2018;16(1):54–63.
- Sakamoto K, Butera MA, Zhou C, Maurizi G, Chen B, Ling L, Shawkat A, Patlolla L, Thakker K, Calle V, et al. Overnutrition causes insulin resistance and metabolic disorder through increased sympathetic nervous system activity. Cell Metab. 2025;37(1):121–137.e126.
- Bergman R. Abdominal obesity, fatty acids and insulin resistance. FASEB J. 2011;25:196.3.
- Enos R, Davis J, Velázquez K, McClellan J, Day S, Carnevale K, Murphy E. Influence of dietary saturated fat content on adiposity, macrophage behavior, inflammation, and metabolism: composition matters. J Lipid Res. 2013;54:152–63.

- Lee C-C, Huang C-C, Hsu K-S. Insulin promotes dendritic spine and synapse formation by the PI3K/Akt/mTOR and Rac1 signaling pathways. Neuropharmacology. 2011;61(4):867–79.
- Chiu S-L, Chen C-M, Cline HT. Insulin receptor signaling regulates synapse number, dendritic plasticity, and circuit function in vivo. Neuron. 2008;58(5):708–19.
- Adeva-Andany MM, Domínguez-Montero A, Adeva-Contreras L, Fernández-Fernández C, Carneiro-Freire N, González-Lucán M. Body fat distribution contributes to defining the relationship between insulin resistance and obesity in human diseases. Curr Diabetes Rev. 2024;20(5):e160823219824.
- Babaei P, Damirchi A, Ghouroughchi AP. The Effect of Estrogen on Visceral Fat, Serum Omentin-1 and Insulin Resistance in Ovariectomized Rats. J Ardabil Univ Med Sci. 2016;16:189–99.
- Sandeep S, Gokulakrishnan K, Velmurugan K, Deepa M, Mohan V. Visceral & subcutaneous abdominal fat in relation to insulin resistance & metabolic syndrome in non-diabetic south Indians. Indian J Med Res. 2010;131:629–35.
- Yang F, He Y, Zhao L, Huang J, Du F, Tian S, Zhang Y, Liu X, Chen B, Ge J, et al. Leptin drives glucose metabolism to promote cardiac protection via OPA1-mediated HDAC5 translocation and Glut4 transcription. Funct Integr Genomics. 2025;25(1):28.
- Jana P, Khan MM, De S, Sinha A, Guha S, Khan G, Maiti S. Estriol inhibits dermcidin isoform-2 induced inflammatory cytokine expression via nitric oxide synthesis in human neutrophil. Curr Mol Med. 2019;18(10):672–8.
- Kumral Z, Memi G, Ercan F, Yeğen B. Estrogen alleviates acetic acidinduced gastric or colonic damage via both ERα- and ERβ-mediated and direct antioxidant mechanisms in rats. Inflammation. 2013;37:694–705.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.