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Association of menarche, menopause, and reproductive history with cognitive performance in older US women: a cross-sectional study from NHANES 2011–2014

Anquan Hu[1†], Lu Xiong[1†], Huijun Wei[1], Liangyan Yuan[1], Yumeng Li[2], Heyan Qin[2], Feng Chen[3*] and Tao Liu[2*]

Abstract

Background With the increasing global aging population, cognitive impairment, particularly Alzheimer's disease (AD), has become an escalating public health and economic concern. Recent research has increasingly focused on the relationship between female reproductive factors and cognitive health. This study explores the association between reproductive history factors and cognitive performance in women aged 60 and older in the US, providing insights for the prevention and management of cognitive impairment.

Methods We analyzed participants in the National Health and Nutrition Examination Survey (NHANES) between 2011 and 2014. The cognitive performance was assessed by the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word Learning sub-test, Animal Fluency test (AFT), and Digit Symbol Substitution Test (DSST), in relation to reproductive history variables like age of menarche, menopause, reproductive span, number of pregnancies, and parity. Statistical analyses included weighted linear regression for continuous variables and weighted chi-square tests for categorical variables, with adjustments for age, BMI, alcohol intake, smoking, PIR, education, race/ethnicity, hypertension, and diabetes.

Results A total of 698 (weighted sample was 25,558,437) women aged 60 years or older were included in the study. Parity negatively impacted cognitive performance, women with ≥ 5 parity showing reductions in AFT (β = -2.1, $p = 0.032$), DSST (β = -14, $p < 0.001$), CERAD trial 1 (β = -0.41, $p = 0.031$), and CERAD Total scores (β = -1.3, $p = 0.033$) all in model 2. Delayed menopause was positively associated with cognitive function, showing improvements in CERAD trial 1 (β = 1.2, $p = 0.002$) and total recall (β = 2.1, $p = 0.031$) both in model 3. Longer reproductive span was linked to better cognitive function, particularly in immediate recall and processing speed (β = 0.12, $p < 0.001$ for DSST) in model 3.

[†]Anquan Hu and Lu Xiong contributed equally to this work.

*Correspondence:
Feng Chen
fenger0802@163.com
Tao Liu
ltao829@163.com

Full list of author information is available at the end of the article

Conclusion Higher parity was negatively correlated with processing speed and memory. In contrast, delayed menopause and a longer reproductive span were positively correlated with global cognition and processing speed. These findings suggest that reproductive factors play a potential role in cognitive aging among older women.

Keywords Cognitive function, Menarche, Menopause, Reproductive history, NHANES

Introduction

The global population is experiencing an increase in age, leading to a significant rise in cognitive impairment, which has emerged as a critical issue for public health. Aging is a complex biological process with profound implications for health and society [1]. The aging woman population is increasing, with women generally living longer than men and comprising the majority of older persons, especially at the most advanced ages. In the US, AD affects approximately 6.7 million adults aged 65 and older, a number projected to nearly double by 2060 without medical breakthroughs to mitigate its progression [2]. Women, in particular, experience a higher prevalence of cognitive decline and AD [3]. In the past two decades, the greatest increase in female deaths has been from AD and other dementias, with deaths nearly tripling between 2000 and 2021 [4]. Factors such as reproductive history and hormonal changes are likely contributing to this disparity in cognitive health. The complex relationship between female reproductive factors cognitive function has received considerable attention in medical research. Reproductive events are not only biological milestones but also important determinants of women's long-term health, particularly cognitive function later in life [5].

Some findings illustrate the intricate relationship between female reproductive health and cognitive development. Song et al. found that older age at menarche and menopause and longer reproductive cycles are associated with lower risks of mild cognitive impairment and AD [6]. Jett et al. highlight the link between female reproductive factors and AD risk, focusing on endogenous and exogenous estrogen exposure. Key factors include reproductive lifespan, menopause status (spontaneous vs. induced), parity, and hormonal therapies such as contraceptives, menopause hormone therapy, and anti-estrogen treatments. Understanding how these factors influence brain aging through sex-specific pathways is essential for developing AD prevention and treatment strategies [7]. Despite these advances, significant research gaps remain. Existing studies have primarily focused on isolated reproductive factors or specific cognitive outcomes, leaving a lack of systematic investigation into how different reproductive stages collectively influence multiple cognitive domains, such as language memory, executive function, and processing speed, in older women. To address these gaps, this study leverages the NHANES 2011–2014 database, known for its broad representativeness and systematic data collection, providing a unique perspective and detailed data support that enhances the innovation and generalizability of the research. The novelty of this study lies in its investigation of the relationship between reproductive histories and cognitive function in women aged 60 and the elder. In particular, multiple cognitive tests such as CERAD, AFT, and DSST are used to comprehensively assess various aspects of cognitive function, including language memory, fluency, executive function, processing speed, and working memory [8]. By further investigating the potential impact of various reproductive histories on cognitive function, this study aims to provide new evidence to support future intervention strategies for preventing dementia in women.

Methods

Study design and population

This research is a cross-sectional analysis utilizing the NHANES database. The NHANES is an extensive and intricate multistage survey that targets the noninstitutionalized population of the United States. This survey is administered by both the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics, with the aim of delivering representative national estimates regarding health and nutritional conditions [9]. In each survey cycle, individuals from diverse geographic regions across the United States are selected through a stratified sampling process involving various census blocks or segments of census block groups, thereby ensuring that NHANES constitutes a nationally representative sample [10]. The detailed sampling method adopted has been published elsewhere [11]. The NHANES 2011–2014 data have been widely used in recent research to explore various aspects of cognitive function [12, 13]. From the NHANES 2011–2014 public release dataset ($n = 19,931$), we excluded individuals aged below 60 years ($n = 16,299$), resulting in 3,632 participants aged 60 and older. We further excluded males ($n = 1,760$), leaving 1,872 female participants. After excluding populations with missing data on key variables and cognitive test scores ($n = 1,038$), 834 participants remained. Finally, we excluded individuals with missing data on reproductive history variables, including age at menarche, age at menopause, number of pregnancies, reproductive span, and parity ($n = 136$), resulting in 698 participants eligible for analysis. The detailed selection process for study inclusion is illustrated in Fig. 1.

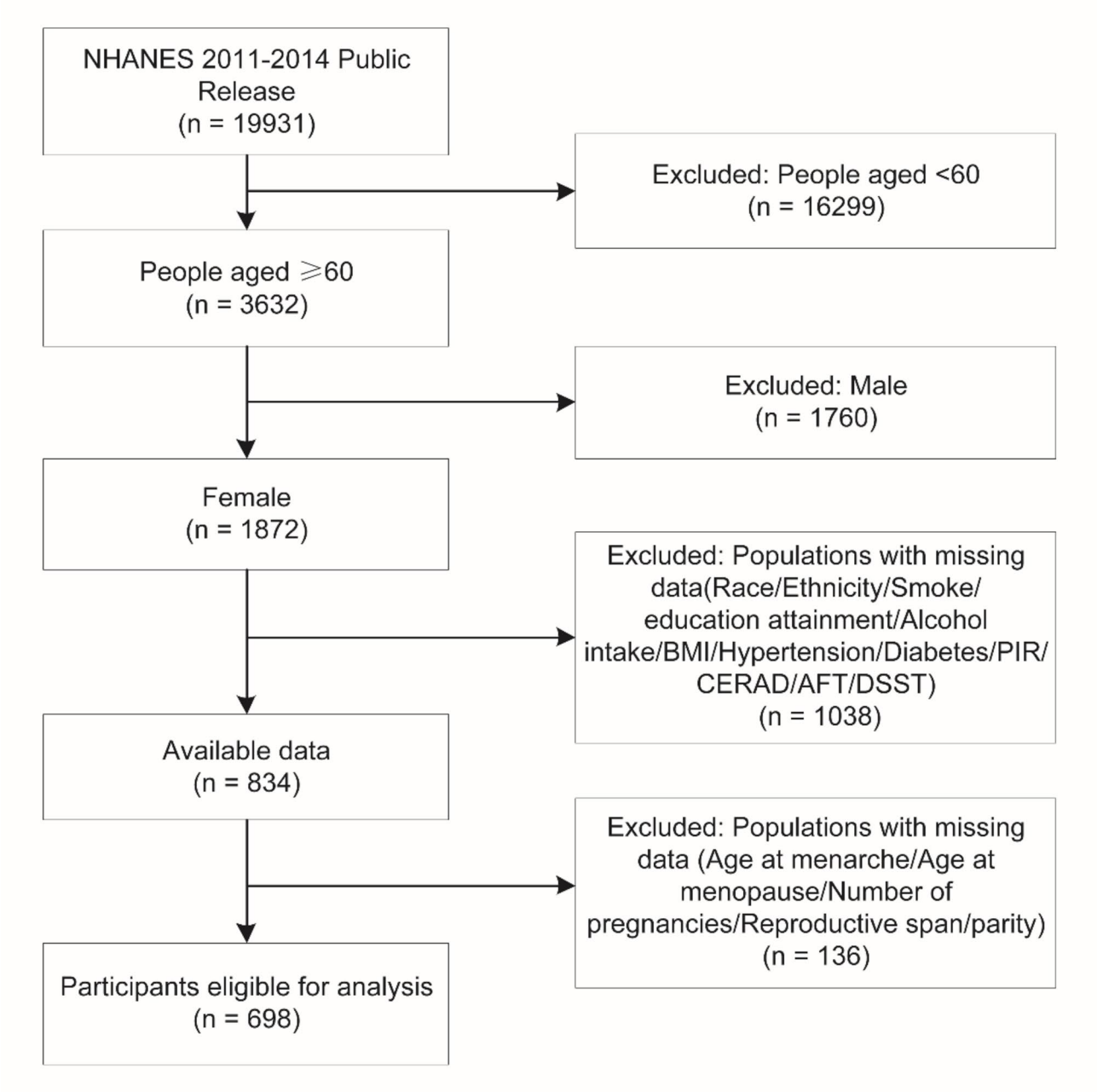

Fig. 1 Flow chart of participants selected

Measurement of cognitive function

Cognitive assessments were conducted by highly trained interviewers during initial private interviews. NHANES uses the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word Learning test, Animal Fluency test (AFT), and Digit Symbol Substitution test (DSST) to assess different cognitive functions [14]. Voice recordings were essential for both the CERAD Word Learning (WL) and the Auditory Functional Test (AFT). If permission for the voice recording was not provided, only the Digit Symbol Substitution Test (DSST) was administered. The CERAD-WL evaluates memory, focusing on verbal memory and comprises four trials [15]. In the first three trials, participants read aloud ten words and then immediately recalled them. The total number of correctly recalled words from these trials formed the immediate recall score (range: 0 to 30). After completing the AFT and DSST (approximately 8–10 min after the CERAD-WL), participants were asked to recall as many of the ten words as possible. The total number of correct recalls was used to calculate their delayed recall score [16]. The AFT assesses semantic fluency, in which

participants are challenged to name as many animals as they can within a 60-second timeframe, with each animal named contributing a point to their score, is used to evaluate executive function [17]. The DSST is a test of sustained attention, working memory and processing speed. Participants were provided with a test sheet featuring 9 numbers at the top, each paired with a corresponding symbol key. Below the key, there was a sequence of 133 numbers. They were asked to match each number with the correct symbol within 2 min. One point was awarded for each accurate match, with a maximum possible score of 133 points [18]. Improved scores on these assessments reflect superior cognitive functioning, a conclusion backed by considerable research [19].

Covariates

Covariates consisted of various demographic characteristics, including sex, age in years, age group (60–69 years, 70–79 years, ≥ 80 years), race/ethnicity, family income (poverty income ratio, PIR), educational attainment (less than a high school education, some high school, high school graduate, some college or associate's degree, college graduate or more), alcohol intake (non-drinker, 1 to < 5 drinks/month, 5 to < 10 drinks/month, or ≥ 10 drinks/month), and smoking status (current, former, or never smoker), body mass index (BMI), hypertension, and diabetes [20]. Race/ethnicity in NHANES are self-identified, as previously reported [21, 22]. The categories included: Non-Hispanic White, Non-Hispanic Black, Mexican American, Other Hispanic, and Other/multiracial [23]. The age of menarche, age of menopause, pregnancy, and parity were obtained from the NHANES database using the reproductive health questionnaire [24, 25]. Specifically, the age of menarche was obtained from RHQ010 (Age when first menstrual period occurred), and the age of menopause was obtained from RHQ060 (Age at last menstrual period). Women experiencing menopause were classified further according to the cause: natural menopause or surgical menopause. Natural menopause refers to the ending of menstrual periods for over 12 consecutive months resulting from physiological factors, while excluding influences like surgical procedures or medical interventions [26]. Surgical menopause, on the other hand, was attributed to the surgical removal of both ovaries before the typical age of natural menopause [27]. The number of pregnancies was obtained from RHQ160 (How many times have been pregnant?), and RHQ171 (How many deliveries resulted in a live birth?) to determine parity. In the research analysis, age at menarche was categorized into three groups: age at menarche < 12, 12 ≤ age at menarche ≤ 13, and age at menarche > 13. The number of pregnancies was categorized into three groups: number of pregnancies ≤ 2, 3 ≤ number of pregnancies ≤ 4, and number of pregnancies ≥ 5. The parity was categorized into three groups: parity ≤ 2, 3 ≤ parity ≤ 4, and parity ≥ 5. Reproductive span was defined as the difference between the age at menopause and the age at menarche (age menopause– age menarche). Age at menopause was categorized into three groups: age at menopause < 45 defined early menopause, 45 ≤ age at menopause ≤ 55 defined normal menopause, and age at menopause > 55 defined delayed menopause [28, 29].

Statistical analysis

Since NHANES uses a probability sampling strategy, we applied the 2-year weight (wtsa2yr) for NHANES 2011–2012 and 2013–2014. When combining the two cycles, the final weight (1/2 wtsa2yr) was adjusted [30]. We divided WTDRD1 by 2 as the new sample weight. All statistical analyses utilized NHANES sample weights to maintain representativeness. Continuous variables were represented as medians (Q1, Q3), whereas categorical variables were shown as both unweighted counts and weighted percentages, the latter indicating the subject distribution following the application of sample weights. P values for continuous and categorical variables were calculated using weighted linear regression and chi-square tests, respectively. Linear regression was conducted on menarche, menopause age, pregnancy, parity, reproductive span, and cognitive function. Multivariable models were adjusted as follows: model 1:no adjusted; model 2: adjusted for age; model 3: were adjusted for age, BMI, alcohol intake, smoking, PIR, education, race/ethnicity, hypertension, and diabetes [31]. The reference groups for the models were defined as follows: age of menarche < 12 years for menarche age, early menopause for menopause status, ≤ 2 pregnancies for the number of pregnancies, and parity ≤ 2 for parity. Variables with a linear regression result $p < 0.05$ were subjected to forest plot visual analysis. All statistical tests were performed using R (version 4.2.2. https://www.r-project.org/).

Results

Baseline characteristics of the participants

A total of 698 participants were enrolled in this study from two cycles of the NHANES database. Based on the NHANES sampling design, the weighted data analysis provided a population estimate of 25,558,437, representing US women aged 60 and older. Data included cognitive function, reproductive history (including menarche, pregnancy, parity, menopause, and reproductive span), as well as other relevant covariates such as sex, age, race/ethnicity, smoking status, education attainment, alcohol intake, BMI, diabetes status, and PIR.

Menarche and cognitive function

Our analysis did not find any significant statistical association between the age at menarche and cognitive function in later life. Median scores for the CERAD test, AFT, and DSST did not show significant differences among age at menarche < 12, 12 ≤ age at menarche ≤ 13, and age at menarche > 13 groups ($p > 0.05$) (Table 1). Linear regression analysis: These results suggest that age at menarche

Table 1 Characteristics and cognitive function of study participants grouped by age at menarche

Characteristic	Age of menarche < 12, *N* = 138 (20.40%)[1]	12 ≤ Age of menarche ≤ 13, *N* = 366 (54.21%)[1]	Age of menarche > 13, *N* = 194 (25.39%)[1]	*p*-Value[2]
Age group				> 0.9
60–69 years	73 (50.75%)	175 (47.69%)	101 (49.41%)	
70–79 year	35 (26.70%)	114 (29.55%)	51 (28.68%)	
≥ 80 years	30 (22.55%)	77 (22.76%)	42 (21.91%)	
Race/Ethnicity				0.024
Non-Hispanic White	75 (80.38%)	199 (79.09%)	81 (71.57%)	
Non-Hispanic Black	28 (9.19%)	88 (10.45%)	36 (9.26%)	
Mexican American	14 (3.66%)	31 (3.67%)	25 (6.18%)	
Other Hispanic	17 (4.75%)	27 (2.70%)	19 (4.13%)	
Other/multiracial	4 (2.01%)	21 (4.09%)	33 (8.86%)	
Education attainment				0.3
Less Than 9th Grade	9 (4.76%)	30 (5.20%)	28 (7.24%)	
9-11th Grade	18 (9.90%)	66 (13.77%)	29 (13.70%)	
High School Graduate/GED	45 (35.88%)	80 (21.37%)	53 (29.72%)	
Some College or AA degree	43 (28.52%)	111 (34.01%)	56 (30.29%)	
College Graduate or above	23 (20.95%)	79 (25.64%)	28 (19.04%)	
Alcohol intake				0.3
1–5 drinks/month	56 (43.41%)	167 (48.52%)	71 (41.90%)	
5–10 drinks/month	5 (3.97%)	8 (2.04%)	5 (3.31%)	
≥ 10 drinks/month	9 (11.53%)	45 (15.72%)	14 (9.02%)	
Non-drinker	68 (41.10%)	146 (33.72%)	104 (45.77%)	
Smoke group				0.8
Current smoker	16 (12.40%)	44 (12.16%)	22 (9.97%)	
Former smoker	45 (38.42%)	119 (35.19%)	54 (32.81%)	
Never smoker	77 (49.18%)	203 (52.64%)	118 (57.22%)	
BMI group				0.057
Underweight (< 18.5)	0 (0.00%)	7 (1.33%)	4 (0.91%)	
Normal (18.5 to < 25)	19 (17.39%)	82 (26.90%)	59 (25.81%)	
Overweight (25 to < 30)	39 (28.13%)	115 (33.74%)	55 (35.85%)	
Obese (30 or greater)	80 (54.48%)	162 (38.02%)	76 (37.43%)	
Hypertension	109 (74.53%)	283 (74.14%)	141 (67.87%)	0.4
Diabetes	65 (42.46%)	145 (34.58%)	81 (35.94%)	0.4
PIR				0.15
≤ 1.3	48 (23.30%)	113 (20.78%)	72 (23.32%)	
1.3 < to ≤ 3.5	54 (41.95%)	158 (41.55%)	85 (53.39%)	
> 3.5	36 (34.74%)	95 (37.67%)	37 (23.29%)	
CERAD1	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	0.2
CERAD2	8.00 (6.00, 9.00)	8.00 (6.00, 9.00)	7.00 (7.00, 9.00)	0.7
CERAD3	9.00 (7.00, 9.00)	8.00 (7.00, 10.00)	8.00 (7.00, 9.00)	0.5
CERAD total	21.0 (18.0, 24.0)	21.0 (18.0, 24.0)	21.0 (17.0, 24.0)	0.5
CERAD delay recall	7.00 (5.00, 9.00)	7.00 (5.00, 8.00)	7.00 (5.00, 8.00)	0.15
AFT	18.0 (14.0, 20.0)	17.0 (14.0, 20.0)	17.0 (14.0, 20.0)	0.8
DSST	52 (42, 62)	53 (40, 64)	50 (42, 64)	> 0.9

[1] n (weighted %); Median (IQR)

[2] chi-squared test with Rao & Scott's second-order correction; Wilcoxon rank-sum test for complex survey samples

Abbreviation: CERAD, Consortium to Establish a Registry for Alzheimer's Disease; AFT, Animal Fluency test; DSST, Digit Symbol Substitution Test; BMI, body mass index; PIR, poverty income ratio; GED, General educational development; AA, Associate of Arts

did not have a significant impact on cognitive function, as assessed by these tests (Supplementary table S1, Supplementary table S2, Supplementary table S3).

Pregnancy and cognitive function

Significant demographic differences were found across pregnancy groups, particularly in age ($p < 0.001$), race/ethnicity ($p < 0.001$), and education ($p = 0.013$). DSST scores also showed a significant difference ($p < 0.001$), with median scores of 54 (IQR 45–67) for ≤ 2 pregnancies, 51 (IQR 41–64) for 3–4 pregnancies, and 49 (IQR 33–61) for ≥ 5 pregnancies, suggesting a potential decline in cognitive function with more pregnancies. (Table 2). Linear regression analysis showed that the association between pregnancies and cognitive function varied across models and domains. For CERAD trial 1, ≥ 5 pregnancies were positively associated with cognitive performance in model 3 ($p = 0.040$). In CERAD delayed recall, 3–4 pregnancies were negatively associated in model 1 ($p = 0.018$). For DSST scores, ≥ 5 pregnancies were negatively associated in models 1 ($p < 0.001$) and 2 ($p < 0.001$). These associations were not consistent across all models or domains. (Supplementary table S1, Supplementary table S2, Supplementary table S3).

Parity and cognitive function

Our study found significant differences in cognitive function related to parity. The demographic analysis revealed disparities in age group ($p < 0.001$), race/ethnicity ($p < 0.001$), and educational levels ($p < 0.001$) across parity groups. Cognitive function assessments demonstrated statistically significant differences in CERAD trial 1, CERAD trial 2, CERAD trial 3, CERAD trial total, CERAD delay recall, AFT, and DSST (Table 3). Linear regression analysis showed that women with ≥ 5 parity had a significant negative impact on AFT ($p = 0.032$), DSST ($p < 0.001$), and CERAD total scores ($p = 0.033$) in model 2. Women with 3 ≤ parity ≤ 4 showed slight decreases in AFT and CERAD total, with a significant reduction in DSST. Parity ≥ 5 was associated with a significant decrease in CERAD trial 1 in models 1 and 2. However, all associations were non-significant in model 3, indicating that higher parity's impact on processing speed and memory may be attenuated after adjustment. (Supplementary table S1, Supplementary table S2, Supplementary table S3).

Parity ≥ 5 was negatively correlated with cognitive function, manifesting in lower scores for AFT, DSST, CERAD trial 1 and CERAD trial total in model 1 and model 2, but it was insignificant in model 3. The results were visually depicted using a forest plot (Fig. 2).

Menopause and cognitive function

The delayed menopause group had higher alcohol intake ($p < 0.001$) and a greater proportion of normal to overweight BMI ($p = 0.041$). Hypertension was more prevalent in the early menopause group ($p = 0.022$) (Table 4). Linear regression analysis showed that normal menopause was positively associated with CERAD trial 1 scores, with higher scores compared to the reference group ($p = 0.004$) in model 1 and ($p = 0.005$) in model 2. Delayed menopause had a significant positive effect on CERAD trial 1 scores across all models, with the strongest association in model 1 ($p < 0.001$) and maintaining significance in model 3 ($p = 0.002$). It also showed a strong positive correlation with CERAD total scores, particularly in model 1 ($p = 0.007$), remaining significant in model 3 ($p = 0.031$). Delayed menopause also positively affected CERAD delayed recall scores in all models, with the strongest association in model 1 ($p < 0.001$), persisting through to model 3 ($p = 0.006$).

These findings indicate a positive correlation between the age at menopause onset and cognitive function, with delayed menopause consistently linked to higher cognitive scores in CERAD trial 1, CERAD total, and CERAD delayed recall. The results were visually depicted using a forest plot (Fig. 3).

Reproductive span and cognitive function

In linear regression analysis, reproductive span remained significantly associated with CERAD trial 1 across all models ($p < 0.001$) and CERAD total recall ($p < 0.001$ in models 1 and 2, $p = 0.019$ in model 3). A strong positive association with DSST was observed in models 1 and 2 ($p < 0.001$), persisting after full adjustment in model 3 ($p = 0.018$). However, associations with CERAD delayed recall and AFT were not significant in model 3 ($p = 0.12$ and $p = 0.2$, respectively). These findings suggest that longer reproductive span is associated with better cognitive performance, particularly in verbal memory, attention, and processing speed (Table 5).

Discussion

The findings of this study highlight the complex relationships between various physiological stages, reproductive histories, and cognitive function in women in later life. We observed a negative association between higher parity (five or more) and cognitive performance, particularly in CERAD trial 1, CERAD trial total, AFT, and DSST. However, this relationship was attenuated after adjusting for factors such as BMI, alcohol intake, smoking, PIR, education, race/ethnicity, hypertension, and diabetes. Our findings also suggest that delayed menopause is positively associated with better cognitive performance. An elevated risk of several health problems, such as cardiovascular conditions, osteoporosis, and cognitive decline,

Table 2 Characteristics and cognitive function of study participants grouped by number of pregnancies

Characteristic	Number of pregnancies ≤ 2, *N* = 217 (36.94%)[1]	3 ≤ Number of pregnancies ≤ 4, *N* = 274 (38.78%)[1]	Number of pregnancies ≥ 5, *N* = 207 (24.28%)[1]	*p*-value[2]
Age group				< 0.001
60–69 years	122 (59.29%)	135 (42.89%)	92 (42.06%)	
70–79 years	54 (22.35%)	77 (31.46%)	69 (34.14%)	
≥ 80 years	41 (18.36%)	62 (25.64%)	46 (23.80%)	
Race/Ethnicity				< 0.001
Non-Hispanic White	128 (82.70%)	143 (78.69%)	84 (67.45%)	
Non-Hispanic Black	33 (5.35%)	64 (10.76%)	55 (15.42%)	
Mexican American	13 (2.26%)	21 (3.46%)	36 (8.78%)	
Other Hispanic	17 (2.62%)	23 (2.94%)	23 (5.67%)	
Other/multiracial	26 (7.07%)	23 (4.15%)	9 (2.69%)	
Education attainment				0.013
Less Than 9th Grade	14 (4.03%)	11 (3.06%)	42 (12.17%)	
9-11th Grade	17 (6.54%)	46 (15.45%)	50 (18.75%)	
High School Graduate/GED	52 (24.37%)	77 (27.53%)	49 (27.88%)	
Some College or AA degree	81 (38.32%)	80 (28.10%)	49 (28.39%)	
College Graduate or above	53 (26.74%)	60 (25.85%)	17 (12.80%)	
Alcohol intake				0.3
1–5 drinks/month	100 (50.36%)	101 (41.20%)	93 (46.19%)	
5–10 drinks/month	8 (3.02%)	6 (2.91%)	4 (2.11%)	
≥ 10 drinks/month	24 (13.86%)	31 (15.44%)	13 (8.46%)	
Non-drinker	85 (32.76%)	136 (40.45%)	97 (43.24%)	
Smoke group				0.5
Current smoker	24 (12.72%)	30 (9.68%)	28 (13.19%)	
Former smoker	72 (37.56%)	80 (32.85%)	66 (35.56%)	
Never smoker	121 (49.73%)	164 (57.47%)	113 (51.24%)	
BMI group				0.4
Underweight (< 18.5)	5 (1.23%)	3 (0.47%)	3 (1.31%)	
Normal (18.5 to < 25)	55 (26.98%)	63 (25.31%)	42 (20.19%)	
Overweight (25 to < 30)	59 (28.81%)	77 (33.37%)	73 (39.32%)	
Obese (30 or greater)	98 (42.98%)	131 (40.85%)	89 (39.17%)	
Hypertension	167 (75.50%)	204 (69.74%)	162 (72.87%)	0.5
Diabetes	83 (38.27%)	102 (30.36%)	106 (43.76%)	0.064
PIR				< 0.001
≤ 1.3	56 (17.18%)	68 (16.58%)	109 (37.74%)	
1.3 < to ≤ 3.5	92 (42.64%)	130 (46.29%)	75 (45.04%)	
> 3.5	69 (40.18%)	76 (37.13%)	23 (17.22%)	
CERAD1	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	0.6
CERAD2	8.00 (7.00, 9.00)	7.00 (6.00, 9.00)	7.00 (6.00, 9.00)	0.4
CERAD3	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	0.6
CERAD total	21.0 (19.0, 24.0)	21.0 (17.0, 24.0)	21.0 (17.0, 24.0)	0.4
CERAD delay recall	7.00 (6.00, 9.00)	7.00 (5.00, 8.00)	7.00 (5.00, 8.00)	0.078
AFT	17.0 (15.0, 21.0)	17.0 (14.0, 20.0)	17.0 (13.0, 19.0)	0.2
DSST	54 (45, 67)	51 (42, 64)	49 (33, 62)	< 0.001

[1] n (weighted %); Median (IQR)

[2] chi-squared test with Rao & Scott's second-order correction; Wilcoxon rank-sum test for complex survey samples

is associated with early menopause [32]. Using early menopause as the reference group allowed for a clearer comparison of how different reproductive factors influence cognitive outcomes. The delayed menopause group displayed higher scores in immediate recall (CERAD trial 1), CERAD delayed recall, and the total score of CERAD trials when compared to the early menopause group. Moreover, reproductive span demonstrated a steady positive correlation with cognitive functioning, especially in the context of CERAD trial 1, as well as total recall and DSST scores, throughout all models. The consistent positive association between delayed menopause and

Table 3 Characteristics and cognitive function of study participants grouped by parity

Characteristic	Parity ≤ 2, *N* = 304 (49.79%%)[1]	3 ≤ Parity ≤ 4, *N* = 275 (37.05%)[1]	Parity ≥ 5, *N* = 119 (13.15%)[1]	*p*-value[2]
Age group				< 0.001
60–69 years	180 (60.27%)	127 (38.37%)	42 (34.38%)	
70–79 years	73 (23.02%)	77 (31.64%)	50 (42.26%)	
≥ 80 years	51 (16.71%)	71 (29.99%)	27 (23.36%)	
Race/Ethnicity				< 0.001
Non-Hispanic White	171 (81.80%)	143 (77.39%)	41 (61.13%)	
Non-Hispanic Black	57 (6.91%)	60 (10.95%)	35 (18.21%)	
Mexican American	18 (2.27%)	28 (4.71%)	24 (10.88%)	
Other Hispanic	22 (2.36%)	27 (3.78%)	14 (6.89%)	
Other multiracial	36 (6.67%)	17 (3.17%)	5 (2.89%)	
Education attainment				< 0.001
Less Than 9th Grade	14 (2.99%)	19 (4.62%)	34 (18.48%)	
9-11th Grade	31 (7.47%)	51 (17.28%)	31 (21.60%)	
High School Grad/GED	67 (22.17%)	84 (31.33%)	27 (28.93%)	
Some College or AA degree	116 (38.24%)	72 (26.23%)	22 (24.24%)	
College Graduate or above	76 (29.14%)	49 (20.55%)	5 (6.75%)	
Alcohol intake				0.047
1–5 drinks/month	137 (49.79%)	107 (41.77%)	50 (42.01%)	
5–10 drinks/month	10 (3.01%)	7 (2.42%)	1 (2.73%)	
≥ 10 drinks/month	37 (15.03%)	27 (14.35%)	4 (2.72%)	
Non-drinker	120 (32.17%)	134 (41.46%)	64 (52.53%)	
Smoke group				0.4
Current smoker	39 (13.77%)	28 (8.66%)	15 (12.09%)	
Former smoker	96 (35.99%)	88 (35.71%)	34 (31.14%)	
Never smoker	169 (50.24%)	159 (55.63%)	70 (56.77%)	
BMI group				0.5
Underweight (< 18.5)	7 (1.16%)	4 (1.02%)	0 (0.00%)	
Normal (18.5 to < 25)	74 (27.87%)	63 (22.56%)	23 (18.62%)	
Overweight (25 to < 30)	86 (30.14%)	82 (35.25%)	41 (38.51%)	
Obese (30 or greater)	137 (40.84%)	126 (41.17%)	55 (42.88%)	
Hypertension	230 (72.13%)	211 (73.12%)	92 (73.11%)	> 0.9
Diabetes	112 (35.19%)	111 (33.22%)	68 (50.99%)	0.045
PIR				< 0.001
≤ 1.3	81 (17.37%)	85 (21.73%)	67 (39.83%)	
1.3 < to ≤ 3.5	126 (41.90%)	128 (46.62%)	43 (49.44%)	
> 3.5	97 (40.74%)	62 (31.65%)	9 (10.73%)	
CERAD1	5.00 (4.00, 7.00)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	0.010
CERAD2	8.00 (7.00, 9.00)	7.00 (6.00, 9.00)	7.00 (6.00, 8.00)	0.038
CERAD3	9.00 (7.00, 10.00)	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	0.016
CERAD total	21.0 (19.0, 25.0)	20.0 (17.0, 23.0)	21.0 (17.0, 23.0)	0.013
CERAD delay recall	7.00 (6.00, 9.00)	7.00 (5.00, 8.00)	6.00 (5.00, 7.00)	0.008
AFT	18.0 (15.0, 22.0)	17.0 (14.0, 20.0)	15.0 (12.0, 19.0)	0.018
DSST	57 (45, 68)	50 (39, 62)	45 (25, 56)	< 0.001

[1]n (weighted %); Median (IQR)

[2]chi-squared test with Rao & Scott's second-order correction; Wilcoxon rank-sum test for complex survey samples

cognitive function across various measures suggested that an extended reproductive lifespan may contribute to better cognitive health. Furthermore, our study highlights the impact of socioeconomic factors on both parity and cognitive outcomes. The relationship between number of pregnancies and cognitive function is a complex and controversial topic. In some cognitive tasks, such as CERAD trial 1, women with a higher number of pregnancies performed better, while in others, like DSST and CERAD delayed recall, they exhibited poorer cognitive performance. This discrepancy may be attributed to differential sensitivity of specific cognitive domains to parity, as well as to the potential confounding effects of factors such as

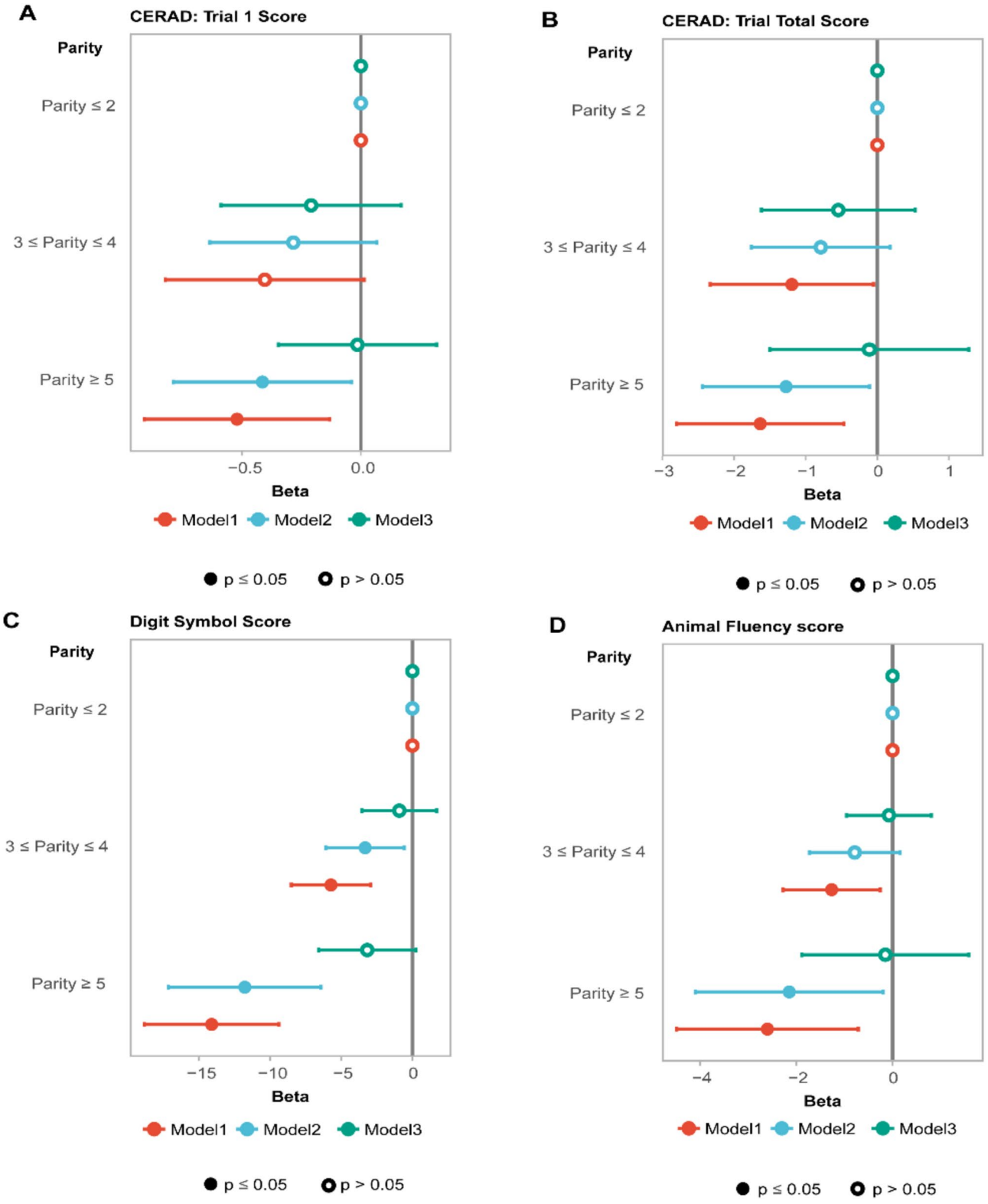

Fig. 2 Forest plot of the associations between parity and cognitive test scores for CERAD trial 1, CERAD trial total, AFT, and DSST. Parity ≤ 2 was used as the reference group. Parity ≥ 5 was negatively correlated with cognitive function, manifesting in lower scores in model 1 and model 2, but it was insignificant in model 3. Model 1: no adjusted; Model 2: adjusted for age; Model 3: were adjusted for age, BMI, alcohol intake, smoking, PIR, education, race/ethnicity, hypertension, and diabetes

Table 4 Characteristics and cognitive function of study participants grouped by menopause status

Characteristic	Early menopause, *N* = 264 (39.05%)[1]	Normal menopause, *N* = 388 (54.26%)[1]	Delayed menopause, *N* = 46 (6.69%)[1]	*p*-value[2]
Age group				0.8
60–69 years	125 (47.47%)	200 (49.20%)	24 (52.55%)	
70–79 years	78 (27.05%)	111 (30.23%)	11 (26.61%)	
≥ 80 years	61 (25.48%)	77 (20.57%)	11 (20.85%)	
Race/Ethnicity				0.8
Non-Hispanic White	143 (77.88%)	190 (77.18%)	22 (77.02%)	
Non-Hispanic Black	64 (11.01%)	76 (8.99%)	12 (10.75%)	
Mexican American	22 (3.48%)	45 (5.21%)	3 (1.83%)	
Other Hispanic	20 (3.04%)	38 (3.70%)	5 (4.24%)	
Other/multiracial	15 (4.59%)	39 (4.92%)	4 (6.16%)	
Education attainment				0.4
Less Than 9th Grade	31 (7.96%)	32 (4.02%)	4 (5.13%)	
9-11th Grade	38 (11.79%)	66 (12.79%)	9 (21.20%)	
High School Grad/GED	76 (27.46%)	90 (26.30%)	12 (21.80%)	
Some College or AA degree	83 (34.04%)	115 (30.73%)	12 (29.64%)	
College Graduate or above	36 (18.76%)	85 (26.17%)	9 (22.23%)	
Alcohol intake				< 0.001
1–5 drinks/month	119 (52.00%)	158 (41.85%)	17 (41.55%)	
5–10 drinks/month	6 (1.68%)	6 (2.22%)	6 (13.36%)	
≥ 10 drinks/month	18 (7.14%)	44 (16.58%)	6 (20.53%)	
Non-drinker	121 (39.18%)	180 (39.34%)	17 (24.57%)	
Smoke group				0.078
Current smoker	38 (16.00%)	39 (8.60%)	5 (11.06%)	
Former smoker	98 (38.56%)	101 (32.72%)	19 (36.44%)	
Never smoker	128 (45.44%)	248 (58.68%)	22 (52.50%)	
BMI group				0.041
Underweight (< 18.5)	4 (0.65%)	6 (1.20%)	1 (0.78%)	
Normal (18.5 to < 25)	44 (16.83%)	106 (29.30%)	10 (33.06%)	
Overweight (25 to < 30)	89 (35.79%)	108 (31.20%)	12 (33.31%)	
Obese (30 or greater)	127 (46.74%)	168 (38.30%)	23 (32.85%)	
Hypertension	222 (79.82%)	276 (67.70%)	35 (70.66%)	0.022
Diabetes	126 (43.28%)	148 (33.26%)	17 (23.78%)	0.075
PIR				0.2
≤ 1.3	95 (22.30%)	125 (22.51%)	13 (15.14%)	
1.3 < to ≤ 3.5	111 (46.86%)	167 (44.30%)	19 (34.38%)	
> 3.5	58 (30.83%)	96 (33.18%)	14 (50.48%)	
CERAD1	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	6.00 (5.00, 7.00)	< 0.001
CERAD2	7.00 (6.00, 8.00)	8.00 (6.00, 9.00)	8.00 (7.00, 9.00)	0.047
CERAD3	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	9.00 (7.00, 10.00)	0.14
CERAD total	21.0 (18.0, 23.0)	21.0 (18.0, 24.0)	23.0 (20.0, 27.0)	0.006
CERAD delay recall	7.00 (5.00, 8.00)	7.00 (5.00, 8.00)	8.00 (7.00, 9.00)	0.002
AFT	17.0 (13.0, 20.0)	18.0 (14.0, 21.0)	17.0 (14.0, 22.0)	0.2
DSST	49 (40, 61)	54 (42, 65)	58 (45, 67)	0.013

[1]n (weighted %); Median (IQR)

[2]chi-squared test with Rao & Scott's second-order correction; Wilcoxon rank-sum test for complex survey samples

overall health status, hormonal fluctuations, and physiological changes.

In our study, the parity had a nuanced relationship with cognitive function. A higher parity, particularly more than five, was negatively associated with cognitive function, especially in terms of delayed recall and word learning. It was consistent with the research results of others. Yang et al. discovered an inverse relationship between the number of children and cognitive functioning among older adults. In contrast to older adults who have four children, those with more than five children exhibited a notable decline in their Mini-Mental State Examination

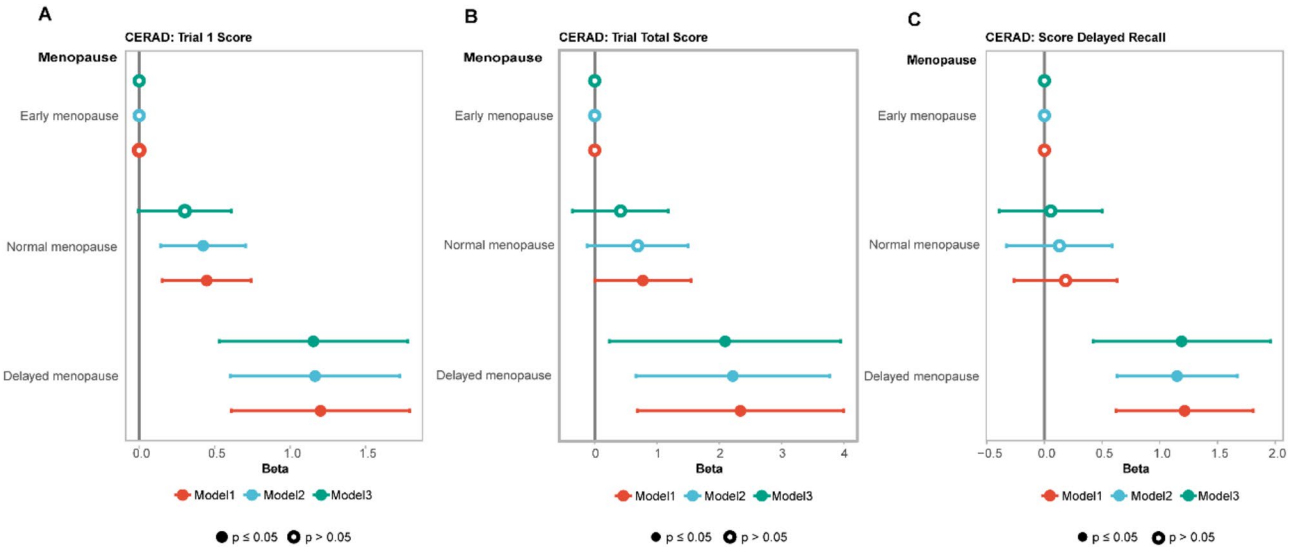

Fig. 3 Forest plot of the associations between menopause and cognitive test scores for CERAD trial 1, CERAD trial total, and CERAD delayed recall. Early menopause was used as the reference group. There existed a positive correlation between the age at menopause and cognitive function. A later onset of menopause is associated with higher cognitive scores in CERAD trial 1, CERAD trial total, and CERAD delayed recall. Delayed menopause exhibited the most robust positive correlation with cognitive function, with statistical significance consistently observed across model 1 and model 2, and model 3. Model 1: no adjusted; Model 2: adjusted for age; Model 3: were adjusted for age, BMI, alcohol intake, smoking, PIR, education, race/ethnicity, hypertension, and diabetes

Table 5 Linear regression β(95%CI) of the association between reproductive span and cognitive function

Reproductive span						
Characteristic	**Model 1**	***p*-value**	**Model 2**	***p*-value**	**Model 3**	***p*-value**
CERAD1	0.04 (0.03, 0.06)	< 0.001	0.04 (0.03, 0.06)	< 0.001	0.04 (0.02, 0.05)	< 0.001
CERAD2	0.01 (0.00, 0.03)	0.081	0.01 (0.00, 0.03)	0.14	0.01 (-0.01, 0.03)	0.5
CERAD3	0.02 (0.01, 0.03)	0.003	0.01 (0.00, 0.02)	0.005	0.01 (0.00, 0.02)	0.13
CERAD total	0.07 (0.04, 0.10)	< 0.001	0.07 (0.04, 0.10)	< 0.001	0.05 (0.01, 0.09)	0.019
CERAD delay recall	0.02 (0.00, 0.04)	0.025	0.02 (0.00, 0.04)	0.037	0.02 (0.00, 0.04)	0.12
AFT	0.06 (0.01, 0.12)	0.031	0.06 (0.01, 0.11)	0.032	0.03 (-0.02, 0.08)	0.2
DSST	0.28 (0.16, 0.40)	< 0.001	0.27 (0.15, 0.39)	< 0.001	0.12 (0.03, 0.22)	0.018

Model 1: no adjusted

Model 2: adjusted for age

Model 3: were adjusted for age, BMI, alcohol intake, smoking, PIR, education, race/ethnicity, hypertension, and diabetes

scores [33]. The association between increased parity and cognitive decline may involve multiple factors, including brain structure, hormonal regulation, metabolic burden, and inflammation. Pritschet et al. discovered that as the number of pregnancies rises, there is a notable decrease in gray matter volume as well as in vital areas such as the hippocampus, hypothalamus, thalamus, and brainstem. Notably, the volume of the hippocampus persisted in declining with multiple pregnancies, while a consistent reduction was observed in the para-hippocampal cortex. Such alterations in structure can negatively affect memory, emotional management, and cognitive regulation, resulting in a progressive decrease in cognitive function [34]. Hoekzema et al. found that the volume of gray matter decreases during pregnancy, and this reduction does not return to baseline levels for a minimum of two years after giving birth [35]. Long-term hormonal fluctuations also contribute to cognitive decline, as elevated levels of estrogen and progesterone during pregnancy enhance short-term neuroplasticity [36]. However, as parity increases, the adaptive effects of these hormones may diminish, especially during the postpartum period when estrogen levels drop, potentially exacerbating neurodegenerative processes [37]. Furthermore, higher parity is associated with chronic diseases such as hypertension and diabetes, which can trigger inflammatory responses. Long-term low-grade inflammation may negatively affect the nervous system, contributing to cognitive impairment or dementia [38]. Jung's research indicates that having many children may enhance the risk of cognitive deterioration or elevate the likelihood of dementia in elderly women by worsening atrophy in the hippocampus or cortex, independent of amyloid factors [39]. While our study initially demonstrated significant associations

between higher parity (≥5) and cognitive outcomes, including AFT, DSST, and CERAD trials, these associations were attenuated and became non-significant after adjusting for covariates in fully adjusted models. This attenuation suggests that the observed effects of parity on cognitive outcomes may be explained by other factors, such as age, education level, socioeconomic status, or comorbidities, which are closely related to both parity and cognitive function. It is essential to recognize that parity might not serve as a direct risk factor; instead, it may function as a proxy for a complex interaction of biological, social, and environmental factors that together affect cognitive health [40]. For instance, higher parity is frequently correlated with lower levels of socioeconomic status and educational attainment [41]. Moreover, physiological alterations linked to multiple pregnancies, such as changes in hormone levels, shifts in nutritional status, and heightened caregiving duties, could lead to variations in cognitive function [42]. When examining the link between parity and cognitive function, it is essential to consider the interplay of various factors, including race/ethnicity, education level, smoking habits, alcohol consumption, diabetes, and hypertension on cognitive performance.

Delayed menopause was consistently associated with better cognitive performance across multiple cognitive measures. Our study was consistent with the conclusions of others. For instance, Needham et al. demonstrated that a later age at menopause is linked to better cognitive performance, particularly in areas like memory, visuospatial skills, and assessments such as the DSST and face-name association tasks [43]. Similarly, a study using data from the Medical Research Council's pioneering National Survey of Health and Development showed that later menopause is associated with improved performance on various cognitive tests, including the Addenbrooke's Cognitive Examination - Third Edition total score and verbal fluency [44]. The link between delayed menopause and cognitive function is likely attributed to prolonged exposure to estrogen, which has been shown to have protective effects on brain health. Estrogen contributes to protecting neurons, promoting the formation of synapses, and improving memory and learning abilities [45]. Research supports the idea that increased estrogen exposure throughout a woman's life is associated with a reduced risk of AD and that estrogen deficiency negatively impacts brain structure and function [46]. Research conducted by Fan et al. demonstrates that estrogen receptors exhibit high expression levels in areas such as the hippocampus and prefrontal cortex, both of which are essential for cognitive functions like memory and attention [47]. Additionally, findings from Ishunina et al. indicate that estrogens might have positive effects on cognitive functions reliant on the hippocampus, potentially acting through the mediation of estrogen receptor alpha [48]. In our study, the delayed menopause group had higher alcohol intake, while hypertension was more common in the early menopause group. It is known that alcohol may increase estrogen levels in the body [49], and since estrogen has a protective effect on ovarian function, this could potentially delay the onset of menopause. Furthermore, alcohol may reduce oxidative stress in ovarian tissue, thereby protecting ovarian function and contributing to a later onset of menopause [50]. On the other hand, the loss of estrogen's protective effects occurs when estrogen levels decline, impairing its ability to dilate blood vessels, reduce peripheral vascular resistance, and regulate lipid metabolism, all of which are essential for cardiovascular protection. In women with early menopause, the decline in estrogen levels weakens these protective effects, leading to increased vascular constriction, elevated peripheral vascular resistance, and a subsequent rise in blood pressure [51].

Our study indicates that a longer reproductive span is positively associated with better cognitive abilities, particularly in memory and processing speed. Other's study has shown that the hormonal changes associated with a longer reproductive span, including prolonged estrogen exposure, may protect against age-related cognitive decline [52]. In our findings, a longer reproductive span was consistently associated with higher scores in CERAD Immediate recall and total recall, reflecting enhanced verbal memory. This suggests that hormonal factors across a longer reproductive lifespan contribute to enhanced neuroprotection. Additionally, the strong association between reproductive span and DSST scores underscores the role of reproductive health in supporting processing speed.

These findings underscore the importance of reproductive factors in cognitive aging and provide a basis for identifying risk factors for cognitive health in elderly women and developing interventions for dementia prevention. These interventions can range from hormone therapy and lifestyle modifications to advanced medical procedures. Hormone replacement therapy is a widely used method for alleviating menopausal symptoms and may also help in postponing the onset of menopause; however, it is crucial to consider the advantages in relation to possible risks [53]. Lifestyle changes, such as maintaining a balanced diet rich in phytoestrogens, healthy fats, and essential vitamins, engaging in regular physical activity, and practicing mindfulness, can play a significant role in managing menopausal symptoms and possibly delaying its onset [54]. Medical interventions, including the use of rapamycin to prolong ovarian function [55] and ovarian tissue transplantation to preserve fertility and reverse menopause [56], show promise in extending the fertility window and delaying menopause.

A few limitations of the present study needed to be noted. Firstly, the cross-sectional design restricts our ability to draw causal conclusions, and the sample may not represent the full diversity of the population. Secondly, in this observational study, residual and unmeasured confounding factors cannot be completely excluded. Thirdly, the study used a single-sample database, which has certain limitations, and can be further validated using multi-sample databases.

Future research may explore two main potential directions. Firstly, future research should consider longitudinal designs to track women's cognitive function from their childbearing years into later life, allowing for a better understanding of temporal relationships and potential causal mechanisms between the number of pregnancies, age at menopause, and cognitive function. Secondly, to further investigate the impact of parity and menopause on cognitive health, future studies could focus on identifying and evaluating biomarkers related to these reproductive events.

Conclusions

This study explores the association between female reproductive factors and cognitive function in later life. The findings indicate that higher parity is associated with reduced cognitive performance, while a later onset of menopause and a longer reproductive span are linked to better cognitive outcomes. Incorporating reproductive factors into the assessment of risk factors associated with cognitive impairment in older adults provides valuable insights into preventing and addressing cognitive decline and dementia.

Abbreviations

NHANES	National Health and Nutrition Examination Survey
CERAD	Consortium to Establish a Registry for Alzheimer's Disease
AFT	Animal Fluency test
DSST	Digit Symbol Substitution Test
BMI	Body mass index
PIR	Poverty income ratio
AD	Alzheimer's disease
CDC	Centers for Disease Control and Prevention
GED	General educational development
AA	Associate of Arts

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-22966-z.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

T.L. and F.C. were involved in developing and designing the study concept; A.H., H.W., L.Y., Y.L., and H.Q. were involved in the data acquisition and analysis; A.H., L.X. contributed to the initial manuscript writing. All authors revised and agreed to the final version of this article.

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Data availability

The data that support the findings of this study are openly available on the NHANES website and can be accessed at (URL https://wwwn.cdc.gov/nchs/nhanes/, accessed on 15 April 2025).

Declarations

Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations. The Research Ethics Review Board (ERB) of the US National Center for Healthcare Statistics (NCHS) authorized the 2011–2014 NHANES (protocol number: protocol#2011–17 and continuation of protocol #2011–17) (https://www.cdc.gov/nchs/nhanes/about/erb.html). Before initiating data collection and the NHANES physical examinations, all eligible individuals had given their informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Geriatric Center, Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), Haikou 570311, China
[2]Department of Neurology, Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), Haikou 570311, China
[3]Department of Radiology, Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), Haikou 570311, China

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