

Background

- Women experience dynamic hormonal shifts from menarche to menopause, making brain aging uniquely complex.
- Reproductive factors may influence cognitive and brain aging and risk of Alzheimer’s disease and related dementias through lifetime estrogen exposure.
- However, their impact on cognition remains poorly understood, particularly in racially and ethnically diverse populations.

Objective

- We examined whether age at menarche, age at menopause, reproductive lifespan, and parity are associated with cognitive trajectories.

Study population

- The Greater Sacramento Women's Brain Health (GROW) Study is a community-based observational cohort of ethnoracially diverse women aged ≥45 years in the greater Sacramento, CA area (2023-present).
- The study investigates life-course risk and resilience factors for cognitive impairment and dementia through questionnaires, annual physical exams, cognitive testing, saliva, blood draws, and neuroimaging.

Measures

- Reproductive factors included self-reported parity, age at menopause, age at menarche, and reproductive lifespan (years between menarche and menopause).
- The Spanish and English Neuropsychological Assessment Scales assessed Executive function (EF) and verbal episodic memory (VEM) up to 2 visits.
- Covariates: age, race/ethnicity, education, marital status, health status, and practice effects.

Table 1: Characteristics of GROW participants

Demographic Factors (n=408)	N (%) or Mean ± SD
Age, years	66.2±10.0
Race/Ethnicity	
Asian/Multiracial/Other	86 (24.9)
Black	106 (30.7)
Latinx/Hispanic	61 (17.7)
White	92 (26.7)
Education	
≤HS graduate	28 (8.1)
Some college	121 (35.1)
College graduate	120 (34.8)
Graduate School	76 (22.0)
Current Marital Status	
Yes	153 (44.9)
No	188 (55.1)
Health Status	
Excellent/very good	169 (48.8)
Good	116 (33.5)
Fair/Poor	61 (17.6)
Reproductive Factors	
Age at menarche, years (n=218)	12.8±1.9
Age at menopause, years (n=295)	49.8±6.8
Reproductive lifespan, years (n=169)	37.7±6.9
Parity/number of children (n=408)	1.7±1.4

Later age at menarche was associated with lower baseline verbal episodic memory

Table 2: Baseline associations of reproductive factors and cognitive performance

	Estimate (95% CI)	
	Executive Function	Verbal Episodic Memory
Reproductive lifespan	-0.003 (-0.02, 0.02)	0.001 (-0.02, 0.03)
Age at menopause	-0.004 (-0.02, 0.01)	0.002 (-0.01, 0.02)
Age at menarche	0.01 (-0.06, 0.07)	-0.08 (-0.15, -0.01)
Parity	0.03 (-0.04, 0.09)	0.01 (-0.06, 0.08)

Model estimates adjusted for age, race/ethnicity, education, marital status, and health status.

Statistical analysis

- We tested cross-sectional and longitudinal associations of each reproductive factor (modeled continuously) with cognition using separate multivariable linear regression and linear mixed-effects models with random intercepts.
- All models were adjusted for covariates.

Results

- Demographic and reproductive characteristics are shown in table 1.
- Mean longitudinal follow-up was 7.2±6.1 months (median: 11.5 months; maximum: 18.4 months).
- Cross-sectionally, later age at menarche was associated with lower VEM. No other associations were observed between reproductive factors and baseline EF or VEM (Table 2).
- Longitudinal analyses showed no associations between reproductive factors and cognition.

Conclusions

- Later age at menarche was associated with lower baseline verbal episodic memory, but not with cognitive change in either domain.
- No other reproductive factors were associated with baseline cognition or longitudinal change.
- The shorter follow-up period and small number of repeated measures may have limited our ability to detect associations.
- Future studies with longer follow-up are needed to confirm these findings.

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Greater Sacramento Women’s
Brain Health Program