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Reproductive history and cognitive aging: The Bogalusa Heart Study

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Abstract

Background—Although it has become increasingly clear that pregnancy-related health predicts later-life cardiometabolic health, the relationship between reproductive history and cognitive health is less frequently studied. Although some research has identified associations between parity or hypertensive disorders of pregnancy and cognitive changes, the evidence is mixed.

Objective—To examine the association between reproductive history and midlife cognition in a community-based population

Study design—730 midlife women in the Bogalusa Heart Study completed a brief cognitive battery (memory, attention, executive function, processing speed) and were interviewed about their reproductive history. Reproductive history (parity, age at first pregnancy, breastfeeding) and pregnancy complications (low birthweight, preterm birth, hypertensive disorders, miscarriage) were examined as predictors of cognitive function, with adjustment for potential confounders.

Results—Nulliparous women had an overall lower cognitive score (adjusted beta −1.50, SE 0.41). Adolescent birth was associated with a somewhat better performance on the Trailmaking Test (beta −0.31 SE 0.15 for birth <16 years), while high parity was not strongly associated with any of the cognitive measures. History of pregnancy complications was not strongly associated with cognitive function, whereas history of miscarriage was associated with better cognitive function, as was a history of breastfeeding (beta overall score 0.90 SE 0.29), particularly noticeable for semantic memory and in those with more total breastfeeding time (beta for overall score among those with >24 weeks lifetime breastfeeding, beta 1.21, SE 0.44).

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The authors report no conflict of interest.

Conclusions—Nulliparity and breastfeeding are associated with midlife cognition in women. Future studies should examine possible mechanisms by which these associations are created.

Keywords

breastfeeding; mental status and dementia tests; parity; pregnancy complications

Objective

Although it has become increasingly clear that pregnancy experience and pregnancy-related health predict later-life cardiometabolic health, the relationship between reproductive history and cognitive health is much less studied. Short-term, pregnancy produces changes in memory, with diminished verbal recall memory (but not recognition or working memory) (1). Alzheimer's neuropathology has been found in women with more children (2, 3), but not in men (4), and women with more pregnancies were found to demonstrate a younger age of onset of Alzheimer's in one case series (5). However, another study found more lifetime months of pregnancy was associated with a reduced risk of Alzheimer's disease (6). Studies specifically examining cognitive function are similarly inconsistent. Lower parity was associated with better cognitive function (word recall, Mini-Mental State Examination [MMSE]) in a Chinese cohort (7), but another study found no association between parity and memory in postmenopausal Canadian women (8). Another Chinese study found greater cognitive impairment for women with five or more full-term pregnancies; women with only completed pregnancies (no abortions or miscarriages) also had a significantly higher risk of cognitive impairment (9). Nulliparity has also been found to be associated with less cognitive decline, as measured by the MMSE, in a study of women in Baltimore (10). In rodents, females with a history of giving birth have demonstrated better learning and memory performance (11).

Similarly, although hypertensive disorders and gestational diabetes have been widely studied as predictors of later-life cardiometabolic health, only eclampsia and pre-eclampsia have been studied in detail in relation to cognition. In the Utah population database, women with a history of hypertensive disorders of pregnancy were at increased risk of death due to Alzheimer's (12), although this was contradicted by a Dutch study (13). In mid- to late life history of hypertensive disorders has been associated with worse processing speed (14) and mild cognitive impairment/dementia (15). Several studies also demonstrate brain changes, such as increased white matter lesions, among those with a history of eclampsia or pre-eclampsia (16, 17). However, most detailed studies of cognitive function have been conducted in relatively young women, with generally ambiguous results. While some studies do show subtle cognitive differences in women with a history of eclampsia or pre-eclampsia (18, 19), often there seems to be some confounding by psychological comorbidity, which is more common than cognitive impairment in younger women and may be the result of a complicated pregnancy.

Other pregnancy complications have not been examined to any great extent, although one study indicated poorer cognitive function in women with gestational diabetes during pregnancy (20). Pregnancy and related complications contribute to both hormone-related

cognitive changes (21) as well as cardiometabolic risk profile (22). Given the inconsistencies in the literature, the ubiquity of pregnancy, and the growing incidence of Alzheimer's disease, more research is clearly needed. In this study, we examine several indicators of reproductive history and their relationship to cognitive health at midlife within the Bogalusa Heart Study, a long-term study of cardiovascular health. We hypothesized that indicators of worse pregnancy health, such as maternal and infant complications, would be associated with worse cognitive function. More specifically, we hypothesized that cognitive function would follow patterns seen with the relationships between pregnancy history and later-life cardiometabolic health (22): worse cognition would be associated with higher parity, nulliparity, and adolescent pregnancy (23). We also hypothesized strong negative associations between hypertensive disorders and gestational diabetes – the complications most strongly associated with poor cardiometabolic health – and weaker but still negative associations with adverse birth outcomes like low birthweight and preterm birth. For similar reasons, we hypothesized that lactation would be protective (24).

Methods

Study sample

The Bogalusa Heart Study is a series of studies of cardiovascular risk, in a semirural, biracial population (65% white and 35% black), founded by Dr. Gerald Berenson in 1973. This analysis combines results from two follow-up studies conducted in 2011–2016: Bogalusa Babies, which examined reproductive outcomes within the BHS, and BiCEPS (Brain, CognitivE and Physical performance Study), which links vascular risk factors across the lifespan with cognitive and physical performance. 1804 women participated in Bogalusa Babies; of those, 731 also participated in BiCEPS and had data on at least one exposure and outcome, while 627 had data on at least one pregnancy. The most common reason for not participating in both was not being available to visit the clinic. In most cases, women completed both studies on the same day, although this was not a requirement.

Inclusion/exclusion

Compared to the overall Babies group, the group with cognitive measures were older (age in 2016 49.3 vs. 43.0); less likely to be black (37% vs. 43%), more postmenopausal (58% vs. 45%, difference mostly due to age), previous smokers (54% vs. 35%), and were less likely to have higher education (26% vs. 31%). Pre-pregnancy BMI was somewhat higher (24.1 vs. 22.4). There was no difference in parity, age at first or last pregnancy, or smoking or weight gain during pregnancy.

Reproductive history

All reproductive history variables in this analysis were self-reported, although women were encouraged to consult a baby book, if they had one. During the interview, women were asked whether they had ever been pregnant, the outcome of each pregnancy, complications, and whether they took any fertility drugs or received any medical procedures to help them get pregnant. Women were also asked whether they ever tried to get pregnant and were unable to. Women who answered "yes" to any one of these three fertility-related questions were considered to have reported fertility difficulties. Although self-report may

underestimate clinical fertility difficulties, it provides an adequate estimate of infertility burden with high specificity (25). Reproductive history assessed included number of pregnancies, number of births, and adolescent pregnancy (<16 or <18 years at first pregnancy).

Pregnancy complications assessed included low birthweight (<2500 g), preterm birth (<37 weeks' gestation), gestational diabetes mellitus (GDM), and miscarriage. Pre-eclampsia and pregnancy-related hypertension were combined for a hypertensive disorders of pregnancy outcome. Mothers typically remember the birthweight and gestational age of their infants quite well, even after many years (26). Recall has been shown to be highly specific (>90%) for hypertensive disorders (27) and accurate for reports of gestational diabetes (GDM) (specificity=98%, sensitivity=92%) (28). Miscarriage is particularly accurately recalled when it occurs late in pregnancy or requires medical attention (29); still, there is no other plausible source of information for history of early miscarriage besides self-report. All exposures were defined as the occurrence at any pregnancy, so if a woman had multiple pregnancies but reported the outcome in only one, she was defined as having had a history of the complication.

For each pregnancy, the participant was asked if she breastfed and for how long; these were summarized as ever breastfeeding and total life length of time breastfeeding.

Cognitive measures

The cognitive domains assessed were consistent with contemporary views of cognitive functioning and compatible with the domains recommended by the NIH Toolbox for the Assessment of Neurological and Behavioral Function: executive function, episodic memory, working memory, processing speed, and attention/concentration (30). Cognitive assessment was conducted by a trained staff member in a private, distraction-free setting. Working memory and executive control were tested with Digit Span Backwards (WAIS-III), in which number strings of increasing length were presented and were to be repeated back to the examiner in reverse order. Number strings increased in length by one digit per test trial, and the test was discontinued after failure of two same-length strings. One point is awarded per correctly reproduced string. Semantic memory was tested using Logical Memory I&II (WMS-III), which presents the subject with two short stories several sentences in length, after which the subject is asked to recall as much target information as possible. Subjects are forewarned that a recall trial will be administered, and recall is tested after a 30-minute delay. Scoring is based on the number of specific story elements correctly recalled. Working memory and processing speed were tested with Digit Symbol Coding (WAIS-III). A key of digit-symbol pairs is presented to the participant followed by lines of unpaired digits. The subject is instructed to write in the correct symbol under each digit according to the key and to complete the task as quickly as possible. It is scored as the number of correct symbols provided by the participant within 90 seconds (higher is better). Attention and executive function were also assessed using the Trailmaking Test, Forms A and B. On Form A, subjects are presented with a page on which the numbers 1 through 25 are randomly placed, and are instructed to connect the numbers as quickly as possible in sequential order. Form B presents randomly placed numbers and letters, and the subject is instructed to connect them

in alternating fashion (1-A-2-B-3-C, etc). It is scored by the number of seconds to complete (lower is better) (31).

Each scale was standardized. In addition, the z-scores were summed across the scales (reverse coded when necessary).

Analysis

Each exposure was examined as a predictor of each of the cognitive measures. Education level (ordinal as listed in Table 1) and single word reading performance as measured by the Wide Range Achievement Test (WRAT) were used to adjust for achieved learning at the time of the cognitive testing. The use of the WRAT reading subtest provides a grade-level score and is considered a suitable proxy for estimation of premorbid education that is generally robust to cognitive decline. Models of fertility and parity were adjusted for age at interview, menopausal status (self-defined as having gone 12 months without a period), race, smoking (ever/never), last reported marital status (married/not married), depressive symptoms (as indicated by the score on the CES-D (32)) and BMI at time of outcome measure. In addition to these covariates, models of pregnancy complications were adjusted for age at first pregnancy. Interaction with menopausal status and race were also examined using an interaction term; results were null except where indicated in the text. Linear models for continuous outcomes were used with multiple imputation (using SAS PROC MI and PROC MIANALYZE) to account for missing data on covariates; most commonly missing was marital status (7.4%) and age at first pregnancy (1.6%). Each linear model was fit in SAS PROC GENMOD which estimates parameters (beta) using maximum likelihood and calculates p-values using Wald chi-square tests with 1 df. All displayed parameters were dichotomous except for time breastfeeding, the p-value for which was calculated for an ordinal variable, 1 df. The results of the imputations (n=10) were combined for analysis; the combined point estimate for the parameter is the average (mean) of the complete-data estimates from the imputation datasets. The variance of this estimate incorporates both within-imputation and between-imputation variance, and is approximately distributed as t. Degrees of freedom depend on the number of imputations and the between- and within-imputation variance; adjusted degrees of freedom were used to avoid having the computed degrees of freedom being much larger than the complete-data degrees of freedom (33). Alpha was set at 0.05 and all tests were two-sided. To assess the effect of multiple comparisons, an analysis of the false discovery rate was conducted with q=0.05; p-values smaller than the critical value are marked in the tables.

The Biceps and Babies studies, as well as the overall BHS, were approved by the Tulane Institutional Review Board.

Results

The included study sample was approximately two-thirds white and one-third black, and fairly evenly divided between those who were pre- and post-menopausal (Table 1). 14% reported nulliparity.

Nulliparous women had lower scores on memory (Table 2) and digit coding scales, and longer trail making times, for an overall cognitive score that was lower. Adolescent birth was associated with a somewhat lower trail A time, while high parity was not strongly associated with any of the cognitive measures.

History of pregnancy complications was not strongly associated with cognitive function (Table 3). History of miscarriage was associated with better logical memory, digit coding scores, and the summary score.

Ever breastfeeding was associated with better cognitive measures, particularly noticeable for logical memory and in those with more than 12 weeks total breastfeeding time (Table 4).

Conclusions

In this analysis, we examined the relationship between pregnancy history and complications and cognitive function at midlife, hypothesizing that pregnancy complications would indicate risk for worse cognitive health later in life, as they indicate risk for cardiovascular health. Our hypothesis that nulliparity would be associated with worse and lactation with better cognition were borne out, while our hypothesized associations with high parity and adolescent pregnancy were not, nor were there strong negative associations between hypertensive disorders and gestational diabetes.

Our analysis of parity indicated that nulliparity was associated with worse cognitive function. This contradicts some previous studies, which have tended to show better cognitive function with nulliparity (10) and worse cognitive function with more pregnancies (7), although the research is far from consistent (6, 8). Previous studies were conducted in British (6), Chinese (7, 9), Canadian (8) and east Baltimore (US) women (10). The last is likely to be the population most directly relevant, as it is an American study with a high proportion of Black women; there is no clear reason for results to be different, but they had an older, postmenopausal population; a smaller sample size; and investigated change in cognitive function rather than absolute levels, which were very similar at baseline between women who had given birth and those who had not. Also, different instruments were used to measure cognitive function. Nulliparity is a possible indicator of infertility (although there are, of course, other reasons for lack of childbearing as well), which has been associated with earlier mortality (34). Infertility may be an indicator of worse underlying health; this is somewhat supported by the generally positive relationship between cognition and adolescent pregnancy, possibly indicating that strong fertility is associated with good health. Alternatively, a small number of pregnancies may be good for health. We did not find any relationships with high parity, but few women in the study had very high parity (few women with 5+ pregnancies). Studies of cardiovascular health may be instructive, both because health risk often clusters and because cardiometabolic health may directly affect cognition. In such studies, lower parity or nulliparity has tended to be associated with worse health, while associations with high parity were similar for men and women, suggesting at least part of the association was due to shared behavioral or socioeconomic risk factors (22).

We did not find many associations with pregnancy complications, although low birthweight and gestational diabetes were in the direction of being associated with worse cognitive measures. Hypertensive disorders were not associated with worse cognition; these conditions have been associated with later worse cognitive health in some though not all previous studies. In this study, we had very few serious cases (such as severe pre-eclampsia), as well. Miscarriage was associated with better cognitive measures; among other possibilities, this may indicate better memory and attention to medical history among those reporting, although it is interesting that one previous study reported women without a history of incomplete pregnancies had a significantly higher risk of cognitive impairment (9). However, the association with miscarriage could be due to chance, given the large number of associations tested.

History of breastfeeding was strongly associated with better cognitive measures. We are not aware of studies that have addressed this precise question, although one previous study found a reduced risk of Alzheimer's disease with breastfeeding and a longer duration of breastfeeding (35). A few studies also incorporated breastfeeding into their measures of overall reproductive history or number of menstrual cycles (6, 36). Breastfeeding is generally associated with better maternal health, particularly metabolic health, later in life (37). Breastfeeding analysis was limited to parous women, allowing us to examine the effect independent of parity. Reported rates of breastfeeding were relatively low, but the combination of the time period when most of the women were giving birth and lower rates among black and rural women likely explain this.

Multiple mechanisms may explain associations between reproductive history and cognition. Estrogen is one obvious candidate. Several studies hypothesize (3), and in some case demonstrate (6), that greater lifetime exposure to estrogen is associated with better cognition and reduced risk of Alzheimer's. Animal studies also demonstrate hormonal effects on cognition. In rats, females who had previously given birth have brains more responsive to estrogens than those who had not (38). Aspects of memory and neurogenesis vary by parity in rats, and the effect of ovariectomy and estrogen treatment on those differ by parity as well (39). In general, however, randomized trials in humans do not show any effects of hormone replacement on improved cognition (40). While we did not test this directly, the relationship with breastfeeding (generally a low-estrogen time) and nulliparity do not suggest that estrogen was protective in this case. A second possible mechanism is cardiometabolic risk. Pregnancy complications, nulliparity, and not breastfeeding are all associated with increased cardiovascular risk (37, 41), and cardiovascular risk factors such as hypertension are associated with cognitive decline and dementia (42).

Several tests of cognitive function were used, as well as a sum of z-scores. Such a use of z-score, particularly for summary scores, is controversial, and a more flexible or principal components analysis may be more theoretically justified. Still, this provides a simple, summary scale, and the individual scales provide more detail. The study sample is midlife; at this age, very few people meet clinical cut-offs and the goal of the instruments is not to provide a diagnostic or screening limit for a clinical diagnosis. Therefore, any relationships are with subtle cognitive differences. Reproductive history is self-reported; although report of most conditions has been found to be reliable, hypertensive disorders, in particular, may

not be well-reported. Cognitive issues could affect recall of pregnancy as well, perhaps leading to under-reporting of complications. Definitions of hypertensive disorders and gestational diabetes have also changed over the time period of the study. The large number of comparisons means we have limited our consideration of associations that are inconsistent.

In conclusion, this study suggests that cognition in midlife is associated with reproductive history, largely in association with factors suggesting overall better health. Future studies should examine possible mechanisms by which such effects might be occurring. Residual confounding by lifestyle, health literacy, or self-care needs to be ruled out. If the results hold, possible hormonal and cardiometabolic mechanisms should be investigated as biological mediators, as well as the possibility that social connections following pregnancy may have beneficial cognitive effects.

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Highlights

- **What is the primary question addressed by this study?** Are indicators of worse pregnancy health, such as maternal and infant complications, associated with worse cognitive function?
- **What is the main finding of this study?** Nulliparity and breastfeeding are associated with midlife cognition in women, while history of other complications did not predict cognitive measures.
- **What is the meaning of the finding?** These findings support the idea that pregnancy history and lactation are associated with long-term health consequences.

Table 1.

Participants in the Bogalusa Babies and BiCEPS studies, 2011–2016, n=730

	N	%			
race					
black	268	36.8			
white	461	63.2			
menopausal status at interview					
post-menopausal	418	57.6			
pre-menopausal	308	42.4			
total parity					
0	99	13.7			
1	125	17.2			
2	283	39.0			
3+	218	30.1			
education					
<12 years	65	8. 9			
12	239	32.8			
some college/AA	238	32.7			
college degree or higher	187	25.7			
ever smoked	395	54.2			
ever smoked in pregnancy	139	22.1			
	mean	median	SD	min	max
age at interview	47.7	48.2	5.2	32.5	57.8
age at 1st pregnancy	22.9	21.6	5.4	14.0	45.8
age at last pregnancy	28.5	28.0	5.7	15.0	45.8
BMI at last visit	32.0	31.2	8.4	17.9	67.7
pre-pregnancy BMI	22.5	21.2	5.2	13.3	49.4
average pregnancy weight gain	30.8	28.3	15.2	0.0	85.0
total vocabulary score on WRAT	40.2	42.0	10.0	0.0	55.0

AA, associate’s degree; BMI, body mass index; WRAT, Wide Range Achievement Test

Table 2.

Reproductive history and cognitive function, women in the Bogalusa Heart Study

	N[§]	%	logical memory: logical memory 1			logical memory: logical memory 2			logical memory: logical recognition			digit coding: digit coding score		
			B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]
nulliparous	99	13.7	−0.24	0.09	0.01	−0.19	0.09	0.04	−0.24	0.09	0.01	−0.32	0.09	<0.01[**]
any fertility difficulties	128	17.5	−0.10	0.08	0.21	−0.01	0.08	0.89	−0.06	0.08	0.48	0.06	0.08	0.42
birth<16 years	34	5.4	−0.04	0.15	0.81	−0.08	0.16	0.61	0.29	0.15	0.06	0.06	0.15	0.68
birth<18 years	113	18.0	−0.02	0.09	0.86	−0.08	0.09	0.37	0.08	0.09	0.35	0.00	0.09	0.98
Parity 4+	69	9.5	0.00	0.11	0.97	0.08	0.11	0.44	0.16	0.11	0.16	0.08	0.11	0.47
Parity 3+	218	30.1	0.00	0.07	0.95	−0.04	0.07	0.55	0.00	0.07	0.96	0.09	0.07	0.18

	trail making test: trail A time			trail B time			trail B/A ratio (log)			digit span forward, total		
	B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]
nulliparous	0.35	0.10	<0.01[**]	0.12	0.10	0.20	0.02	0.11	0.83	−0.01	0.10	0.90
any fertility difficulties	−0.07	0.09	0.45	−0.03	0.09	0.77	0.14	0.10	0.17	−0.12	0.09	0.18
birth<16 years	−0.31	0.15	0.04	−0.03	0.16	0.86	−0.32	0.19	0.09	−0.20	0.16	0.23
birth<18 years	−0.23	0.08	0.01	−0.04	0.09	0.64	−0.13	0.11	0.22	0.11	0.09	0.28
Parity 4+	−0.06	0.12	0.63	−0.07	0.11	0.52	0.16	0.13	0.22	−0.01	0.12	0.96
Parity 3+	−0.09	0.08	0.27	−0.05	0.07	0.47	−0.01	0.08	0.92	0.02	0.08	0.78

	digit span backward, total			summary score		
	B[*]	SE	p[†]	B[*]	SE	p[†]
nulliparous	−0.16	0.09	0.08	−1.50	0.41	<0.01[**]
any fertility difficulties	−0.12	0.08	0.16	−0.41	0.37	0.27
birth<16 years	0.06	0.16	0.72	0.28	0.69	0.69
birth<18 years	−0.06	0.09	0.52	0.17	0.40	0.67
Parity 4+	0.11	0.11	0.33	0.58	0.49	0.24
Parity 3+	0.02	0.07	0.80	0.24	0.32	0.46

[*] Adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms.

[**] Meets criterion (overall 0.05) for false discovery rate controlling for multiple testing

[†] Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances (adjusted df between 597 and 717).

Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation

[§]725 women had data on parity, 730 on fertility, and 627 on age at first pregnancy

[*]Adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms.

[**]Meets criterion (overall 0.05) for false discovery rate controlling for multiple testing

[†]Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances (adjusted df between 597 and 717).

Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation

[*]Adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms.

[**]Meets criterion (overall 0.05) for false discovery rate controlling for multiple testing

[†]Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances (adjusted df between 597 and 717).

Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation

Table 3.

History of pregnancy complications and cognitive function, women in the Bogalusa Heart Study

			logical memory								
			logical memory 1			logical memory 2			logical recognition		
	N[§]	%	B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]
low birthweight	113	18.1	−0.13	0.09	0.13	−0.09	0.09	0.29	−0.10	0.09	0.26
preterm birth	95	15.1	−0.06	0.09	0.55	0.02	0.09	0.87	0.03	0.09	0.71
gestational diabetes	67	10.7	−0.10	0.11	0.37	−0.17	0.11	0.13	0.00	0.11	0.99
hypertensive disorders	139	22.1	0.02	0.09	0.81	0.05	0.09	0.55	0.04	0.09	0.64
miscarriage	153	21.0	0.16	0.07	0.04	0.06	0.08	0.40	0.10	0.08	0.20

	digit coding			trail making test								
	digit coding score			trail A time			trail B time			trail B/A ratio (log)		
	B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]
low birthweight	−0.14	0.09	0.12	0.10	0.08	0.24	0.05	0.09	0.60	−0.15	0.11	0.15
preterm birth	−0.09	0.09	0.31	0.09	0.09	0.29	0.06	0.09	0.54	−0.08	0.11	0.46
gestational diabetes	−0.18	0.11	0.11	−0.03	0.10	0.79	−0.08	0.11	0.47	0.00	0.13	0.97
hypertensive disorders	0.03	0.08	0.71	0.04	0.08	0.60	0.11	0.09	0.21	0.14	0.10	0.18
miscarriage	0.14	0.07	0.05	−0.03	0.08	0.69	−0.11	0.08	0.15	0.04	0.09	0.63

	digit span forward, total			digit span backward, total			summary score		
	B[*]	SE	p[†]	B[*]	SE	p[†]	B[*]	SE	p[†]
low birthweight	−0.02	0.09	0.87	−0.15	0.09	0.09	−0.64	0.39	0.10
preterm birth	−0.06	0.10	0.54	−0.12	0.09	0.20	−0.37	0.42	0.38
gestational diabetes	−0.12	0.12	0.31	−0.11	0.11	0.33	−0.57	0.48	0.24
hypertensive disorders	0.09	0.09	0.33	0.02	0.09	0.84	0.12	0.38	0.75
miscarriage	0.13	0.08	0.11	0.11	0.08	0.15	0.72	0.34	0.03

[*] adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms. Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation; BMI, body mass index

[†] Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances (adjusted df between 594 and 717).

[§] 625 women had data on birthweight, 629 on preterm birth, gestational diabetes, and hypertensive disorders, and 730 on miscarriage

[*] adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms. Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation; BMI, body mass index

[†] Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances (adjusted df between 594 and 717).

[*] adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms. Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation; BMI, body mass index

† Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances (adjusted df between 594 and 717).

Table 4.

History of breastfeeding and later cognitive function, women in the Bogalusa Heart Study (n=627)

			logical memory								
	N	%	logical memory 1			logical memory 2			logical recognition		
			B*	SE	p†	B*	SE	p†	B*	SE	p†
Ever breastfed	261	41.6	0.20	0.07	<0.01	0.16	0.07	0.03	0.08	0.07	0.26
Total lifetime breastfed											
none	371	59.2			<0.01**			0.01			0.07
<12 weeks	101	16.1	0.09	0.09		0.04	0.10		−0.01	0.10	
12–24 weeks	58	9.3	0.25	0.12		0.23	0.12		0.09	0.12	
>24 weeks	97	15.5	0.29	0.10		0.24	0.10		0.18	0.10	

	digit coding			trail making test								
	digit coding score			trail A time			trail B time			trail B/A ratio (log)		
	B*	SE	p†	B*	SE	p†	B*	SE	p†	B*	SE	p†
Ever breastfed	0.14	0.07	0.05	−0.15	0.07	0.02	−0.11	0.07	0.14	0.06	0.08	0.47
Total lifetime breastfed												
none			0.11			0.03			0.15			0.95
<12 weeks	0.16	0.09		−0.11	0.09		−0.07	0.10		0.09	0.12	
12–24 weeks	0.07	0.12		−0.23	0.11		−0.21	0.12		0.08	0.14	
>24 weeks	0.16	0.10		−0.16	0.09		−0.10	0.10		−0.02	0.12	

	digit span forward, total			digit span backward, total			summary score		
	B*	SE	p†	B*	SE	p†	B*	SE	p†
Ever breastfed	−0.01	0.08	0.90	0.12	0.07	0.09	0.95	0.32	<0.01
Total lifetime breastfed									
none			0.74			0.29			<0.01**
<12 weeks	−0.08	0.10		0.17	0.10		0.53	0.42	
12–24 weeks	0.15	0.13		−0.01	0.12		1.18	0.52	
>24 weeks	−0.09	0.11		0.12	0.10		1.21	0.44	

*adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms.

**Meets criterion for false discovery rate under multiple testing

†Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address mis sing data; average value ~t with df depending on within- and between-imputation variances (adjusted df between 594 and 614).

Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation; BMI, body mass index

*adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms.

**Meets criterion for false discovery rate under multiple testing

† Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances.

Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation; BMI, body mass index

* adjusted for age, menopausal status, race, smoking, education, vocabulary, BMI, last known marital status, depressive symptoms.

** Meets criterion for false discovery rate under multiple testing

† Linear models fit using maximum likelihood. Parameters combined across multiple (n=10) imputations to address missing data; average value ~t with df depending on within- and between-imputation variances.

Outcomes are standardized to mean=0, SD=1. Summary score sums the individual standardized measures.

SE, standard error; SD, standard deviation; BMI, body mass index