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Research Article

Higher Number of Children Is Associated With Increased Risk of Generalization Deficits in Older African American Women

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Abstract

Objectives: The objectives of this project were to: (1) examine the relationship between the number of biological children and hippocampal-dependent cognitive performance among older African American women and (2) determine the influence of socioeconomic status (i.e., age, education, marital status, median household income), if any, on this relationship.

Methods: A total of 146 cognitively unimpaired African American women aged 60 and older were recruited from the greater Newark area and reported their number of biological children, marital status, educational level, and age. We retrieved median household income from census tract data based on the participants' addresses. Participants' cognitive performance was assessed using the Rey Auditory Verbal Learning Test (RAVLT) long delay recall and a Rutgers generalization task (Concurrent Discrimination and Transfer Task).

Results: As the number of biological children a woman has had increases, the number of generalization errors also increased, indicating poorer hippocampal-dependent cognitive performance when controlling for age, education, marital status, and median household income. There was no significant relationship between the number of children and performance on a standardized neuropsychological measure of episodic memory (RAVLT), although education was a significant covariate.

Discussion: Generalization tasks may better capture early changes in cognitive performance in older African American women who have had children than standardized neuropsychological assessments. This finding may be explained by the fluctuations in estrogen associated with having children. Future studies should explore how these findings can be applied to protecting cognitive function and preventing Alzheimer's disease in older African American women who have had children.

Keywords: Alzheimer's disease, Biological children, Cognitive function

About 10.7% of Americans aged 65 and older have Alzheimer's disease (AD; Gaugler et al., 2022). A growing body of evidence reveals that African Americans may be two to three times more likely to develop AD as compared to their non-Hispanic, White counterparts (Barnes & Bennett, 2014). The risk of dementia and AD reveals sex disparities in its epidemiology (Bae et al., 2020). Studies show that women have a higher prevalence of dementia than men (Cao et al., 2020). This may put African American women at a disproportionate risk for AD.

One factor that may play a role in AD development is the number of biological children a woman has had (also known as "parity"). Prior research suggests that parity may be associated with a higher risk for AD-related neuropathology, including neurofibrillary tangles and neuritic plaques (Beeri et al., 2009). Mostly among White/European study cohorts, there is no consensus on whether the number of children a woman has had is related to cognitive decline. Some studies report significant correlations between the number of children a woman has had and cognitive decline/dementia (Najar et al., 2020; Ptok et al., 2002), whereas others mention that pregnancy may be neuroprotective (Fox et al., 2018; Peterson & Tom, 2021). Additionally, some studies found that adverse outcomes of pregnancy may affect women's cognition in later life, but having children provides a neuroprotective effect when compared to having no children (Peterson & Tom, 2021). This cognition–pregnancy effect may be due to the relationship between hormonal levels and cognitive function. Specifically, estrogen has shown to be neuroprotective against AD/dementia (Bernstein et al., 1985). Estrogen levels increase during pregnancy and decrease after childbirth—influencing estrogen levels later in life (Sobow & Kloszewska, 2004). In other words, women who are nulliparous (i.e., have had no biological children) have higher levels of estrogen than women who are multiparous, that is, have had multiple children (Beeri et al., 2009). These decreases in estrogen levels due to the gestational process and childbirth may be associated with increased AD neuropathology in the brain (Beeri et al., 2009). Overall, these findings suggest that estrogen depletion may play a role in AD development.

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Ptok et al. (2002) found that having children is associated with a diagnosis of AD in women but not in men. This study also suggests that estrogen therapy may be a preventative measure against AD such that nulliparous women have more natural estrogen. A large epidemiological study that included White/European and Asian women across 11 countries and three continents found that having five or more biological children is associated with a greater risk of dementia(s), but this finding is not uniform across regions and dementia types (Bae et al., 2020). These mixed findings suggest that there are differences in the association between the number of children a woman has had and risk for cognitive decline for women of different ethnic/racial groups. While the mechanisms linking the number of biological children a woman has had and cognitive dysfunction/decline remain unclear, socioeconomic status may play a role (Zhang, 2022).

As such, this paper examined the relationship between the number of children a woman has had and cognitive function in older African American women living in the greater Newark area. We hypothesized that older African American women who have had several (>1) children will demonstrate poorer cognitive function. This project also examined demographic and socioeconomic factors that may be influenced by having children (e.g., age, educational level, marital status, median household income) and how these factors may further affect African American women's cognitive performance. Given the paucity of research on women's health and cognitive function in later life, especially within African American women, the current analyses focused on older African American women. To assess women's cognitive performance, this study utilized the Rey Auditory Verbal Learning Test (RAVLT) and a Rutgers generalization task (Concurrent Discrimination and Transfer Task). RAVLT is a standardized neuropsychological test that assesses episodic and verbal memory, often used to diagnose various forms of dementia (Rey, 1964). Past studies have shown that the Rutgers generalization task is associated with medial temporal lobe (MTL) dysfunction and is sensitive to early changes in cognitive function in preclinical phases of AD (Petok et al., 2018). Because this study's population consists of cognitively unimpaired older African American women, it was anticipated that the generalization task may reveal earlier changes in cognition that other standard neuropsychological assessments fail to capture.

Method

Participants

Participants in this study were selected from a larger ongoing parent study that aims to understand the associations between cognitive decline and biological (genetics, cognition, etc.) and social factors in older African Americans. Participants were recruited through the *Aging and Brain Health Alliance*, a university–community partnership at Rutgers University–Newark. Potentially eligible candidates met the following inclusion criteria: identify as postmenopausal, African American or Black, be 60 years or older, and were assigned female sex at birth. Initial screening was done over the phone and exclusion factors included: a diagnosis of dementia/mild cognitive impairment (MCI), self-reported memory issues, and the use of medication that affects cognitive ability. Participants responded to self-reported health items including (but not limited to):

Do you have any serious memory problems that you feel are worse than normal for a person your age (e.g., frequently forgetting a family member's name)?

Have you ever experienced any sleep problems (e.g., sleep apnea, chronic insomnia, trouble falling or staying asleep)?

Do you consume alcohol? If yes, what, how much, and how often?

Other exclusion factors included taking birth control (including any oral contraceptives) and hormone replacement therapy; diagnoses of sleep disorders; color blindness (due to some tasks requiring ability needed to differentiate between colors); alcohol use disorder and/or the use of illicit drugs; inability to see a computer screen from a normal distance; psychiatric and seizure disorders; and any significant cardiovascular disease including: myocardial infarction, coronary artery bypass grafting, and angioplasty or other cardiac condition in the past year. However, individuals with controlled/treated cardiovascular diseases such as hypertension, hypotension, heart disease, and having experienced transient ischemic attacks more than 6 months prior to screening are eligible for the *Pathways* study.

Other medical disorders such as cancers and chronic pain/arthritis were not necessarily excluded; however, if participants were excluded if they were currently undergoing chemotherapy or radiotherapy for cancer. Participants were also excluded if they were taking medications that affect cognition (e.g., long-term use of benzodiazepines).

All participants were required to be fluent in English and were consented prior to being enrolled in the study. Ethical approval was granted by the Rutgers University institutional review board and experiments were done in accord with the Helsinki Declaration of 1975.

Materials

Demographics

If candidates passed initial eligibility criteria, no more than 2–4 weeks elapsed between screening/enrollment and the neuropsychological testing appointment (described in next section). Participants reported their age and educational level during the initial screening. We retrieved median household income using census tract data based on participants' home addresses. Marital status and the number of children each participant has had were reported through Cohen's Social Network Index (Cohen et al., 1997). Each participant responded to the following prompt: "How many children do you have?" with a focus on biological children only. Each participant also indicated whether they were (1) currently married and living together or living with someone in a marital-like relationship; (2) never married and never lived with someone in a marital-like relationship; (3) separated; (4) divorced or formerly lived with someone in a marital-like relationship; and (5) widowed. If participants indicated that they were currently married and living together, or living with someone in a marital-like relationship or that they were widowed, they were considered married for the purposes of our study. If participants indicated that they never married and never lived with someone in a marital-like relationship, were separated, or divorced or formerly lived with someone in a marital-like relationship, they were considered not married for the purposes of our study. As such, marital status was coded as 0 = married/widowed and 1 = never married.

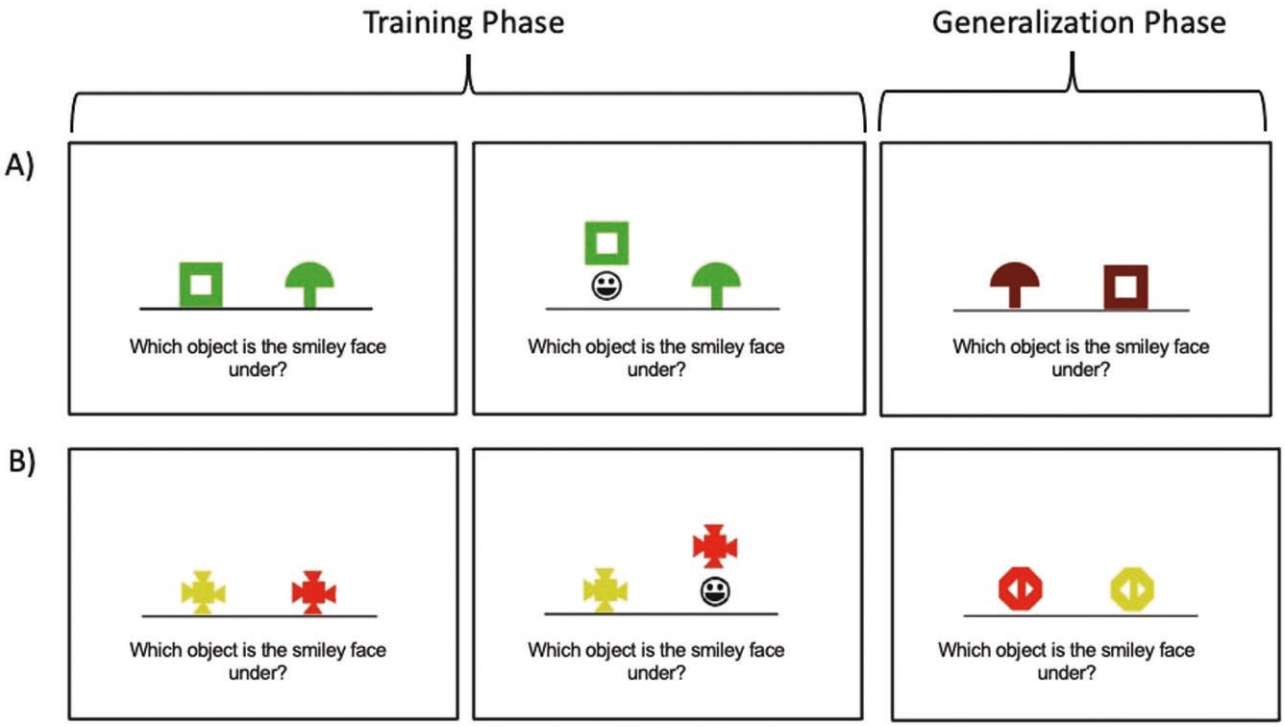

Figure 1. Rutgers generalization task. (A) As part of the training phase, the participants learn to choose the hollow green box as opposed to the green mushroom. This is supposed to indicate to the participants that shape is predictive of where the smiley face will be, while color is not. In the generalization phase, the participants are once again presented with a hollow box and a mushroom, but this time the color has changed to brown; in this case, the participant should realize that shape is still predictive of where the smiley face will be, while color is irrelevant. (B) In this example, the color becomes the predictive feature while the shape is irrelevant.

Standardized neuropsychological assessments

Potentially eligible candidates were invited to attend a neuropsychological testing session about 2–4 weeks following the initial telephone screening. The neuropsychological tests were administered within a two to two-and-a-half-hour time frame on the same day. Participants were given breaks as needed to mitigate any fatigue. The Mini-Mental State Examination (MMSE) is the most widely used mental status screening tool in clinical practice. The MMSE includes various questions to assess the attention, orientation, verbal memory, and concentration of participants (Kurlowicz & Wallace, 1999). Scores on the MMSE range from 0 to 30 points (higher scores indicate better mental status). The MMSE can be used to distinguish cognitively unimpaired participants from those with probable MCI/dementia (Arevalo-Rodriguez et al., 2015). Participants scoring between 20 and 30 points on the MMSE were initially eligible for the study. The MMSE criterion was accompanied by additional psychometric criteria to confirm cognitively unimpaired status via published protocols. Using the National Institute on Aging's recommendation (Albert et al., 2011), any individual who scored at least 1.5 *SD*s below what was expected for the participants' age and education on one or more standardized neuropsychological assessment(s) was excluded from the study.

The RAVLT assesses episodic and verbal memory (Rey, 1964). Participants are asked to recall a list of 15 words after the examiner has enunciated them at a rate of one word per second. This assessment is repeated five times, followed by a distraction list, and then the participant is asked to recall the original list one last time without the examiner repeating the words again. After a 20-min delay, participants are once again asked to recall as many words as they can remember from the first list. The outcome variable of interest for the current study is total number of words recalled after the 20-min delay (long delay recall; higher scores indicate better performance).

Experimental paradigm

The Rutgers generalization task (Concurrent Discrimination and Transfer Task) is a computerized task that assesses the ability to generalize past learning to novel conditions and has been shown to be sensitive to early changes in the MTL and hippocampus circuits linked to preclinical AD (Myers et al., 2008). In these tasks, the participant is told to find which object (differing in colors and shapes) the "smiley face" is under. At first, the participant must guess, and after each attempt, the computer indicates whether the selection was correct or incorrect. In this case, the participants should learn which shapes and colors to associate with the smiley face. The task involves two phases: (1) a training phase during which participants learn to discriminate between correct and incorrect objects with feedback and (2) a generalization phase during which participants apply previously learned rules in the training phase to new contexts. An example of this assessment is shown in Figure 1. The outcome variables of interest are the number of errors committed during both training and generalization phases of the task.

Power Analysis

A power analysis using G*Power software version 3.1.9.6 (Faul et al., 2009) determined that a sample size of 146 has at least 80% power to detect a medium effect size for

Table 1. Descriptive Statistics of the Analytic Sample (N = 146)

Variables	Minimum	Maximum	Mean	*n*	*SD*	%
Age (years)	60	91	71.67		6.62	
Education (years)	5	20	13.95		2.31	
Number of children	0	7	2.08		1.52	
Median household income (USD)	9,860	228,388	50,730		36,917	
Marital status—married	—	—		69		47.26
RAVLT long delay recall	0	15	8.31		3.52	
MMSE (20–30 points)	20	30	27.00		2.25	
Generalization errors	0	58	12.03		15.46	
Generalization training errors	3	58	22.31		13.82	

Notes: MMSE = Mini-Mental State Examination; RAVLT = Rey Auditory Verbal Learning Test; *SD* = standard deviation; USD = U.S. dollars. Generalization errors and generalization training errors from the Concurrent Discrimination and Transfer Task.

a significant main effect of number of children on episodic memory and generalization outcomes (α = 0.05, two-tailed).

Statistical Analyses

Statistical analyses performed included analyses of covariance (ANCOVAs) exploring the possible differences between number of children groups (0, 1, 2, 3, and ≥4 children) and cognitive function. ANCOVAs were used specifically to examine the threshold at which the number of children groups is associated with worse cognitive function outcomes. As such, the independent variable of number of children groups was better emphasized via ANCOVA (as opposed to regression). Cognitive function outcomes included generalization errors, generalization training errors, and RAVLT long delay recall. Age, educational level, marital status, and median household income were entered as covariates for all ANCOVAs.

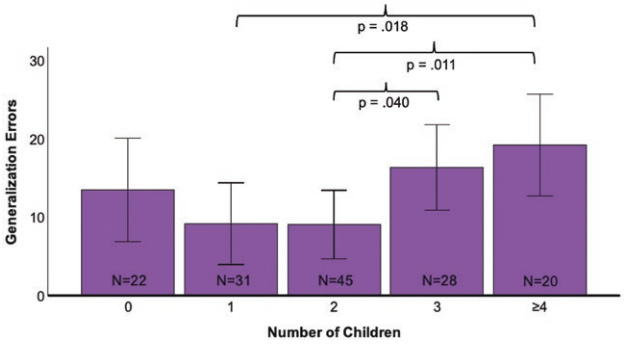

Figure 2. The relationship between number of children groups and generalization errors, controlling for age, education, marital status, and median household income.

Results

Participants

Descriptive statistics for the 146 participants are included in Table 1. The participant pool consisted of only females. Participants' ages ranged from 60 to 91 years old but averaged approximately 72 years old. Most participants completed, on average, some college coursework, but educational level ranged from fifth grade to graduate/doctoral level degree. The median household income ranged from $9,860 to $228,388. The number of children the participants had ranged from 0 to 7 children, with the mean being two children. MMSE scores ranged from 20 to 30 with a mean of about 27 points.

Cognitive Outcomes

Separate ANCOVAs were conducted to test associations between the number of children groups on cognitive outcomes (generalization and generalization training errors, RAVLT long delay recall). There was an overall significant effect of the number of children groups on generalization errors (Figure 2), controlling for median household income, marital status, age, and educational level, $F(4, 146) = 3.13$, $p = .040$, $\eta_p^2 = 0.072$. There was a significant difference on generalization errors when comparing 1 and ≥4 children groups ($p = .018$); 2 and 3 children groups ($p = .040$); and 2 and ≥4 children groups ($p = .011$; Figure 2). Marital status and educational level were both significant covariates ($B = -4.02$, $p = .047$; $B = -1.61$, $p = .004$, respectively). As educational level increases, generalization errors decrease. On the other hand, being married was associated with having fewer generalization errors. Median household income and age were not significant covariates ($B = 3.8473E\text{-}6$, $p = .912$; $B = 0.21$, $p = .290$).

There was no significant difference between performance on generalization training errors and the number of children (Figure 3), $F(4, 146) = 1.74$, $p = .144$, $\eta_p^2 = 0.050$. Marital status and education were both significant covariates ($B = -0.57$, $p = .033$ and $B = -1.43$, $p = .004$, respectively).

There was no significant difference between performance on RAVLT and the number of children (Figure 4), $F(4, 146) = 0.63$, $p = .61$, $\eta_p^2 = 0.019$. Education was a significant covariate ($B = 0.29$ and $p = .034$).

Discussion

The current study found that, generally, older African American women who have had more children demonstrate greater difficulty generalizing prior learning to new situations and contexts. On the other hand, there was no effect of the number of children a woman has had on episodic memory performance as measured by a standardized neuropsychological assessment. Thus, parity appears to be associated with hippocampal-dependent cognitive performance that is sensitive to early changes in AD but is not captured by standardized tests of episodic memory.

Consistent with some studies, there was poorer memory performance among women who have had children (Ning et al., 2020; Ptok et al., 2002; Zhang et al., 2023). Similarly,

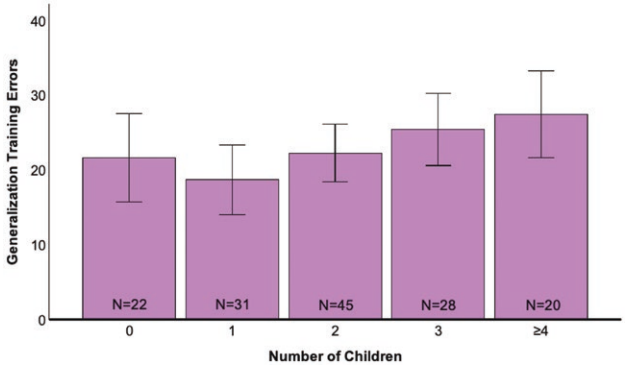

Figure 3. The relationship between number of children groups and generalization training errors, controlling for age, education, marital status, and median household income. *p*s > .05.

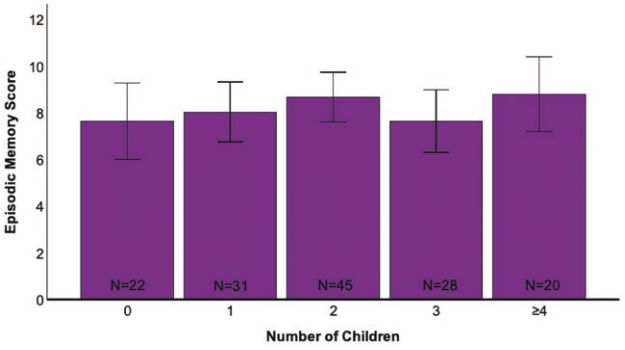

Figure 4. The relationship between number of children groups and episodic memory score (using Rey Auditory Verbal Learning Test), controlling age, education, marital status, and median household income. *p*s > .05.

one study consisting of White/European and Asian cohorts of women across three different continents found that women with five or more biological children had a greater risk of cognitive decline (Bae et al., 2020). As such, many of these studies consisted of general population cohorts (e.g., census data). In our cohort of cognitively unimpaired African American women, a standardized measure of episodic memory may not capture the early cognitive changes associated with the number of children a woman has had in later life.

Generalization, however, may detect subtle hippocampal-dependent cognitive changes. Previous studies show that the Rutgers generalization tasks can predict cognitive status among older adults across a 2-year follow-up at 91% specificity as compared to an episodic memory measure of delayed paragraph recall with a specificity of 82% (Myers et al., 2008). Similarly, generalization performance is impaired among autosomal dominant AD genetic mutation carriers decades before overt clinical symptoms appear (Petok et al., 2018). Overall, these studies highlight the predictive ability of the Rutgers generalization tasks to capture early cognitive changes in later life. While consistent with findings of parity and increased AD neuropathology (Beeri et al., 2009), this is the first study to explore the relationship between parity and cognitive performance among older African American women.

Although mechanisms underlying parity and cognitive dysfunction are outside the scope of the current study, possible biological links include: (1) fluctuations in estrogen and progesterone levels during and after pregnancy and (2) changes in endocrine activity, which result in metabolic changes and influence the cardiovascular and other systems (Clapp & Capeless, 1997). The "estrogen hypothesis" claims that the gonadal steroid hormone, estrogen, may play a neuroprotective role against AD through its effects on the development of neuronal dendritic spines (Rahman et al., 2019). Estrogen also plays a role in adaptive immunity, influencing the levels of circulating antibodies and aiding in the development of T cells (Ding & Zhu, 2008; Phiel et al., 2005; Staples et al., 1999). The greatest fluctuations in estrogen concentrations are during pregnancy, with estrogen levels up to 60 times higher than in nonpregnant women. As a result, pregnant women display altered immune and inflammatory responses that may contribute to late-life cognitive performance (Harding & Heaton, 2022). Thus, nulliparous women may have higher estrogen levels that protect them against pathological cognitive decline (Bernstein et al., 1985).

Additionally, parity can influence parents' social and financial contexts and thus affect their health. A greater number of children may diminish economic resources and exacerbate fatigue and poor health, thus reducing parents' time and abilities to take care of themselves (Floderus et al., 2008; Zhang, 2022). Participants in our sample were mostly recruited from the same geographical area with low socioeconomic variability, which could contribute to the lack of an effect of median household income. Moreover, having a lower socioeconomic status may render an impoverished social network (Hoff & Laursen, 2019), which is associated with higher rates of dementia (Trani et al., 2022). A community-based, longitudinal study by Fratiglioni concluded that larger social networks protect against dementia (Fratiglioni et al., 2000; Sharifian et al., 2022). Overall, the financial and social tax associated with child-rearing may put mothers at disproportionate risk for developing AD and cognitive dysfunction.

Furthermore, this study revealed marital status and educational attainment as significant covariates. This shows that we need to consider such demographic and social factors to fully understand the cognitive health of African American women and mothers. These findings are consistent with studies that show that those who have been diagnosed with AD or other related dementias were more likely to have never been married and have lower educational attainment (Liu et al., 2019; Yang et al., 2022).

While there are parity-related changes in generalization, the number of children a woman has had reveals no significant relationship with episodic memory. Our sample is cognitively unimpaired, and episodic memory is rarely affected until an individual demonstrates overt cognitive decline; in other words, standardized measures of episodic memory (e.g., RAVLT) are not sensitive enough to detect early preclinical changes in cognitive function (Andersson et al., 2006). This suggests that the Rutgers generalization task may be superior to RAVLT for earlier detection of cognitive dysfunction associated with increased risk for AD.

This study has several limitations. While estrogen depletion may seem like a plausible mechanism, we have not collected estrogen levels from our participants. Future studies can incorporate estrogen measurements in postmenopausal women and determine its role in AD development. Further, our study is limited to self-reported number of *biological* children and cross-sectional data, and information on the ages of the women at the time of childbirth was not available.

Longitudinal follow-up studies linking estrogen levels, parity, and AD risk will clarify the direction of this relationship. Given that physical well-being may be strained among women who are multiparous, future studies should also incorporate health and lifestyle factors as potential confounders.

Conclusion

In conclusion, our findings suggest older African American women who are multiparous may be at greater risk for cognitive dysfunction. In addition, not being married and lower educational level further exacerbate this risk. Future studies should explore how these findings can be applied to preserving cognitive function in older African American women who have had children.

Funding

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Conflict of Interest

None.

Data Availability

The data supporting the findings of this study are available on request without undue reservation from the corresponding author. This study was not preregistered.

Acknowledgments

We are grateful for helpful feedback from Dr. Michal Beeri. We are indebted to the thousands of community members who have participated in our brain health events since 2006, and from over 500 community members who have enrolled, to date, as VIPs (Very Important Participants) in our *Pathways to Healthy Aging in African Americans* study.

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