Effects of early-life adversity on cognitive decline in older African Americans and whites

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ABSTRACT

Objectives: Early-life adversity is related to adult health in old age but little is known about its relation with cognitive decline.

Methods: Participants included more than 6,100 older residents (mean age = 74.9 [7.1] years; 61.8% African American) enrolled in the Chicago Health and Aging Project, a geographically defined, population-based study of risk factors for Alzheimer disease. Participants were interviewed at approximately 3-year intervals for up to 16 years. The interview included a baseline evaluation of early-life adversity, and administration of 4 brief cognitive function tests to assess change in cognitive function. We estimated the relation of early-life adversity to rate of cognitive decline in a series of mixed-effects models.

Results: In models stratified by race, and adjusted for age and sex, early-life adversity was differentially related to decline in African Americans and whites. Whereas no measure of early-life adversity related to cognitive decline in whites, both food deprivation and being thinner than average in early life were associated with a slower rate of cognitive decline in African Americans. The relations were not mediated by years of education and persisted after adjustment for cardiovascular factors.

Conclusions: Markers of early-life adversity had an unexpected protective effect on cognitive decline in African Americans. *Neurology*® 2012;79:2321-2327

GLOSSARY

MMSE = Mini-Mental State Examination.

A growing body of evidence suggests that early-life adversity may contribute to the development and progression of disease in old age.¹⁻⁴ Children subjected to adverse conditions such as poverty or abuse may have an increased risk of cardiovascular disease and mental disorders in adulthood.^{5,6} Although the mechanisms have not been elucidated, investigators have hypothesized that brain alterations due to chronic stress or ineffective coping strategies that predispose to poor health behaviors such as smoking and alcoholism may be potential mediators.⁷⁻⁹ It is fairly well established that early-life factors such as socioeconomic position, cognitive environment, and childhood health may contribute to late-life cognitive function,^{3,10-12} but few studies have examined whether adverse social conditions in childhood may increase the risk of cognitive decline in old age.

In this study, we tested whether greater childhood adversity is associated with a faster rate of cognitive decline in older age using data from more than 6,100 older residents in a population-based study of Alzheimer disease. In a previous analysis of these data, we found that childhood socioeconomic position and cognitive milieu were associated with late-life cognitive function, but not with cognitive decline.¹¹ In the present analysis, we focused more specifically on markers of childhood adversity, using a broader range of social and health-related conditions and a longer follow-up period to determine whether early-life adversity is associated with late-life cognitive decline. In addition, we examined childhood adversity in relation to cognitive decline in older age for African Americans and

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non-Hispanic whites separately. During the early 1900s, African Americans and whites lived in profoundly different physical and social environments as a result of severe residential and occupational segregation, poverty, discrimination, and restricted access to education and medical care.¹³ Thus, to avoid making potentially invalid comparisons across disparate social conditions, effects of adversity were modeled separately by race.

METHODS Study population. Participants were enrolled in the Chicago Health and Aging Project.¹⁴ Of 7,813 eligible residents identified in a census of households in the area, 6,158 (78.9%) participated (non-Hispanic African Americans: 61.4%; non-Hispanic whites: 37.7%; Hispanic or race/ethnicity unreported: 0.9%). In-home baseline interviews were conducted from 1993 to 1997, followed by successive interview cycles at approximately 3-year intervals consisting of structured questions on a wide range of characteristics, including socio-demographic and psychosocial factors, medical history, and physical and cognitive performance.

Standard protocol approvals, registrations, and patient consents. All study procedures were approved by the Institutional Review Board of Rush University Medical Center and all participants provided written informed consent.

Assessment of early-life adversity. Early-life adversity was conceptualized as disadvantage in childhood grouped into 3 distinct categories: the home cognitive environment, health, and family financial conditions. For childhood cognitive environment, participants rated how frequently someone in the home told stories to or played games with them. For childhood health, participants rated their health compared with other children their own age, and their body size at age 12 with similar-aged children. Family financial status during childhood was assessed with 2 questions, including family's financial situation when they were very young, and how often the respondent went

without enough food to eat. To form the adversity measures, we collapsed the response options for each individual indicator into a binary response option (adversity = 1; no adversity = 0) based on the frequency distribution such that adversity was defined as the most extreme disadvantage present in at least 5% of the population. For example, for the cognitive environment, adversity was being read to or playing games with someone less than once a year.

Assessment of cognitive function. Four brief tests of cognitive function were administered at each interview: 2 measures of episodic memory, immediate and delayed recall of 12 ideas contained in the East Boston Story¹⁵; 1 test of perceptual speed, the oral version of the Symbol Digit Modalities Test¹⁶; and the Mini-Mental State Examination (MMSE).¹⁷ A composite of all 4 tests was used in analyses. As previously described,¹⁸ the raw scores on each test were converted to *z* scores, using the baseline mean and SD in the population, and then the *z* scores were averaged, with higher scores indicating better cognitive function.

Other covariates. Other variables used in the analysis included age at baseline, sex, and race (African American or white as determined by self-report using the 1990 US Census questions). Years of educational attainment and height were self-reported. Data on 4 chronic medical conditions were obtained from self-report of heart attack or myocardial infarction, hypertension, stroke, and diabetes mellitus.

Because of regional differences in social and economic conditions for African Americans and whites born in the early 1900s, we included geographic region of birth based on the US Census definitions. From this, we distinguished participants who were born in the southern states from those born in any other state. Seventy percent of African Americans in the cohort were born in the south vs only 2% of whites. Therefore, we only examined the effect of region of birth among African Americans.

Data analysis. We conducted a series of mixed-effects models¹⁹ to examine the relation of each adversity indicator with rate of decline in global cognition. In subsequent models, we examined whether education mediated the effects of early adversity on cognitive decline. We then conducted sensitivity analyses in which we repeated the first model after sequentially excluding persons at the lowest 10th and 20th percentile of cognitive function, and persons scoring <24 on the MMSE at baseline. Next, we repeated the core models with terms added for chronic health conditions. We also conducted a secondary analysis within African Americans to examine whether any significant findings depended on place of birth.

Model assumptions, particularly regarding normality of the random effects and residual errors, were assessed graphically and analytically, and were adequately met. Programming was performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC).²⁰

RESULTS A total of 6,105 participants with nonmissing data on the early-life indicators and at least 2 cycle interviews were included in the current analyses. African Americans tended to be younger, had fewer years of education, and had lower global cognitive function scores at baseline compared with whites (table 1).

A higher percentage of African Americans experienced early-life adversity, with the exception of "not told stories" and "being much thinner than average" (table 1). Differences between African Americans and whites were most striking for cognitive (not playing games) and financial (being very poor) conditions in early life. Table 2 shows the frequency distribution of all possible responses for each adversity measure.

Table 1 Sample characteristics of participants in the Chicago Health and Aging Project (N = 6,105)

Characteristic	African Americans (n = 3,772)	Whites (n = 2,333)
Age, y, mean (SD)	73.9 (6.8)	76.6 (7.3)
Education, y, mean (SD)	10.7 (3.5)	13.5 (3.4)
Gender, % female	59.9	62.2
Global cognitive <i>z</i> score, mean (SD)	−0.23 (0.90)	0.31 (0.79)
Cognitive adversity in early life		
Told stories (% once a year or less)	20.8	18.3
Played games (% once a year or less)	28.4	15.3
Financial adversity in early life		
Family's financial situation (% very poor)	28.7	11.4
How often not enough food (% sometimes, often, always)	5.8	2.6
Health adversity in early life		
Self-rated health (% fair or poor)	12.6	8.6
Body size at age 12 y (% much thinner than average)	8.4	7.9

Table 2 Frequency distribution (%) of early-life conditions in African Americans and whites

	African Americans	Whites
Told stories		
Every day	33.2	30.7
Several times/week	26.0	25.6
Several times/month	14.0	17.2
Several times/year	5.9	8.2
Once a year or less	20.8	18.3
Played games		
Every day	32.3	29.3
Several times/week	23.4	29.0
Several times/month	11.6	19.5
Several times/year	4.2	6.9
Once a year or less	28.4	15.3
Financial situation		
Very well off	1.4	2.6
Somewhat well off	5.3	12.3
About average	41.6	51.9
Somewhat poor	23.0	21.9
Very poor	28.7	11.4
Go without food		
Never	87.6	92.8
Very rarely	4.2	2.7
Rarely	2.4	1.9
Sometimes, often, always	5.8	2.6
Self-rated health		
Excellent	41.5	47.8
Good	45.9	43.6
Fair	10.5	6.3
Poor	2.1	2.2
Body size		
Much heavier than average	2.2	1.5
Somewhat heavier than average	9.5	10.0
About average	57.5	55.8
Somewhat thinner than average	22.4	24.8
Much thinner than average	8.4	7.9

At baseline, scores on the global measure of cognitive function among African Americans ranged from -4.31 to 1.54 (mean = -0.23 , SD = 0.90), with higher scores indicating better cognitive function. In mixed models adjusted for age, sex, and current height, the global cognitive score decreased approximately 0.059 units annually, as shown by the term for time (since baseline) for each adversity indicator (table 3, model 1). Being very poor, being told stories infrequently, and playing games infrequently were associated with poorer cognitive

function at baseline, as shown by the term for adversity in each model. Contrary to our hypothesis, early-life adversity indicators of going without food and being thinner than average were significantly associated with a slower rate of cognitive decline (table 3, model 1).

Because early-life adversity could have an indirect effect on late-life cognition by affecting other determinants of cognition (e.g., educational attainment), we tested whether the effect of early-life adversity was independent of education. Adjustment for education mainly affected the association between indicators of early-life adversity and baseline cognitive function (table 3, model 2). Controlling for education weakened the associations of telling stories and playing games with baseline cognitive function by approximately one-third each, and reduced the term for being very poor by approximately 15%; only telling stories remained significant after adjustment. However, adjustment for education did not change the relationships between adversity measures and cognitive decline (table 3, model 2). To test the extent to which the effect of being thinner than average was attributable to food deprivation, we included both adversity conditions in the same model. They were each independently associated with a slower rate of cognitive decline (both p values <0.01).

Because it is possible that the inclusion of persons with mild, undiagnosed Alzheimer disease could influence the findings, we repeated the core analysis 3 times after sequentially excluding persons at the lowest 10th and 20th percentiles of cognitive function at baseline, and persons scoring <24 on the MMSE at baseline. The association between the adversity markers and slower cognitive decline remained significant in each case (see table e-1 on the *Neurology*[®] Web site at www.neurology.org). To determine whether differences in health affected findings, we repeated the core analysis with indicators for the presence of 4 cardiovascular conditions or diseases at baseline and results were unchanged (see tables e-2 and e-3).

For whites, the scores on the global measure of cognitive function at baseline ranged from -4.31 to 1.56 (mean = 0.31 , SD = 0.79). The global cognitive score decreased approximately 0.070 units annually. Similar to African Americans, being told stories infrequently and playing games infrequently were associated with poorer cognitive function at baseline. In addition, not having enough food to eat was associated with worse performance at baseline (table 4, model 1). No measure of early-life adversity was related to rate of decline in whites. In contrast to the findings in African Americans, being thinner than average was related to a faster rate of decline in whites, although this effect failed to reach statistical significance (coefficient = -0.016 , $p = 0.06$).

Among whites, adjusting for education also reduced baseline associations of the cognitive adversity measures (being told stories and playing games infrequently) with

Table 3 Mixed-effects models of the relation of childhood adversity and change in cognitive function in African Americans (n = 3,772)^a

	Model 1	Model 2
Cognitive adversity		
Time	−0.058 (0.003) ^b	−0.060 (0.003) ^b
Infrequent stories	−0.190 (0.033) ^b	−0.065 (0.031) ^c
Time × infrequent stories	−0.000 (0.005)	−0.004 (0.005)
Time	−0.058 (0.003) ^b	−0.060 (0.003) ^b
Infrequent games	−0.119 (0.030) ^b	−0.028 (0.027)
Time × infrequent games	0.002 (0.004)	−0.001 (0.004)
Financial adversity		
Time	−0.058 (0.003) ^b	−0.061 (0.003) ^b
Very poor	−0.066 (0.030) ^c	0.043 (0.027)
Time × very poor	0.001 (0.004)	−0.001 (0.004)
Time	−0.060 (0.003) ^b	−0.062 (0.003) ^b
Not enough food	−0.029 (0.056)	0.006 (0.050)
Time × not enough food	0.021 (0.008) ^d	0.019 (0.008) ^d
Health adversity		
Time	−0.059 (0.003) ^b	−0.061 (0.003) ^b
Poor health	−0.051 (0.041)	−0.035 (0.036)
Time × poor health	0.000 (0.005)	−0.000 (0.006)
Time	−0.061 (0.003) ^b	−0.064 (0.003) ^b
Thinner than average	0.080 (0.047)	0.031 (0.042)
Time × thinner than average	0.021 (0.006) ^d	0.022 (0.006) ^b

^a Model 1 includes age, sex, current height, adversity indicator, time, and their interactions with time. Model 2 includes all terms from model 1 and education.

^b $p < 0.001$.

^c $p < 0.05$.

^d $p < 0.01$.

cognitive function by approximately one-third, but they both remained significant. In contrast, adjusting for education reduced the association of going without food with baseline cognition by a little more than half, and the association was no longer significant. Education did not influence the null results for early-life adversity and decline among whites (table 4, model 2).

Next, we conducted a secondary analysis within the African Americans to explore the relationships between the 2 significant adversity measures and rate of decline. In analyses stratified by US region of birth (south vs north), not having enough food was related to a slower rate of cognitive decline in African Americans born in the north (estimate = 0.030, $p = 0.034$), and being thinner than average was related to a slower rate of cognitive decline in African Americans born in the south (estimate = 0.025, $p < 0.001$).

DISCUSSION We examined the relation of several childhood adversity measures with rate of cognitive decline in more than 6,100 older African Americans

and whites participating in a population-based study on the south side of Chicago. Over a follow-up of up to 16 years, going without food and being thinner than average as a child were related to a *slower* rate of cognitive decline in older African Americans. These results were not influenced by educational attainment, cardiovascular factors, or the presence of persons with cognitive impairment at baseline, but the effects of going without food on cognition seemed to be stronger for African Americans born in the north, and the effects of being thinner than average were stronger for African Americans born in the south. By contrast, no early-life adversity was related to rate of decline in older whites.

These results build on a previous report in this population that focused on socioeconomic and cognitive conditions in early life and their relations to late-life cognition. The current analysis is different in 3 ways: 1) our focus was on adverse conditions (i.e., absolute disadvantage) in early life using a broader range of indicators; 2) we had an explicit interest in race and examined these effects among African Americans and whites separately; and 3) we had a longer follow-up time. The results are consistent with previous research that suggests that early-life factors are related to late-life cognition. Conflicts in the home and father's social class,^{10,21} early-life nutrition and socioeconomic status,^{3,12} and early-life cognitive activity¹¹ have been associated with worse cognitive function in old age. To our knowledge, only 2 studies in older adults have been longitudinal,^{11,21} and only 1 specifically examined the degree to which the effects of early-life experiences on late-life cognition vary by race.¹² We are not aware of any previous study that has examined the race-specific effects of early-life adversity on change in cognitive function in older adults.

The protective effect of adversity in older African Americans was unexpected and the biological basis of the association is unknown. One mechanism is suggested by the potential link between food insecurity and obesity in late life.^{22,23} Although African Americans in general have higher rates of obesity than whites,²⁴ a finding observed in our population as well, we have not found obesity in late life to be related to cognitive decline.²⁵ We also did not find an association between our adversity measures and body mass index, making obesity less tenable as a potential mechanism. There is evidence that caloric restriction delays the onset of various age-related physiologic changes and increases the lifespan, particularly in animal models. Only a limited number of studies have been conducted in humans, but findings suggest a role for caloric restriction in improved cardiovascular and glucoregulatory health,^{26–28} and attenuation of oxidative stress.^{29,30} One intervention study showed that caloric restriction improved memory performance in older adults,³¹ but the caloric restriction arm in this study was limited to only 3 months. Mechanisms linking caloric restriction with improved health

Table 4 Mixed-effects models for relation of childhood adversity to change in cognitive function in whites (n = 2,333)^a

	Model 1	Model 2
Cognitive		
Time	−0.068 (0.004) ^b	−0.069 (0.004) ^b
Infrequent stories	−0.233 (0.038) ^b	−0.173 (0.037) ^b
Time × infrequent stories	−0.012 (0.008)	−0.011 (0.008)
Time	−0.071 (0.004) ^b	−0.071 (0.004) ^b
Infrequent games	−0.194 (0.040) ^b	−0.132 (0.038) ^b
Time × infrequent games	−0.011 (0.008)	−0.010 (0.008)
Financial		
Time	−0.072 (0.003) ^b	−0.074 (0.004) ^b
Very poor	−0.083 (0.044)	−0.002 (0.042)
Time × very poor	−0.001 (0.008)	0.002 (0.008)
Time	−0.072 (0.003) ^b	−0.073 (0.004) ^b
Not enough food	−0.197 (0.086) ^c	−0.087 (0.082)
Time × not enough food	0.006 (0.016)	0.008 (0.016)
Health		
Time	−0.072 (0.003) ^b	−0.074 (0.004) ^b
Poor health	0.021 (0.051)	0.050 (0.048)
Time × poor health	0.004 (0.009)	0.004 (0.010)
Time	−0.070 (0.003) ^b	−0.071 (0.004) ^b
Thinner than average	−0.018 (0.049)	−0.012 (0.047)
Time × thinner than average	−0.016 (0.009)	−0.016 (0.009)

^a Model 1 includes age, sex, current height, adversity indicator, time, and their interactions with time. Model 2 includes all terms from model 1 and education.

^b $p < 0.001$.

^c $p < 0.05$.

are not understood, but reduced inflammation and enhanced energy metabolism have been proposed, and would be consistent with a protective effect on cognitive decline.^{32,33} Studies of historical events, such as famine and war, have shown associations of severe undernutrition during adolescence with a higher risk for heart disease, high blood pressure, and diabetes in old age,^{34,35} as well as overall mortality.³⁶ Although not consistent with our findings that food deprivation may have beneficial cognitive health effects later in life, it is possible that the health consequences of food deprivation may depend on the timing. For example, food deprivation during pregnancy and immediately post-natal may be distinguishable from food deprivation during early childhood or adolescence. Although several studies have examined the link between critical windows of development and subsequent diseases of aging, data are inconclusive on the actual timing of nutritional or behavioral exposures for later health.³⁷ In addition, what people retrospectively recall when responding to the questions on early-life conditions may be a general memory of being hungry that cannot

be linked to a specific window of development during early life.

Finally, our findings could be attributable to a selective survival effect. Older adults with early adversity may represent the hardest and most resilient; those with the most extreme adversity may have died before reaching old age.³⁸ Of note, any of these potential mechanisms could apply to whites as well, but early-life adversity among whites in our population may have not been severe enough to observe an effect.

Strengths of the study include the prospective design, a large population-based sample of African Americans and whites, and several years of follow-up. Also, we used a psychometrically sound measure of global cognition, which enhanced our ability to reliably measure individual differences in change in cognition. There are also limitations. Early-life adversity was based on recall of events that occurred several decades earlier, possibly biasing results. However, results were unchanged after excluding persons with cognitive impairment at baseline, increasing confidence in the retrospective recollections. Although we examined a broad range of adverse conditions, we did not capture adversities such as abuse and neglect. Both are related to poor health in older age, but were not available in the current study. We did not have information on residential characteristics in early life (e.g., urban vs rural), which have been linked to mortality among African Americans.³⁸ It is not clear how or whether these factors may have influenced the current results. Results are from an urban setting in the Midwest and may not be generalizable to elders in other parts of the country. Finally, we had relatively few whites report early-life adversity in our population, potentially limiting power to detect an effect of adversity on decline among whites.

AUTHOR CONTRIBUTIONS

L. Barnes made a substantive contribution to the manuscript including conceptualization of the study, analysis and interpretation of the data, and drafting/revising the manuscript for content. R. Wilson, S. Everson-Rose, and M. Hayward contributed to drafting/revising the manuscript for content. D. Evans is responsible for the study design and contributed to drafting/revising the manuscript for content. C. Mendes de Leon contributed to conceptualization of the study, analysis and interpretation of the data, and drafting/revising the manuscript for content.

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