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Stressful Life Events and Racial Disparities in Cognition Among Middle-Aged and Older Adults

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Abstract

Background: It is well-documented that African Americans have elevated risk for cognitive impairment and dementia in late life, but reasons for the racial disparities remain unknown. Stress processes have been linked to premature age-related morbidity, including Alzheimer's and related dementias (ADRD), and plausibly contribute to social disparities in cognitive aging.

Objective: We examined the relationship between stressful life events and cognitive decline among African American and White participants enrolled in the Wisconsin Registry for Alzheimer's Prevention (WRAP).

Methods: Linear mixed models including demographic, literacy, and health-related covariates were used to estimate (1) relationships between a life event index score and decline in cognitive test performance in two domains of executive function (Speed & Flexibility, Working Memory) and one domain of episodic memory (Verbal Learning & Memory) among 1,241 WRAP enrollees,

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stratified by race, and (2) contributions of stressful life events to racial differences in cognition within the full sample.

Results: African Americans (N = 50) reported more stressful life events than Whites (N = 1,191). Higher stress scores associated with poorer Speed & Flexibility performance in both groups, though not with declines across time, and partially explained racial differentials in this domain. Among African Americans only, stressor exposure also associated with age-related decline in Verbal Learning & Memory. Stressor-cognition relationships were independent of literacy and health-related variables.

Conclusions: Greater lifetime stress predicted poorer later-life cognition, and, in a small sample of African Americans, faster declines in a key domain of episodic memory. These preliminary findings suggest that future work in large minority aging cohorts should explore stress as an important source of modifiable, socially-rooted risk for impairment and ADRD in African Americans, who are disproportionately exposed to adverse experiences across the life course.

Keywords

African Americans; Alzheimer's disease; life course; stress

INTRODUCTION

The prevalence of Alzheimer's disease and related dementias (ADRD) and age-related cognitive impairment are increasing across sociodemographic strata as the U.S. population ages, but the burden is not equally distributed [1]. Though African Americans continue to be underrepresented in cognitive aging research, there is substantial evidence that when compared with age-matched Whites, they are at increased risk for dementia [2-4]. Cognitive function in midlife and early old age may be an important determinant of ADRD onset in racial minority populations [5], and studies in diverse combined [6] and population-based [7] cohorts demonstrate that African Americans also experience more subclinical impairment in both episodic memory and executive function. Cognitive aging disparities remain underexplained: genetic factors such as the apolipoprotein E (*APOE*) *ε*4 allele that contribute to ADRD-related changes in predominantly White cohorts [8, 9] appear more prevalent but less relevant in African Americans [10], and substantial efforts dedicated to identifying cardiovascular mechanisms that might operate differentially by race have also failed to fully account for the disproportionate risk [3, 11].

In this paper, we propose that stress-related mechanisms empirically shown to contribute to cognitive aging processes are likely to be an important determinant of cognitive outcomes among older African Americans, and to play a role in racial disparities in cognitive health. Exploration of socioenvironmental contexts across the life course is likely to clarify disproportionate risk for dementia and age-related cognitive impairment in racial and ethnic minorities including African Americans. Health disparities frameworks posit African American race as a fundamental determinant of health [12] operating through pervasive structural and institutionalized inequalities that shape more proximal risk exposures and systematically disadvantage members of minority racial groups across the life course. As such, at a population level African American race is often a risk marker for a number of

independent ADRD risk factors including neighborhood disadvantage, reduced healthcare access, undertreated comorbidities, and socioeconomic deprivations including poorer quality of early life schooling [13, 14]. Given these associations, it is unsurprising that a substantial body of evidence suggests African Americans of all ages also report experiencing more acute and chronic stressors than their White counterparts [15-17].

Disproportionate exposure to stressors plausibly contributes to racial disparities in age-related cognitive impairment and ADRD risk. In cross-sectional and longitudinal studies, measures of both objective and perceived stress have been associated with poorer cognitive function [18, 19] and increased risk for Alzheimer's disease [20, 21]. Stress may impact memory and executive function processes directly through structural and functional changes in key brain regions: chronic stress associates with lower hippocampal volume in animal [22, 23] and human [24, 25] models, and cumulative exposure to adverse life events has been linked to reduced volume in the hippocampus [26] and the medial prefrontal cortex [27]. Additionally, stress exposures have been associated with longer-term metabolic and vascular disorders such as diabetes [28] and hypertension [29] that represent strong independent risk factors for cognitive decline and dementia in later life [30, 31], and to acute risk factors for impairment such as depression [32, 33] and sleep disturbance [34, 35].

Despite well-established dual associations between African American race and stress, and between stress and cognitive aging, the contribution of stress to cognitive aging processes among African Americans and to racial disparities in cognitive health has only rarely been explored [15, 36, 37]. In this paper, we describe an analysis designed to preliminarily assess the role of cumulative stressful life events. We utilize a middle-aged and older cognitive aging study cohort that includes a small but well-characterized sample of African American participants. In primary analyses, we stratify by race to explore within-group relationships [38] between a life event index score and rate of cognitive decline over time in three cognitive domains vulnerable to early age-related changes [39]. In secondary analyses, we explore the contribution of stressful life event exposure to race differentials in cognitive function among the sample as a whole.

METHODS

Participants

Participants were selected from the Wisconsin Registry for Alzheimer's Prevention (WRAP). The WRAP study is a longitudinal study of cognitive aging in a cohort of middle-aged and older adults enriched for a parental history of Alzheimer's disease [40]. Participants in the parental history-positive group (73% of all WRAP enrollees) have at least one biological parent with dementia attributed to Alzheimer's disease as determined by a review of parental medical records (and autopsy records, when available) or by administering a Dementia Questionnaire [41] to the adult child. Most WRAP participants volunteered for the study after learning of it via statewide educational presentations or word of mouth. A portion of the parental history-positive participants were recruited during a clinical evaluation of their parent in a University of Wisconsin or satellite Memory Assessment Clinic. WRAP participants were between the ages of 40 and 65 at enrollment, were cognitively intact at enrollment as determined by neuropsychological test performance,

and speak English as their primary language. Enrollment began in 2001 and has been conducted on a rolling basis with recent efforts prioritizing racial diversification of the cohort [42].

The WRAP protocol includes a baseline visit (Wave 1), a second visit after approximately four years (Wave 2), and subsequent visits approximately every two years (Waves 3–6). Visits are conducted at one of three study sites: a large urban center, a mid-sized city that is home to a state university, and a small city. A majority (90%) of African American participants attend the site based in the large urban center. The Wave 1 protocol does not include collection of social data; a stressful life events questionnaire was included in the Wave 2 protocol between 2006 and 2015. WRAP participants were only included in the current analytic sample if they attended their Wave 2 visit within that time frame and provided complete lifetime experience data. Seven participants who were determined by clinical consensus to meet diagnostic criteria for mild cognitive impairment, Alzheimer's disease, or another dementia at any follow-up WRAP study visit were excluded. Finally, 35 participants who identified their primary race as Hispanic/Latino, American Indian, Asian, or Other were excluded from analyses because their numbers were not large enough to create independent racial categories. The analytic sample ultimately included 1,191 White participants and 50 African American participants. Of these 1,241 individuals, the number of participants who most recently completed a Wave 2, 3, 4, 5, or 6 visit was 92, 161, 319, 469, or 200, respectively. 91% of White participants and 92% of African American participants in the analytic sample remained actively enrolled at the time of analysis. This study was conducted with the approval of the University of Wisconsin Health Sciences Institutional Review Board and all participants provided signed informed consent prior to enrollment.

Measures

Each WRAP visit is approximately five hours in duration, and participants provide self-reported data on health history, psychosocial factors, and lifestyle. A nurse collects blood samples and clinical data. A trained psychometrist administers a battery of neuropsychological tests. A detailed description of the WRAP study protocol and overall sample characteristics is available in a recent publication [40].

Cognitive outcomes

Key cognitive outcome variables included three cognitive factor scores from each WRAP visit, determined via a previously published factor analysis [43]. These composite factor scores represent domains of episodic memory and executive function, and were used to reduce the potential for measurement error and Type I error associated with multiple comparison testing. The cognitive factors in this analysis, Speed & Flexibility, Working Memory, and Verbal Learning & Memory were selected for their sensitivity to age-related change. Speed & Flexibility is derived from time to completion on Trailmaking Tests A & B [44] and the number of items completed on the Stroop Test Color-Word Interference condition [45]. A second measure of executive function, Working Memory, is derived from the number of correct items on the Digit Span Forward, Digit Span Backward, and Letter-Number Sequencing subtests of the Wechsler Adult Intelligence Scale-III [46]. Verbal Learning & Memory, representing episodic memory, was derived from the Rey Auditory

Verbal Learning Test (RAVLT), specifically RAVLT Learning Trials 3–5 and the RAVLT Delayed Recall Trial [47]. Factor scores have been standardized [~$N(0,1)$] into z-scores, using means and SDs obtained from the WRAP Wave 1 baseline sample.

Lifetime stressors

Data were drawn from a Stressful Life Events Inventory adapted from a Midlife in the United States study [48] measure [49] that was itself based on standard life event instrumentation [50]. The inventory, administered at Wave 2 visits for every participant, included 27 different potentially stressful events (e.g., flunking out of school, parental alcohol abuse, involuntary unemployment, the death of a child) spanning the life course. Lifetime stressor exposure was operationalized as a count of self-reported events. Every event a participant reported experiencing was scored as a "1" on a binary 0-1 scale and these were summed to create a cumulative index of stressful life events.

Self-identified race and covariates

WRAP participants are asked to specify their race/ethnicity at their baseline visit and questionnaire formatting requires participants to select a single response. The current study included those participants who identified as "White/Caucasian" or as "Black/African American".

Covariates were chosen *a priori* based on a review of cognition and disparities literature. Demographic covariates included age at visit, gender, and educational attainment. Age was calculated for each visit based on date of birth and analyzed as a continuous variable. To maximize model parsimony and minimize collinearity, baseline age was not included, and it should be noted that with this approach, age-at-visit estimates represent a weighted average of the within-person (time) effects and between-person (cohort) age effects [51]. Gender was self-reported as "Male" or "Female" and analyzed as a binary variable. Educational attainment was reported and analyzed as a continuous variable but was winsorized at a maximum of 20 years. In addition to base demographics, covariates included *APOE ε*4 carrier status and a control for practice effects, operationalized as the number of visits completed following Wave 1. Late-life literacy, as measured by the WRAT 3 Reading Score [52], was included as a proxy for cumulative educational quality in early life and intellectually enriching activities in adulthood [13]. Two stress-correlated health variables, smoking status and body mass index (BMI), were also included in final models. Participants were coded as never, ever, or current smokers. Height and weight were measured at the time of visit and BMI was calculated as kg/m^2.

Data analyses

Analyses were performed using SAS version 9.4 and R version 3.5.1. Characteristics of African American and White participants were compared using Mann-Whitney U tests and Chi-squared tests within the analytic sample. In our primary stratified analyses, we utilized linear mixed effects regression within White and African American samples. We modeled each of the three cognitive factor scores as a function of the life event index score while adjusting for additional covariates. Time was operationalized as the age at each WRAP visit. Covariates were sequentially added to three nested models to assess the contributions of

each set to stress-cognition relationships. Ultimately, the three cognitive factor scores were regressed on the life event index in (1) a base model controlling for time [age at visit, centered at sample mean across all visits], gender, years of education, *APOE ε*4 carrier status, practice effects, the interaction of stress*age, and subject specific random effects for intercept and age-related slope; (2) a model that added a measure of literacy to assess any confounding of stress-cognition relationships by poor educational quality; and (3) a model, including literacy, that added two health-related factors, smoking and BMI, that potentially confound relationships between stress and cognitive health.

In order to directly assess the contribution of stressful life event exposure to racial disparities in cognitive function, we utilized the combined African American and White sample. In order to assess potential disparity in level of cognitive test performance and in rate of decline, we first explored the main effect for African American race and a race*age interaction term in mixed models similarly structured to Model 3 above. Where significant race effects were observed, we then quantified the attenuation of race estimates when life event index score and the life event*age interaction term were included in models. Naïve non-parametric bootstrapping was used to construct 95% confidence intervals around each attenuation estimate. 2,000 replicates were performed for each attenuation analysis and the bootstrap quantile method was used to construct the confidence intervals.

In unconditional growth models used to assess inter-individual variability for all cognitive domains, null hypotheses were rejected, indicating that intercepts and slopes should be included in conditional models. Regression diagnostics were performed on the model with the most parameters for each race/ethnicity and cognitive factor pairs (6 model total). Each of these models was checked for residual outliers, heteroscedasticity, trends, distribution, and random effects' distribution and correlation with residuals. No concerning violations were noted for these models.

RESULTS

Sample characteristics

A total of 1,241 participants had completed at least two WRAP visits and had complete data available. Participant characteristics from their baseline WRAP visit are presented in Table 1. Only a small percentage of the analytic sample (4%) identified as African American or Black. African Americans had completed fewer WRAP visits on average than White participants, reflecting the implementation of a priority outreach program beginning in 2008 [42]. There were no significant differences by race in age at enrollment, proportion identifying as female, or proportion of *APOE ε*4 carriers. African American participants were more likely to currently smoke and on average had a higher BMI. African Americans also reported marginally fewer years of educational attainment, and showed worse performance on a measure of literacy and on the outcome measures of Speed & Flexibility, Working Memory, and Verbal Learning & Memory.

African Americans reported experiencing significantly more stressful life events than their White counterparts. The mean number of life events among African Americans was nearly 84% higher, and as seen in Fig. 1, the upper tail of the index score distribution was longer.

Stressful life events and cognitive outcomes in African Americans

Associations between the life event index score and cognitive outcomes in nested models can be seen in Table 2. Within the small African American stratum and utilizing Model 1, greater exposure to stressful life events marginally associated with poorer overall level of performance within the domain of Speed & Flexibility (β = −0.11, $p = 0.06$), but not with rate of decline. Though literacy was strongly and positively associated with level of function in this domain (β = 0.07, $p < 0.001$), its inclusion in the analytic model does not appear to change the association between lifetime stressor index and level of performance (β = −0.12, $p = 0.02$), nor does the inclusion of BMI and smoking status. No associations were seen between stressful life events and performance on tests of another domain of executive function, Working Memory.

Within this African American sample, stressful life events were associated with rate of decline in the Verbal Learning & Memory domain (β = −0.01, $p = 0.05$) in Model 1, and again, this negative relationship did not change after controlling for literacy (β = −0.01, $p = 0.04$) and health factors (β = −0.01, $p = 0.02$).

Lifetime stressful events and cognitive outcomes in Whites

Within the much larger White stratum, greater exposure to stressful life events significantly associated with poorer level of performance on tests of Speed & Flexibility (β = −0.03, $p = 0.008$) in the Model 1 and, as in African Americans, this association does not appear to be attenuated by the inclusion of literacy and health factors in regression models. Also, similarly to the African American cohort, there were no associations between life events and rate of decline in Speed & Flexibility skills over time, or with any cognitive outcomes in the Working Memory or Verbal Learning & Memory domains.

Racial disparities across domain and attenuation by stress and stress related decline

African American race was significantly associated with poorer level of test performance across all three cognitive domains, but was not associated with rate of decline in Speed & Flexibility (β = −0.01, $p = 0.37$), Working Memory (β = 0.001, $p = 0.86$), or Verbal Learning & Memory (β = −0.01, $p = 0.40$) domains. Results from secondary analyses conducted to directly assess contributions of stressful life event exposure to racial disparities in level of cognitive test performance can be seen in Table 3. In otherwise full models excluding the life event index score and its interaction with age, African American race was associated with poorer overall performance in all three domains of cognition. Inclusion of life event index terms (stress and stress*time) led to attenuation of the association between African American race and Speed & Flexibility by 6.9% (95% CI: 4.4, 8.8). However, no significant stress-related attenuation of associations between African American race and level of Working Memory [0.02% (95% CI: −1.8, 6.0)] or Verbal Learning & Memory [1.5% (95% CI: −1.8, 13.1)] was observed.

DISCUSSION

In a sample of cognitively normal middle-aged and older adults, we explored associations between stressful life events and cognitive decline across time. Although there were only a

small number of African American participants with full stressor and cognitive data available, we disaggregated the sample by race for assessment of within-group stress-cognition relationships. This approach is advantageous because the lifetime social environment and experiences of White and African American participants are likely to differ in significant ways, with unique implications for adversity, resilience, and health [38]. Data were aggregated only to preliminarily quantify the contribution of lifetime stressful events to racial disparities in cognition seen among the whole sample. Racial disparity was observed only in level of performance: African American participants performed more poorly in each cognitive domain but no differences by race were observed for rate of decline. Our analysis ultimately showed that exposure to self-reported lifetime stressful events associated negatively with cognitive test performance within both White and African American participants, though the domains affected varied by race. African Americans also reported significantly greater exposure to stressors. Cumulative stressful life events, as measured here, partially accounted for observable racial gaps in Speed & Flexibility. The attenuation of <10% observed in this study was quite modest compared to results reported for the most well-studied social determinants of cognitive health disparity, educational quality and literacy, which are robust predictors of cognitive aging trajectories in racial and ethnic minority populations [53, 54] and have been shown to attenuate racial disparities in both executive function and episodic memory by as much as 32% [13] and to the point of non-significance [55]. Here, we provide evidence that another social determinant, lifetime stress, contributes to later-life cognitive outcomes, including memory decline, for African American communities. In our study, this relationship appears robust to controls for literacy and for BMI and smoking, two additional cognitive aging risk factors that are more prevalent in individuals with a history of stressful life events [56, 57].

Our findings regarding stress and executive function are generally consistent with the current body of literature. A relationship between stressful life events and overall level of performance on tests of Speed & Flexibility, observed in both subsamples, echoes previous findings on stress and cognition in WRAP. Our group has reported cross-sectional relationships between *recent* stressful events and poorer performance in the same domain [19]. That earlier study was conducted in a small subset of the current study's White sample, and when paired with our current findings suggests robustness in the associations of both past and present stressful experiences with this measure of executive function within our cohort. Past studies in both White and African American cohorts have reported consistently negative associations of stress constructs including negative life events [58] and perceived stress [36] with overall level but not decline in processing speed. However, given strong experimental evidence suggesting that induced stress is associated with cognitive detriment in both domains of executive function across all ages [59], the lack of observable relationships between stressful life events and tests of working memory in the current data is somewhat surprising. In the small sample of African Americans, this may be due primarily to limited estimate precision. And among White participants in the WRAP cohort, Working Memory performance has previously been shown to have a strong genetic component [60]. Additionally, the timing of events could be important: some prior work has suggested that recency of stress exposure may be important in working memory, with recent stressors negatively impacting working memory through cognitive interference [61]. We did not

distinguish recent from distal experiences in this analysis, though we also reported a lack of association in the previously mentioned study on recent stress [19].

A relationship between stressful life events and episodic memory was seen only in the African American sample, where greater number of events associated with faster rate of decline. Though research on stress and cognition in African Americans is still rare, this association is consistent with findings from a recent study that showed perceived stress to be associated with faster rate of decline in performance on word list recall tasks in a much larger cohort of older African Americans [36]. Racial differences in stressor-episodic memory relationships may be consistent with "weathering," a model commonly used to account for health disparities [62], which posits that accumulating disadvantage across the life course provokes systemic dysregulation, accelerated biological aging [63], and premature onset of age-related morbidities including cognitive aging [64]. Executive function has been shown to mediate the association between age and episodic memory [65] and between vascular pathology and episodic memory [66]. As such, early age-related declines in episodic memory are likely to be most observable in a sample of African American participants disproportionately experiencing both stress-related weathering and poorer executive function. Interestingly, our findings differ from those reported in a seminal study [10] assessing early life adversity and later-life cognitive change in a large, population-based African American and White sample. Barnes and colleagues also observed a lack of association among Whites, but found that African Americans who self-reported two markers of childhood adversity, being thinner than average and not having enough food to eat during childhood, exhibited slower rates of cognitive decline than their peers who did not experience these conditions [15]. The Barnes et al. sample included much older adults than the current sample, and the adversity measure differed substantially from the life events inventory utilized in this analysis. The contrasting findings highlight the need for additional research that parses both nature and timing of adverse events.

Our reported findings on stress and cognition within a small sample of African Americans provide suggestive preliminary data that should inform replicating or expanded research questions to be answered within larger and population-based cohorts. Both African American and White samples were drawn from a cohort enriched for AD risk, and sampling on family history of AD may limit generalizability based on issues of ancestry, selection into the cohort, and prevalence of dementia caregiving. Only WRAP participants who were interested enough and healthy enough to attend the first WRAP follow-up visit and provide the stressful life events data that were collected for the Wave 2 protocol were included in the analytic sample. The high educational attainment in both samples similarly limits generalizability. Further, information on recruitment source (from a memory clinic during the clinical evaluation of a parent versus community-based) was not available for WRAP participants, but Gleason and colleagues [67] recently used a national cognitive aging database to illustrate how restricting the use of strong participatory research-based recruitment programming [42] to underrepresented racial minority communities while sampling White participants from memory clinic settings can result in selection bias and threats to internal validity when race is a predictor of interest.

In addition to sample limitations, there are measurement issues that bear mention. First, it must be noted that while cognitive trajectories began at each participant's baseline visit, they did not provide information on their experiences of stressful life events until a follow-up visit Wave 2 visit four years later. Exposure over that four-year period is reflected in the index score despite it having occurred after the first outcome measure timepoint, and exposure that occurred after Wave 2 was not reflected. Additionally, as mentioned earlier, stress operationalization in a given study is likely to influence findings. Our measure, a count of binary 0/1 responses indicating the absence or presence of a given experience on a finite checklist of possible life events, is commonly used and is appropriate for studies incorporating accumulation-of-risk models [48]. However, such models do not account for potentially synergistic detriment arising from repeated stressor exposures, nor do they incorporate appraisal [16], and in fact they have been shown to underestimate stressor exposure in African Americans and other underrepresented groups [17].

Finally, our small African American sample did not allow for disambiguation of age, cohort, and period effects on the relationships between stressful life events and cognitive outcomes in older age. Recent epidemiological work has suggested that consideration of cohort effects in dementia and impairment, and how they differ by race, is critical [4] given that risk exposures and their influence are likely to be influenced by the year an individual was born, schooled, entered the labor force, encountered health problems, and so on. As *de jure* and *de facto* environments that shape key modifiable cognitive risk factors such as education quality and access to cardiovascular health care shift, the relationships between exposures and cognitive outcomes are also likely to change. Period effects may also differ between the predominantly White adults enrolled at the beginning of the study and similarly-aged African American adults enrolled ten years later. Future studies in larger middle-aged and older cohorts should explore potentially distinct age, cohort, and period effects in relationships between stress and health [68].

The current study nonetheless contributes additional evidence to a growing body of literature that suggests that life course socio-environmental factors are important determinants of later-life cognitive trajectories and dementia risk, and that this may be particularly true for racial minority and other historically disadvantaged populations. Further, cumulative disadvantage as measured by a life event index may influence cognitive trajectories independent of other strong, well-established social determinants including education quality and literacy. Observed racial differences in stress-cognition relationships highlight the need for prioritization of cohort diversity, and delineation of AD-specific biomarker and other relevant brain changes in non-White populations. Social-biological processes represent a modifiable source of ADRD and impairment risk, one that with further study could clarify underexplained disparity and illuminate strategic points for targeted intervention.

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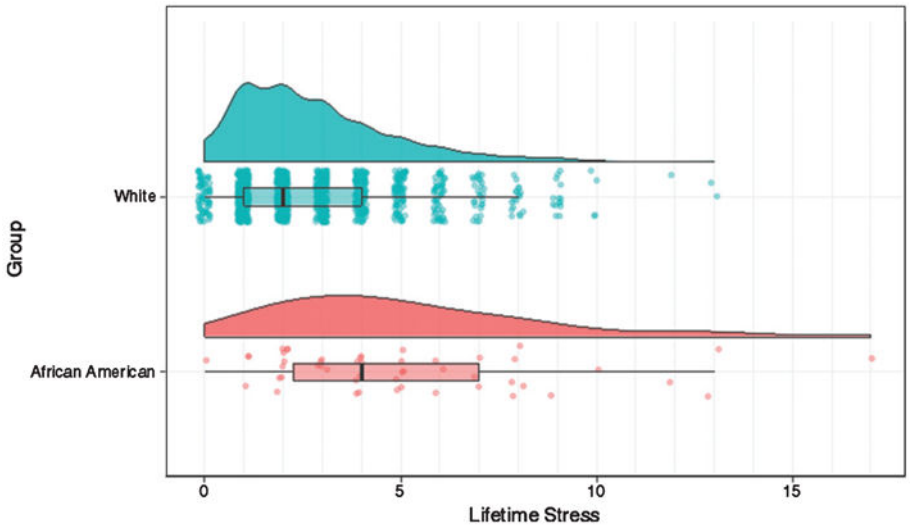

Fig. 1.
Distribution of lifetime stressful experiences by race.

Table 1

Descriptive statistics by race for study participants (*N*== 1,241) at Visit 1

Variable	African American (*n* = 50)	White (*n* = 1,191)	Group comparison (p)
Age in years, M (SD)	54.84 (6.55)	53.91 (6.70)	0.19
Female gender, N (%)	36 (72)	834 (70)	0.74
Years of education, M (SD)	**15.36 (2.51)**	**16.09 (2.45)**	**0.02**
*APOE ε*4 carriers, N (%)	25 (50)	453 (38)	0.13
WRAP visits completed, M (SD)*	**3.4 (1.1)**	**4.5 (1.1)**	**<0.001**
Body mass index, M (SD)	**33.43 (7.34)**	**28.77 (6.16)**	**<0.001**
Smoking status, N (%)			
Never	**19 (38)**	**707 (59)**	**<0.001**
Past	**15 (30)**	**397 (33)**	
Current	**16 (32)**	**87 (8)**	
Life Event Index Score, M (SD)	**5.12 (3.51)**	**2.79 (2.01)**	**<0.001**
Literacy Score, M (SD)	**46.28 (6.48)**	**51.02 (4.35)**	**<0.001**
Speed & Flexibility, M (SD)	**−0.96 (1.03)**	**0.10 (0.95)**	**<0.001**
Working Memory, M (SD)	**−0.70 (0.98)**	**0.06 (0.98)**	**<0.001**
Verbal Learning & Memory, M (SD)	**−0.55 (1.11)**	**0.07 (0.97)**	**<0.001**

*Number of WRAP visits completed was based on most recent (last) visit rather than Visit 1.

Table 2

Regression coefficients (95% confidence intervals) for stressful life events and change in cognitive function by domain, race, and model

Speed & flexibility	**African American (N = 50)**			**White (N = 1191)**		
	Model 1	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
Stress	−0.11 (−0.23, 0.006)	−0.12 (−0.23, −0.02)*	−0.13 (−0.24, −0.03)*	−0.03 (−0.05, −0.01)*	−0.03 (−0.05, −0.01)*	−0.03 (−0.05, −0.01)*
Age	−0.07 (−0.12, −0.02)*	−0.08 (−0.13, −0.03)†	−0.08 (−0.14, −0.04)†	−0.05 (−0.06, −0.05)†	−0.06 (−0.06, −0.05)†	−0.06 (−0.07, −0.05)†
Stress*Age	0.003 (−0.007, 0.013)	0.001 (−0.008, 0.011)	0.001 (−0.009, 0.010)	−0.000 (−0.001, 0.002)	−0.000 (−0.001, 0.002)	−0.000 (−0.002, 0.002)
Literacy	–	0.07 (0.03, 0.11)†	0.07 (0.03, 0.11)†	–	0.03 (0.02, 0.05)†	0.03 (0.02, 0.05)†
BMI	–	–	0.01 (−0.02, 0.04)	–	–	−.001 (.−0.007, 0.005)
Past smoking	–	–	0.10 (−0.49, 0.69)	–	–	−0.03 (−0.12, 0.07)
Current smoking	–	–	−0.14 (−0.77, 0.50)	–	–	−0.13 (−0.26, 0.01)
Working memory	**African American (N = 50)**			**White (N = 1191)**		
	Model 1	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
Stress	−0.06 (−0.15, 0.03)	−0.05 (−0.13, 0.02)	−0.06 (−0.13, 0.02)	0.01 (−0.02, 0.03)	0.01 (−0.01, 0.03)	0.01 (−0.02, 0.03)
Age	−0.03 (−0.07, 0.02)	−0.04 (−0.08, −0.001)*	−0.04 (−0.08, −0.005)*	−0.01 (−0.02, −0.01)†	−0.01 (−0.02, −0.01)†	−0.01 (−0.02, −0.01)†
Stress*Age	0.00 (−0.01, 0.01)	−0.001 (−0.006, 0.005)	−0.002 (−0.007, 0.004)	−0.000 (−0.001, 0.001)	0.000 (−0.001, 0.001)	0.000 (−0.001, 0.002)
Literacy	–	0.10 (0.06, 0.13)†	0.10 (0.07, 0.14)†	–	0.09 (0.08, 0.10)†	0.09 0.08, 0.10)†
BMI	–	–	0.02 (−0.01, 0.04)	–	–	−0.002 (−0.007, 0.004)
Past smoking	–	–	0.12 (−0.41, 0.65)	–	–	0.13 (0.04, 0.23)*
Current smoking	–	–	0.06 (−0.49, 0.60)	–	–	0.21 (0.09, 0.34)*
Verbal learning & memory	**African American (N = 50)**			**White (N = 1191)**		
	Model 1	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
Stress	0.00 (−0.08, 0.08)	−0.001 (−0.08, 0.08)	−0.01 (−0.09, 0.08)	−0.002 (−0.03, 0.02)	−0.002 (−0.03, 0.02)	−0.002 (−0.03, 0.02)
Age	0.01 (−0.03, 0.04)	0.01 (−0.04, 0.04)	−0.01 (−0.05, 0.04)	−0.03 (−0.04, −0.02)†	−0.03 (−0.04, −0.03)†	−0.03 (−0.04, −0.03)†
Stress*Age	−0.01 (−0.02, 0.00)	−0.01 (−0.02, −0.001)*	−0.01 (−0.02, −0.002)*	0.001 (−0.001, 0.003)	0.001 (−0.001, 0.003)	0.001 (−0.001, 0.003)
Literacy	–	0.02 (−0.01, 0.06)	0.02 (−0.01, 0.06)	–	0.05 (0.04, 0.06)†	0.05 (0.04, 0.06)†
BMI	–	–	−0.01 (−0.04, 0.01)	–	–	0.003 (−0.003, 0.009)
Past smoking	–	–	−0.07 (−0.58, 0.44)	–	–	−0.04 (−0.13, 0.06)

Speed & flexibility	African American (N = 50)			White (N = 1191)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Current smoking	–	–	−0.45 (−1.06, 0.16)	–	–	−0.11 (−0.26, 0.03)

All models additionally adjust for gender, years of education, *APOE ε4* carrier status, and practice effects.

*Significant at the $p < 0.05$ level.

†Significant at the $p < 0.001$ level.

Table 3

Attenuation of race differences in level of cognitive function by lifetime stress in each cognitive domain

	Speed & flexibility		Working memory		Verbal learning & memory	
	Model 1	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
African American race	−0.93 (−1.18, −0.69) †	−0.87 (−1.12, −0.62) †	−0.39 (−0.63, −0.15) *	−0.39 (−0.63, −0.15) *	−0.33 (−0.58, −0.09) *	−0.33 (−0.58, −0.08) *
Stress	–	−0.04 (−0.06, −0.01) †	–	0.00 (−0.02, 0.02)	–	–0.003 (−0.03, 0.02)
Stress * Age	–	0.00 (0.00, 0.00)	–	0.00 (−0.001, 0.001)	–	0.00 (−0.002, 0.002)
Attenuation (%, CI)	–	6.91 (4.43, 8.78) *	–	0.02 (−1.77, 5.97)	–	1.51 (−1.83, 13.06)

All models additionally adjust for age at visit, gender, years of education, *APOE ε*4 carrier status, and practice effects.

*Significant at the $p < 0.05$ level.

†Significant at the $p < 0.001$ level.