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Perceived Stress and Cognitive Decline in Different Cognitive Domains in a Cohort of Older African Americans

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Abstract

Background—Research indicates that stress is linked to cognitive dysfunction. However, few community-based studies have explored the relationship between perceived stress and cognitive decline, and fewer still have employed cognitive domains rather than a global measure of cognition.

Objective—We examined the relation between perceived stress and the rate of decline in different cognitive domains.

Method—Participants were older African Americans without dementia from the Minority Aging Research Study (MARS; N=467, mean age: 73 SD=6.1). A battery of 19 cognitive tests was administered at baseline and at annual intervals for up to 9 years (mean follow up=4 years), from which composite measures of global cognitive function and five specific cognitive domains were derived. The 4-item Cohen's Perceived Stress Scale (PSS) was also administered at baseline.

Results—In linear mixed-effects models adjusted for age, sex, education, and vascular risk factors, higher perceived stress was related to faster declines in global cognition ($\beta=-0.019$; SE=0.008; $t_{(1951)}=-2.46$), episodic memory ($\beta=-0.022$; SE=0.011; $t_{(1954)}=-1.99$), and visuospatial ability ($\beta=-0.021$; SE=0.009; $t_{(1939)}=-2.38$) all $p < .05$. Findings were similar in subsequent models adjusted for demographics, vascular diseases, and depressive symptoms.

Conclusions—Results indicate that older African Americans with higher levels of perceived stress have more rapid declines in global cognition than those with lower levels, most notably for episodic memory and visuospatial ability.

Keywords

African Americans; Cognition; Cognitive Domains; Cognitive Decline; Perceived Stress

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Conflicts of Interest

There are no relationships, financial or otherwise, that could be considered conflicts of interests affecting this manuscript. No Disclosures to Report.

INTRODUCTION

It has been well documented that stress, defined as a consequence of environmental events or demands (stressors) that exceed an individual's perceived ability to cope⁽¹⁾, can affect a person's physical and psychological health. Research has described the detrimental effects of chronic stress on psychological well-being and cognitive functioning, with an emphasis on the relationship between stress and memory⁽²⁾. However, much of the evidence regarding the relation between stress and cognition comes from clinical observations and basic neuroscience studies involving biological measures of the physiological stress response⁽³⁾. Few community-based studies have explored the relationship between the perception of stress, which precedes the physiological response, and cognition, and fewer still have examined the full range of cognition rather than memory alone. The focus on memory in stress and cognition research stems from the fact that both animal and human studies show that psychosocial stress can lead to a spectrum of cellular changes in the hippocampus, a part of the limbic system that is important for declarative memory processes⁽⁴⁾. The cellular changes seen in the hippocampus occur, at least in part, because of a high number of glucocorticoid/cortisol (also known as the stress hormone) receptors in this area⁽⁵⁻⁷⁾. However, glucocorticoid/cortisol receptors also exist in the prefrontal cortex, suggesting the possibility that psychosocial stress could lead to deficits in executive functioning and attention as well^(8,9).

Research also suggests that chronic stress is associated with inflammatory and hormonal indicators of accelerated aging⁽¹⁰⁾, with reports of greater perceived stress levels increasing the possibility of brain infarcts, reduced brain volume⁽¹¹⁾, and elevated risk of stroke^(12,13). Consequently, these same physiological markers of accelerated aging are also associated with rates of decline in cognition. Taken together, these different lines of research suggest that perceived stress may be related to cognitive decline by causing cellular changes within the hippocampus or via an association with inflammatory and hormonal markers of brain aging. We are aware of only one population-based study that examined perceived stress and change in cognition⁽¹⁴⁾. While this study confirms a relationship between perceived stress and cognitive decline, they used only a brief global measure of cognitive function consisting of four tests. Thus, the potential relationship between perceived stress and *specific* declines in memory and attention, as suggested by previous literature, is still an unanswered question.

Previous research has suggested that African Americans experience a disproportionate burden of stressful life experiences linked to poverty, racism, and residential segregation, due, in part, to their relative low social status in US society⁽¹⁵⁻¹⁸⁾. For example, African Americans are more likely to experience stressful life conditions such as unfair treatment, environmental stressors such as impoverished neighborhoods, and limited job opportunities^(19,20). Yet most research on psychosocial stress and health outcomes has been conducted in the majority white population. In addition, several studies have documented high rates of cognitive impairment in older African Americans⁽²¹⁾. Examination of the link between perceived stress and cognition in a population characterized by societal inequalities and high rates of cognitive impairment^(16,18,21) would represent an important step in delineating whether psychosocial stress may be a modifiable risk factor for cognitive decline. Therefore, we examined the relation between perceived stress and cognitive decline

in a sample of community-dwelling older African American adults. We hypothesized that higher levels of perceived stress would be related to faster rates of cognitive decline, particularly in the well documented area of hippocampus mediated tasks such as memory (as measured by episodic memory specifically) and the projected areas of prefrontal cortex mediated tasks such as executive function and attention (as measured by perceptual speed specifically).

METHODS

Participants

All the participants were enrolled in the Minority Aging Research Study (MARS) and had signed an informed consent form in which they agreed to annual clinical evaluations that included an assessment of lifestyle and psychosocial factors (e.g., depressive symptoms and perceived stress) and cognitive testing, as previously described²². MARS is a longitudinal epidemiological cohort study of risk factors for cognitive decline and Alzheimer's disease in African-Americans, approved by the Rush University Medical Center Institutional Review Board. The participants were older community-dwelling adults, without dementia, recruited from churches, community-based organizations, senior-subsidized housing facilities in the Chicagoland area, and through the Clinical Core of the Rush Alzheimer's Disease Center. Community presentations were held throughout the city on aging and Alzheimer's disease in African Americans during which a description of the study and eligibility were discussed. Interested persons were asked to complete a form describing their level of interest in the study, and were contacted later to have questions answered and obtain further information on the study. At the time of the analysis, 602 older adults had enrolled and completed a baseline evaluation. Follow up time ranged from 1-9 years (approximately 44% of individuals had 2-4 years follow up time, 24% had 5-7 years and 32% had 8-9 years) with an average of 4.0 (SD=3.52) years. Because we are interested in cognitive change, we excluded 116 individuals who had not yet completed at least two clinical evaluations. Based on clinical evaluations conducted at baseline, we excluded another 19 individuals who met criteria for dementia. The remaining 467 participants were included in these analyses.

Clinical evaluation

All participants agreed to annual uniform structured clinical evaluations. These included a complete neurological examination, a detailed medical history, and neuropsychological testing (described below). An experienced clinician classified the participants with respect to dementia diagnosis. Dementia classifications were based on the criteria of the joint working group of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association⁽²³⁾.

Neuropsychological testing

Annual neuropsychological testing consisted of detailed tests selected to assess a broad range of cognitive abilities commonly affected in older adults. It included the Mini-Mental State Examination (MMSE)⁽²⁴⁾, which was used for descriptive purposes only. As previously described⁽²⁵⁾, the remaining tests were used to form summary measures of five cognitive domains (episodic memory, semantic memory, working memory, perceptual speed,

and visuospatial ability) and global cognition. The measures included in each of the cognitive domains are as follows: episodic memory includes Word List Memory, Word List Recall, and Word List Recognition from the procedures established by CERAD⁽²⁶⁾, immediate and delayed recall of the East Boston story⁽²⁷⁾, and, immediate and delayed recall of Story A from the Logical Memory subtest of the Wechsler Memory Test-R (WMS-R)⁽²⁸⁾; semantic memory includes semantic Verbal Fluency from CERAD (animal and fruits/vegetables)⁽²⁶⁾ and a 15-item version of the Boston Naming Test⁽²⁹⁾; working memory includes Digit Span Forward and Backward from the WMS-R⁽²⁸⁾ and Digit Ordering⁽³⁰⁾; perceptual speed includes symbol digit modalities⁽³¹⁾, number comparison⁽³²⁾, and two indices from a modified version of the Stroop Neuropsychological Screening Test: the number of color names correctly read aloud in 30 seconds minus the number of errors and the number of colors correctly named in 30 seconds minus the number of errors⁽³³⁾; visuospatial ability includes a 16-item version of Standard Progressive Matrices⁽³⁴⁾ and a 15-item version of Judgment of Line Orientation⁽³⁵⁾. As described previously⁽²⁵⁾, the composite scores of the five cognitive domains were created by converting the raw scores of the measures for each cognitive domain into z scores and then averaging the z scores. The global cognitive score was derived by averaging the z scores of all measures.

Stress measure

Stress was assessed using Cohen's Perceived Stress Scale (PSS)⁽³⁶⁾. The PSS is an index of the degree to which a person finds their lives unpredictable, uncontrollable, and overloading - characteristics central to the evaluation of stress. Initially Cohen introduced the full length version (14 items) and a short version (4 items) of the scale, later another short version of the scale with 10 items was introduced. Validation studies of the English versions of the PSS conducted by the creators demonstrate acceptable internal consistency across all versions (Chronbach's alpha = .78, .75, .60 for -14, -10, and -4 item versions respectively)⁽³⁷⁾. We used the 4-item version of the measure and asked participants to rate the frequency at which they perceived these characteristics within the last month. The responses were coded in a Likert scale format ranging from 0 (never) to 4 (very often), with higher scores indicating higher levels of perceived stress. Scale items included "In the last month, how often have you felt.... (1) that you were unable to control the important things in your life?, (2) confident about your ability to handle your personal problems?, (3) that things were going your way?, and (4) difficulties were piling up so high that you could not overcome them?"

Covariates

The covariates included age, sex, education (years of formal schooling), a composite score of vascular risk factors, and depressive symptoms. Vascular risk factors (i.e., the sum of hypertension, diabetes mellitus, and smoking, resulting in a score from 0 to 3 for each individual) and vascular disease (i.e., the sum of heart attack, congestive heart failure, claudication, and stroke resulting in a score from 0 to 4 for each individual) were computed on the basis of self-report questions and inspection of medications, as previously described⁽³⁸⁾. Depressive symptoms were assessed using the 10-item version of the Center for Epidemiologic Studies Depression Scale (CES-D)⁽³⁹⁾. The participants were asked whether they had experienced specific symptoms in the last week. The responses to the

items on the CES-D are coded in a yes/no format, yielding a summary score ranging from 0–10.

Data analysis

We computed descriptive statistics for the PSS, including the mean scores of demographic subgroups and used *t*-tests and one way ANOVAs to compare the mean PSS scores across the different demographic subgroups. Least square means were compared using Tukey-Kramer adjustment for multiple comparisons. The relation of stress and cognitive decline (global cognition and the five separate domains) was examined with linear mixed models with a random intercept and random slope for time, using restricted maximum likelihood and an unstructured covariance structure. All the models controlled for age (centered at the mean), sex, education (centered at the mean), vascular risk factors, and depressive symptoms. In order to ensure a full examination of vascular effects, subsequent models adjusted for vascular disease.

All analyses were programmed using SAS/STAT® software version 9.3 for Linux on a Hewlett Packard DL380 server⁽⁴⁰⁾.

RESULTS

Among the 467 African American participants, 75% were women. They had a mean age of 73.4 (SD = 6.12) years, a mean education of 15.0 (SD = 3.46) years, and a mean MMSE score of 27.9 (SD = 1.91). The mean vascular risk score of the participants was 1.5 (SD = 0.85), and they had a median CES-D score of 1.0 (IQR= 0.0, 2.0) and a mean PSS score of 0.85 (SD = 0.67) (Table 1).

We first examined the mean scores for PSS within demographic subgroups (age: 65-75, 76-85, & 86+; education: <12years, 13-15 years, 16+ years; gender: women, men). In these bivariate analyses, there was only an association between perceived stress level and years of education, such that perceived stress was lower in those with higher education. Perceived stress did not differ as a function of age, or among men and women. (See Table 2).

Next, we constructed mixed-effects models to examine the relation of perceived stress to the rate of cognitive decline, while adjusting for the effects of age (centered at 73 years), sex, education (centered at 15 years), vascular risk, and depressive symptoms. Level of perceived stress was not related to global cognition at baseline, but it was related to global cognitive decline (Table 3), such that persons who scored higher on the PSS declined in global cognition significantly faster than those who scored lower on the PSS (See Figure 1). For example, a typical person with the mean age and education but with a PSS score one point above the mean was estimated to enter the study with a non-significant 0.005 points lower cognition and significantly decline by .019 points per year. In a model adding vascular disease as a covariate the PSS continued to be related to global cognitive decline (data not shown).

In subsequent mixed-effects models, we examined the relationship between perceived stress and each of the five cognitive abilities. We repeated the main analysis while adjusting for the

effects of age (centered at 73 years), sex, education (centered at 15 years), vascular risk factors, and depressive symptoms to determine whether the PSS score was associated with a decline in some domains of cognitive function but not others. Higher PSS scores were associated with a faster decline in episodic memory and visuospatial ability (Table 3; Figures 2 & 3), but not semantic memory, working memory, or perceptual speed. A typical individual from the example above with mean age and education but with a PSS score one point above the mean would decline in episodic memory by .022 points per year and in visuospatial ability by 0.021 points per year. Subsequent models that also adjusted for vascular disease did not change these results (data not shown).

Because persons with less than 12 years of education reported significantly higher levels of perceived stress, in a secondary analysis we examined the relation of perceived stress and cognitive decline in this subgroup, in a model adjusting for the effects of age, sex, education, vascular risk factors, and depressive symptoms. In this model with 133 individuals, higher PSS scores were associated with a faster decline only in episodic memory ($\beta = -.039$; $SE = .019$; $t_{543} = -2.10$, $p = .036$).

Approximately 29% of the sample developed MCI and 9% developed dementia. We conducted separate cox proportional hazards models to test whether perceived stress is associated with a higher risk of MCI and dementia, but there was no relation (data not shown).

DISCUSSION

In this study of 467 African American older adults without dementia at baseline, we found that greater perceived stress was associated with declines in global cognition, episodic memory, and visuospatial ability in models that adjusted for demographics, vascular risk factors, and depressive symptoms. We also adjusted for depressive symptoms in our models to ensure that the results truly reflected perceived stress. These results suggest that older African Americans with higher levels of perceived stress had faster rates of cognitive decline than those with lower levels of perceived stress, independent of vascular risk, vascular disease, and depressive symptoms.

Though previous research examining the relationship of perceived stress to cognition in older African Americans is relatively scarce, one recent population-based study, which included approximately 66% African Americans, reported that higher levels of perceived stress were related to lower cognition scores at baseline, as well as a faster rate of decline in African Americans and whites⁽¹⁴⁾. However, they included a brief global measure of cognition, consisting of four tests, and limiting the ability to examine specific cognitive domains. Our results replicate their finding with global cognition, and extend the finding by demonstrating that perceived stress is also related to faster declines in episodic memory and visuospatial ability.

Overall, our sample had low perceived stress scores, given that our median score was one on a scale that ranged from 0 to 4. This finding contradicts the previous literature, which has suggested high levels of stress among African Americans^(18,41,42). It is possible that the

stress levels in our sample were low due to the overall high level of educational attainment of the participants. Research has indicated that lower levels of educational attainment are related to higher levels of stress^(14,41,43) and this was also seen in our sample, with individuals with less than 12 years of education reporting significantly more stress than individuals with more education. In a secondary analysis examining the relationship of perceived stress to declines in cognition in a subsample with less than 12 years of education, we found that perceived stress was related to faster decline in episodic memory, but not in global cognition or visuospatial ability as observed in the full sample. It is possible that we may have been underpowered with a little over 100 people in the model. Future studies with larger numbers should examine the influence of educational attainment on the relationship between perceived stress and cognition in African Americans. A previous study proposed that individuals with higher levels of education have access to more socioeconomic resources than those with less education and that this access leads to a better ability to cope with life's stressors⁽⁴¹⁾. It is also possible that the low scores reported by participants in this study reflect a general tendency to under-report negative emotions. In addition, research has demonstrated that older adults have reduced emotional reactivity to stress with age⁽⁴⁴⁾. We have also previously reported in this cohort that older African Americans tend to report low levels of another social stressor, perceived discrimination^(45,46). Future studies are needed to explore the relationship of age and stress in minority populations.

To our knowledge, this is the first study to examine the relationship between perceived stress and cognition in specific cognitive domains in general, and in a minority population in particular. We found an association between greater perceived stress and declines in episodic memory, as well as visuospatial ability. However, contrary to our hypothesis, we did not find that perceived stress was related to a faster rate of decline in perceptual speed. Our finding of a link between episodic memory and perceived stress is consistent with the previous literature⁽⁵⁻⁷⁾ and is consistent with the involvement of the hippocampus, which governs episodic memory, in stress processes via the high concentration of glucocorticoid receptors in this region of the brain. Though, the relationship between stress and visuospatial ability has not been extensively explored, we are aware of one study in college-aged males which found that acute, laboratory-based, psychosocial stress improved performance on a visuospatial ability task⁽⁴⁷⁾. In addition, research in visuospatial ability has indicated that healthy individuals recruit prefrontal cortex involvement along with the requisite parietal regions on more difficult visuospatial tasks⁽⁴⁸⁾. These results are at least consistent with the idea that similar to what happens with the abundance of glucocorticoid receptors in the hippocampus, glucocorticoid receptors in the prefrontal cortex could play a role in the current samples association between perceived stress and impaired visuospatial ability. Essentially, it is possible that the over taxing of the glucocorticoid receptors in the prefrontal cortex prevents the individuals from recruiting this region as they should on difficult visuospatial tasks.

Although the mechanisms linking stress to cognition in this study are not clear, the well-established mechanism of hypothalamic-pituitary-adrenal-axis dysregulation in chronic stress^(6,49) may play a role. Our finding of a relationship between perceived stress and declines in episodic memory would be consistent with the hypothalamic-pituitary-adrenal-axis mechanism and its involvement of the hippocampus. Inflammation may also be a

contributing factor. Previous research has demonstrated that discrimination, especially perceived discrimination, is a persistent stressor in African Americans and that perceived discrimination is associated with elevated levels of C-reactive protein⁽³⁹⁾, a marker that signals inflammation in the peripheral bloodstream. Both C-reactive protein levels and discrimination have been linked to psychosocial processes, such as depressive symptoms and chronic stress in African Americans^(15,50), as well as deleterious outcomes, such as cognitive impairment and decline^(51,52). Future studies are needed to test one or both of these mechanisms as potential pathways between perceived stress and cognitive decline.

The limitations of this study must be noted. First, the results of this study are based on a select cohort that may differ from other older African Americans in the US in education or lifestyle. Specifically, given that lower levels of educational attainment are associated with higher levels of stress, the relatively high educational status of our sample may have influenced these results. Therefore, there may be a more modest association with cognition in the present study than in other less educated cohorts. Additionally, we used only educational attainment as a measure of socioeconomic status; it is possible that results may have differed with other socioeconomic indicators. Secondly, the perception of stress is, by nature, a self-report measure. Therefore, it may be susceptible to issues of bias inherent in subjective reporting. In addition, the perceived stress levels in this sample were low, which may have led us to underestimate the relation of perceived stress to rate of decline. Despite this limitation, we were able to detect a relationship between perceived stress and specific domains of cognitive function. Third, while our comprehensive battery of cognitive tests may be a strength of the study, the battery itself was limited in its examination of executive functioning. Given that executive function is one of the prefrontal cortex mediated tasks suggested by previous literature, future studies focusing on executive function measures should be included to highlight the influence of the glucocorticoid receptors in the prefrontal cortex, on the relationship between perceived stress and cognition. In addition, this study did not explore the biological stress response mechanisms that may underlie the association of perceived stress and cognitive decline.

The study also has several strengths. First, we utilized a comprehensive battery of cognitive tests that included not only a global cognition measure but also five cognitive domains that have been shown to be valid and reliable in this sample⁽²⁵⁾. In addition, the use of composite measures of cognition enhanced our ability to identify subtle cognitive changes over time. Second, longitudinal data were available on close to 500 people, providing adequate statistical power. Finally, all the analyses controlled for health and mental status issues that could influence the perception of stress, the risk of cognitive decline, or their association.

In summary, our results indicate that higher levels of perceived stress are related to declines in global cognition and this relationship seems to be driven by more rapid declines in episodic memory and visuospatial ability in older African Americans; effects that appear to be independent of vascular factors and depressive symptoms.

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Figure 1.

Graphical representation of the rate of change in global cognition over time in individual with higher levels of stress (90th percentile perceived stress) versus those with lower levels of stress (10th percentile perceived stress).

Figure 2.

Graphical representation of the rate of change in episodic memory over time in individual with higher levels of stress (90th percentile perceived stress) versus those with lower levels of stress (10th percentile perceived stress).

Figure 3.

Graphical representation of the rate of change in visuospatial ability over time in individual with higher levels of stress (90th percentile perceived stress) versus those with lower levels of stress (10th percentile perceived stress).

Table 1Clinical Characteristics, $n = 467$

	Minimum	Mean/Median	SD/IQR	Max
Age	60.61	73.38	(6.12)	97.59
Years of Education	6.00	14.99	(3.46)	30.00
MMSE score	20.00	27.93	(1.91)	30.00
Perceived Stress Scale	0.00	0.85	(0.67)	3.00
CES-D	0.00	1.00 *	0.00, 2.00 *	9.00
Vascular risk score	0.00	1.50	(0.85)	3.00

Notes. SD = Standard deviation; IQR= Interquartile Range; MMSE = Mini-Mental State Examination; CES-D = Center for Epidemiological Studies Depression Scale

* Median/IQR.

Table 2

Mean PSS Score by Demographic Subgroups, n=467

Characteristics	N	Range	Mean(SD)	F statistic _(DF)
Age groups (years)				
65–75	309	0-3	0.86(0.62)	F _(2,464) =1.32
76–85	130	0-3	0.80(0.69)	
86 +	28	0-2.25	1.03(0.66)	
Education (years)				
<12	133	0-3	1.00(0.72)	F _(2,464) =4.7 *
13–15	146	0-2.5	0.79(0.67)	
16+	188	0-2.5	0.80(0.63)	
Gender				
Women	351	0-3	0.88(0.69)	F _(1,465) =2.79
Men	116	0-2	0.76(0.62)	

Notes. PSS = Perceived Stress Scale; SD = Standard deviation

* indicates a statistically significant least square means difference, adjusting for multiple comparisons with Tukey-Kramer, df=degrees of freedom

Table 3

Relation of Perceived Stress to Baseline Cognition and Cognitive Decline

Model term	Global cognition			Episodic			Semantic			Working			Perceptual speed			Visuospatial		
	β	SE	p	β	SE	p	β	SE	p	β	SE	p	β	SE	p	β	SE	p
Time	-.031	.012	.012	-.024	.017	.157	-.049	.016	.002	-.041	.014	.003	-.038	.012	.001	-.010	.013	.444
Age*	-.029	.003	<.001	-.034	.004	<.001	-.022	.005	<.001	-.012	.005	.026	-.042	.005	<.001	-.023	.005	<.001
Age × time	-.005	.001	<.001	-.005	.001	<.001	-.005	.001	<.001	-.003	.001	.002	-.003	.009	<.001	-.004	.001	.001
PSS	-.050	.031	.111	-.010	.039	.810	-.023	.043	.597	-.081	.048	.094	-.116	.043	.006	-.077	.046	.102
PSS × time	-.019	.008	.014	-.022	.011	.047	-.018	.010	.072	-.011	.009	.243	-.008	.008	.321	-.021	.009	.017

Notes. Six separate linear mixed models, each controlling for age, sex, education, vascular risk, and depressive symptoms. Participants, N = 467; Observations, N = 2428. p values are based on the t values of the coefficients, degrees of freedom=1954. SE: standard error; PSS = Perceived Stress Scale

* centered at 73 years of age.