Cumulative stress burden and cognitive function in African American adults living in low-income neighborhoods

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Abstract

Introduction
Dementia disproportionately affects African Americans. Differences in prevalence may be related to stress: African Americans are more likely to be exposed to stressors as a result of racial discrimination and living in segregated and disadvantaged neighborhoods. Despite this, few studies have considered the role of cumulative stress in cognitive decline across cognitive domains in a longitudinal aging cohort.

Hypothesis
We hypothesize that individuals with higher cumulative stress, as quantified by a cumulative stress burden (CSB) index, will have poorer cognition across all domains.

Methods
Stressors and cognition by domain (executive, attention, memory, visuospatial, and language) were measured in a cohort of 253 participants 50 years and older, recruited from two urban, primarily African American neighborhoods in Pittsburgh, PA. Domains were assessed by z-scores adjusted for age, sex, and educational attainment calculated through combining relevant cognitive tests. Stressors include perceived stress, psychological distress, unfair treatment, post-traumatic stress disorder, neighborhood satisfaction, safety, and walkability. Factor analysis and assessment of
stress variability over time was performed. Three indices were formed by dichotomizing stressor scores and summing: individual-level, neighborhood-level, and a sum of both. Generalized linear models adjusted for covariates were used to assess the relationship between these indices and cognition, as well as the relationship between individual stressors and cognition.

**Results**

The individual CSB index was associated with language ($\beta = -0.11, p = 0.03$) and executive function ($\beta = -0.087, p = 0.04$) in unadjusted and adjusted models. The neighborhood-level CSB index was not significantly associated with cognition. The combined index was significantly associated with language in both unadjusted and adjusted models ($\beta = -0.10, p = 0.01$). When all four components of the individual CSB index were assessed, there were no significant associations between any particular stressor and cognition.

**Conclusion**

These results show that increased cumulative stress is associated with poorer cognitive function in older African Americans. This indicates that a more holistic and comprehensive assessment of cumulative stress is vital in understanding the dimensionality of racialized stress for older adults potentially experiencing cognitive decline. Additionally, this analysis provides evidence for the public health relevance of interventions in African American neighborhoods aimed at decreasing experiences of stress.
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1.0 Introduction

1.1 Aging population and dementia prevalence

The number of older adults in the United States is growing rapidly, with projections that approximately 23.5% of the population will be older than 65 by 2060.\(^1\) As such, research of aging-related chronic conditions has become increasingly important. Of these chronic diseases, dementia is comprised of a collection of diseases characterized by cognitive decline and behavioral changes, of which Alzheimer’s disease (AD) is most common. Affecting approximately 5.7 million Americans, with projected prevalence rapidly increasing in coming years, AD and related dementias are a serious public health issue.\(^2\)

1.2 Definition of dementia and assessment

Dementia is characterized by progressive psychological and cognitive deficits that interfere with daily functioning. Mild cognitive impairment (MCI) is used to describe modest cognitive decline that does not yet significantly impact independent functioning but can progress to dementia over time.\(^3\) Cognitive function can split into different domains: attention, executive, language, memory, visuospatial and social cognition.\(^4\) Depending on type and location of dementia pathology, different domains can be affected at different time points as dementia progresses, affecting clinical presentation of these pathologies.
Attention deficits present as trouble focusing on appropriate stimuli and difficulty in performing more complex tasks or mental calculations. Problems with executive functioning are characterized by difficulties with organization, planning, set-shifting/cognitive flexibility, and reasoning. Memory deficits are defined by problems with learning new information, recall, and increasing reliance on external reminders and lists. This domain is often further split into immediate and delayed memory, which are differentiated by length of time between encoding and recall. Language limitations present as difficulty finding words, using words and grammar incorrectly, or comprehension of language more generally. Visuospatial deficits are characterized by difficulty with navigation and getting lost in previously familiar locations. Limitations in social cognition can present as an inability to recognize emotion and empathize.\(^4\)

Evidently, deficits in these domains are not independent from one another: for example, being unable to find the right words (language deficit) is likely related to difficulty in recall more generally (memory deficit). However, understanding decline in terms of domains is a useful tool for prevention and treatment as compensation for different deficits takes different forms. Furthermore, different underlying pathology can express itself through different patterns of deficits across domains. As such, it is key to develop a valid and reliable battery of assessments to isolate different features of cognitive decline, while keeping in mind that these domains fit into an interrelated picture of global cognitive functioning.
1.3 Burden of dementia

The public health burden of these deficits and accompanying disability encompasses individual, social, and economic harms. On the individual level, dementia often interferes with an individual’s independence and ability to perform everyday tasks without others. The direct cost of care and treatment of AD in 2020 is estimated to be 305 billion dollars, with estimates increasing to more than one trillion by 2050. Additionally, it’s estimated that 75% of care for a dementia patient is performed by unpaid family members or friends. The implications of this are two-fold. One, non-professional caregivers often experience negative health outcomes and decreased productivity linked to their caregiving obligations. With rising prevalence of AD, the psychological and physical burden on non-professional caregivers is likely to increase. And two, the economic costs of AD are likely underestimated as it is difficult to capture loss of productivity and care in unpaid non-professionals; thus, the real economic burden of dementia is likely much higher. Despite these significant harms, research on potential therapeutics for these conditions has been difficult and largely unfruitful. As there are limited effective therapeutic options, there is a unique interest in examining risk factors for cognitive decline for the purposes of prevention.

1.4 Disparities in dementia prevalence, African Americans

African American populations are especially affected by cognitive decline with prevalence of AD being twice as high in African Americans when compared to White Americans. As the aging population in the US becomes more diverse, understanding race specific risk factors underlying disparities in chronic diseases is of growing significance. This difference in prevalence
mirrors disparities in other health conditions such as cardiovascular disease and diabetes, which have been linked in part to increased chronic stress.\textsuperscript{10–13} Past research has also suggested that cognitive decline is associated with socioeconomic status, and environmental and social stressors.\textsuperscript{14–16} This is an especially important consideration as African Americans, when compared to White Americans, are more likely to be exposed to individual, social, and neighborhood level stressors as a result of continued racial discrimination and living in segregated and disadvantaged neighborhoods.\textsuperscript{17}

\section*{1.5 Measures of stress: neighborhood level}

The effects of economic and residential segregation in the U.S., reinforced by social norms and public policies such as redlining, persist to this day with high rates of African American-white segregation in both rural and urban areas. As such, African Americans experience both different kinds and different quantities of stressors. Heavily affected by segregation, neighborhood level factors refer to both the social and built environment in one’s local area/community. Social features involve person-based factors such as social cohesion and perceived safety; the built environment encompasses walkability, aesthetics, land use, etc. There is strong evidence that neighborhood level factors are associated with health outcomes and risk factors that are more prevalent in the African American population. On average, African Americans tend to live in more impoverished and disadvantaged neighborhoods, with reduced opportunity for employment and education and decreased safety.\textsuperscript{18–20} Segregated neighborhoods also have reduced access to healthier foods and higher prevalence of cardiovascular disease and obesity.\textsuperscript{21,22} The combination of both risk factors and health outcomes can act as stressors for those residing in these neighborhoods.
There is evidence that neighborhood level factors could also be associated with cognitive decline through similar mechanisms. In particular, neighborhood features such as land use mix, green space, and street connectivity have been shown to be related to factors like physical activity and depressive symptoms, both of which are associated with cognitive decline.\textsuperscript{23–25} Furthermore, there is strong evidence that engaging neighborhood environments can play a protective role in cognitive aging.\textsuperscript{26} A study examining cross-sectional cognitive functioning with relation to social environment in a cohort of older adults in Florida shows that a better neighborhood social climate, as measured through a questionnaire about neighbor quality, is associated with better cognition.\textsuperscript{27} This study also examined the effect that a local social environment might have on psychological distress, reporting that higher social support mediates the relationship between neighborhood social environment and individual distress.

With regard to the built environment, one study reports that higher neighborhood connectivity, as defined by the number of streets and businesses linked to an individual’s home within a set distance, is associated with better global cognition and less change in cognitive status over two years.\textsuperscript{28} Another study considered neighborhood features measured on the block group level, showing an association with cognitive function trajectories, concluding that in addition to individual factors, a high density of community resources, close proximity to public transport, and well maintained public spaces are associated with slower rates of cognitive decline.\textsuperscript{29} Both suggest that walkability and easy access to community resources likely plays a role in cognitive decline.
1.6 Measures of stress: individual level

Environmental conditions have been shown to have a strong effect on individual stress. Those living in disadvantaged neighborhoods (lack of resources, limited places to go, high crime, etc) report higher levels of individual stress. Additionally, neighborhood environments with lower social cohesion have been linked to increased odds of post-traumatic stress. Individual stress, in part induced by neighborhood level factors, can be uniquely harmful. In response to an acute stress event, an individual may choose to remove themselves from the stressful stimuli and thus end the stress response. However, if one’s neighborhood and environment is consistently stressful, one is unable to meaningfully escape stressors that chronically increase individual stress. As such, it has been hypothesized that African Americans suffer from “weathering” effects, where persistent stress as a consequence of persistent social, economic, and economic discrimination and disadvantaged neighborhoods can lead to higher prevalence and earlier onset of negative health outcomes. In particular, weathering effects have been linked to increased cognitive decline. Thus, self-reported longitudinal individual stress, potentially precipitated by neighborhood level factors is a key risk factor for cognitive decline in African Americans.

Past literature has identified several individual factors linked to cognitive decline in older adults that can couple with neighborhood level factors. For example, a study examining the relationship between perceived stress and cognition in a diverse urban cohort reports that increased levels of perceived stress are associated with both lower cognitive scores in general, but also a faster rate over time. These results are confirmed in a study of older African Americans where self-reported perceived stress was associated with a faster rate of decline in global cognition, memory, and visuospatial ability. Furthermore, mental illness has been associated with greater risk of cognitive decline and dementia. One study reports that late-life depression increases risk of
progression from MCI to vascular dementia.\textsuperscript{36} Additionally, psychological distress, characterized by feeling anxious or depressed, has been linked to poorer cognitive function in general and in older adults.\textsuperscript{37–39} Post-traumatic stress disorder (PTSD) has also been linked to poor cognitive function in older adults.\textsuperscript{40} One longitudinal study reports that PTSD is a risk factor for subsequent dementia; another reports that risk of dementia is almost two times as high in those with PTSD than those without.\textsuperscript{41,42}

Such stressors are affected by and can be compounded by unfair treatment and discrimination. African Americans who report experiencing high levels of racial discrimination also have higher levels of self-reported stress and lower levels of psychological well-being.\textsuperscript{43} In a study using the Minority Aging Research Study cohort, unfair treatment was associated with poorer cognitive function with strongest effect sizes in memory.\textsuperscript{44}

\section*{1.7 Mechanisms of stress and cognitive decline}

Mechanistically, stressors act on the hypothalamic-pituitary-adrenal (HPA) axis, causing downstream release of cortisol. In cases of acute stress events, this process can be protective and help regulate energy supply and neuronal networks, enhancing cognitive abilities short-term.\textsuperscript{45} In these circumstances, cortisol release is self-regulated and levels return to baseline post-event.\textsuperscript{46} However, chronic stress can cause continued and overactive cortisol release, extending the body’s natural stress response and causing hormonal imbalance. Chronically elevated cortisol levels have been associated with a variety of poor health outcomes across multiple systems, including dysfunction in other hormonal pathways, depression, anxiety, and obesity.\textsuperscript{47–49}
Chronically elevated cortisol has also been linked to dementia. One prospective longitudinal study collecting cortisol samples over an average follow up time of 10.56 years in cognitively normal participants at baseline showed that long term exposure to cortisol had significant associations with AD risk. Additional studies show that chronic elevated cortisol may be neurotoxic. The hippocampus, a region with a high number of cortisol receptors and is critical for memory, and the prefrontal cortex are especially vulnerable to this toxicity: chronic stress is associated with decreased hippocampal and frontal cortex volume which, in turn, have been associated with difficulties with memory and executive function respectively.\textsuperscript{50–53} Furthermore, several mouse model studies have shown that increased stress is related to increased amyloid-\textbeta and tau pathology, a defining characteristic of AD.\textsuperscript{54,55} As such, repeated exposure to stress has been shown to increase risk for cognitive decline and AD through dysregulated neuroendocrine responses, autonomic reactivity, and extended inflammatory processes.\textsuperscript{56,57}

1.8 Gaps in research

Despite the high prevalence of dementia in African American populations and previous research supporting the connection between stressors and cognition, there is still a dearth of evidence among African Americans with careful consideration of chronic discrimination. This is likely due, in part, to a lack of African American recruitment in longitudinal studies of aging and difficulties with recruiting longitudinal aging cohorts more generally with the majority of literature on stress and cognition seeming to be cross-sectional.\textsuperscript{58–60} However, due to significant differences in disease prevalence and risk factors, there is a need for a more focused analysis targeting race related stressors, including potential neighborhood consequences of segregation and unfair
treatment. Longitudinal analyses, examining variation in stressors across time, are also required to understand the effect of cumulative repeated stress.

Furthermore, most studies assessing the association between stressors and cognitive decline have not considered an individual’s stress profile. That is, many studies consider one or two stressors, or cortisol levels with relation to cognitive decline.\textsuperscript{34,37,44,51,61,62} However, stressors that an individual experience are not mutually exclusive from one another. For example, if an individual lives in a disadvantaged neighborhood, they are more likely to experience psychosocial stress and “weathering” effects on the individual level: one that lives in a neighborhood with chronically low resources will experience personal stress from this lack.\textsuperscript{60} As such, in order to understand the effect of stress on cognition, we must consider an individual’s cumulative stress burden both over time and over different stressors.

Additionally, studies considering cognitive decline often exclude participants in mid-life, focusing mostly on individuals older than 65 years. It has been previously reported that older African Americans generally perform poorer on cognitive tests when compared to White Americans, but decline at a slower rate than White Americans: as such, cognitive decline likely occurs earlier in African American populations.\textsuperscript{63} As stress potentially contributes to cognitive decline years before symptoms of decline manifest, it is important to capture chronic stress effects in midlife. Furthermore, stressors likely affect individuals who are in early stages of decline differently than those who are cognitively normal. As such, enrolling a younger study population may allow researchers to parse out a stronger temporal relationship between stress and decline.

Finally, prior research lacks robust cognitive testing. Many studies only consider formal dementia/MCI diagnosis, global cognition, or use one measure per cognitive domain as outcomes.\textsuperscript{34,41,62} Only considering global cognition as an outcome leaves out important differences
in decline between domains, especially since past research has shown that chronic elevated cortisol may be especially harmful to particular areas of the brain.\textsuperscript{50,64} Likewise, only considering dementia/MCI diagnosis reduces the important dimensionality of a participant’s cognitive decline. However, using one cognitive measure per domain, while decreasing participant burden, limits reliability. Thus, it is necessary to use a more comprehensive battery of cognitive tests to understand how stress might act on different features of cognition, balanced with patient burden.

\textbf{1.9 Current study}

We aim to investigate the association between stress burden measured over five years and cognitive function in adults over 50 years old by building a cumulative stress burden (CSB) index. The cumulative stress burden index is comprised of self-reported stressors of psychological distress, unfair treatment, PTSD, social cohesion, walkability, and perception of neighborhood factors measured over several rounds of follow up assessment in a cohort of community dwelling older adults who live in two majority African American, low-income neighborhoods. Including adults in mid-life in this analysis is especially important given the population of interest: African Americans are likely to experience cognitive decline before age 65.\textsuperscript{63} Since those who are cognitive impaired potentially respond to stress differently than those who are cognitively normal, it is important to capture individuals prior to decline by using a cut off of 50 years old instead of a more typical 65 years old. Stressors were chosen based on previous research indicating potential associations between these factors and cognitive decline, in addition to plausible coherence and interrelatedness between these subjective variables.\textsuperscript{14,61,65} Furthermore, we chose the above predictors as they capture race-relevant stress, in order to study factors that contribute to the
disparity between AD prevalence in African American populations and White populations. In particular, social, neighborhood, and environmental level factors that contribute to economic and housing segregation have been shown to be related to poor health outcomes.\textsuperscript{13,14,66,67}

Using this CSB index, we hypothesize that those with higher cumulative stress will have lower overall cognitive function and lower cognitive function across all individual domains, with largest effect sizes in executive function and memory. Understanding how different levels (individual, social, and environmental) of stressors come together to impact cognitive function in this understudied population can provide insight on effective public policy and identify appropriate points for intervention.
2.0 Methods

2.1 Sample

Beginning in 2011, the Pittsburgh Hill/Homewood Research on Neighborhood Change and Health (PHRESH) study enrolled a longitudinal cohort comprised of community-dwelling adults from two low-income, predominantly African American neighborhoods that are sociodemographically and geographically similar. Within these neighborhoods, households were randomly selected from the Pittsburgh Neighborhood and Community System (PNCIS) coupled with the postal service data: recruiters went to selected addresses to enroll the household’s primary food shopper. As such, participants tended to be female. Data collection occurred in waves, with different measures collected annually or every other year. Additional details of recruitment and retention are detailed elsewhere.\textsuperscript{68,69}

Of this original PHRESH cohort, a subsample (n=253), called “Think PHRESH”, was enrolled in 2018 to undergo a neuropsychological evaluation. This subsample was enrolled through making contact with PHRESH participants over 50 years old with sufficient stressor data available, and consenting participants who agreed to completing a cognitive battery. Think PHRESH participants tend to be more often female and more educated than the original PHRESH cohort.
2.2 Cognitive function

Different domains of cognitive function were assessed, including executive, attention, memory, visuospatial, and language functions. Domains were created by first z-scoring individual cognitive test scores to have a within-sample mean of zero and a standard deviation of one, then grouping variables into overarching domains based on an iterative process using Cronbach’s alpha scores and theoretical understanding. For example, grouping tests for executive function based solely on alpha scores would be inappropriate, as executive function covers a wide array of cognitive abilities such as set-shifting, inhibitory control, and working memory. As such, this domain had a lower Cronbach’s alpha score due to the heterogeneous nature of the underlying cognitive processes, and subjective categorization based on theoretical understanding was also included. Cognitive z-scores were adjusted for age, gender, and education. Tests within each domain are listed below.

**General/global cognition:** Modified Mini Mental State Examination (3MS)\(^70\), Wide Range Achievement Test 3 (WRAT3)\(^71\)

**Attention:** Wechsler memory scale (WMS-III) digit span forward and backward\(^72\), Wechsler intelligence scale (WAIS-III) Digit Symbol Substitution Test, WAIS-III Digit Symbol Copy\(^73\)

**Executive:** Clock drawing test, Trails Making Test A and B\(^74\), Stroop Color and Word test\(^75\), Digit Ordering Test\(^76\)

**Language:** Boston Naming Test\(^77\), Controlled Oral Word Association Test (COWAT)\(^78\), Category fluency- Animals\(^79\)

**Immediate memory:** WMS-III Logical Memory I Story A and B\(^72\), CERAD Trials 1 through 3\(^80\), WMS-III Visual Reproduction Immediate\(^72\)
**Delayed memory:** WMS-III Logical Memory II Story A and B\textsuperscript{72}, CERAD long-delay recall\textsuperscript{80}, WMS-III Visual Reproduction Delayed\textsuperscript{72}

**Visuospatial:** WMS-III Visual Reproduction Copy\textsuperscript{72}

### 2.3 Individual-level stressors

#### 2.3.1 Post-Traumatic Stress

Symptoms of PTSD were assessed using the six item Post-Traumatic Stress Disorder (PTSD) Checklist (PCL-6) in 2016 and 2018.\textsuperscript{81} Participants were asked to consider how much the following items bothered them in the past month on a scale of one to five, with one being not at all to five being extremely: (1) repeated, disturbing memories, thoughts, or images of a stressful experience from the past, (2) feeling very upset when something reminded you of a stressful experience from the past, (2) avoided activities or situation because they reminded you of a stressful experience from the past, (4) feeling distant or cut off from other people, (5) feeling irritable or having angry outbursts, (6) difficulty concentrating. Scores were totaled across all six items, with a maximum score of 30. Higher scores indicate increased severity of PTSD symptoms.

#### 2.3.2 Psychological distress

Psychological distress was quantified using the Kessler 6 (K6) test in years 2013, 2016, and 2018 and the Patient Health Questionnaire-2 (PHQ-2) as used in years 2014 and 2015.\textsuperscript{82,83} For the K6 instrument, participants were how often they felt the following in the past 30 days: (1)
nervous, (2) hopeless, (3) restless or fidgety, (4) so depressed that nothing could cheer them up, (5) that everything was an effort, (6) worthless. Each item could be answered in a range of zero to four, with zero being not at all to four being all the time.

For the PHQ-2, participants were asked how often they experience (1) little interest or pleasure in doing things and (2) feeling down, depressed, or hopeless, on a scale of zero to three, with zero being not at all and three being nearly every day.

2.3.3 Unfair treatment

Unfair treatment was measured in years 2016 and 2018 using the Everyday Discrimination Scale, Short Version. Participants were asked how often they experienced the following five situations in the last 30 days: (1) you are treated with less courtesy or respect than other people, (2) you receive poorer service than other people at restaurants or store, (3) people act as if they think you are not smart, (4) people act as if they are afraid of you, and (5) you are threatened or harassed. Responses range from zero to five, with zero being never and five being almost every day.

2.3.4 Perceived stress

Perceived stress was measured by a four item survey in 2011, 2014, and 2018 with the following items, where participants were asked how often they felt: (1) unable to control the important things in their life, (2) confident about their ability to handle their personal problems, (3) things are going their way, (4) difficulties were piling up so high that they could not overcome them.
2.4 Social and environmental conditions

2.4.1 Perception of neighborhood environment

Neighborhood perception was measured using subscales adapted from the Neighborhood Environment Walkability Scale (NEWS) and supplemented with additional items about neighborhood infrastructure, satisfaction, and safety in 2011, 2016, and 2018.85,86 Item having to do with perception of neighborhood environment included but were not limited to: your neighborhood streets are well lit at night, the city steps and outdoor stairwells in your neighborhood are safe, there is so much traffic along nearby streets that it makes it difficult or unpleasant to walk in your neighborhood.

2.4.2 Social cohesion

Social cohesion was assessed in 2013, 2016 and 2018, using a six-item survey where participants were asked how much they agree or disagree with the following statements on a five-point likert scale from strongly disagree to strongly agree: (1) people in this neighborhood are willing to help their neighbors, (2) this is a close-knit neighborhood, (3) people in this neighborhood can be trusted, (4) people in this neighborhood generally don’t get along with each other, (5) people in this neighborhood do not share the same values, (6) people in this neighborhood look out for one another, whether they are standing on the streets, sitting on their porches, or just walking around.86
2.5 Covariates

Demographic and socioeconomic variables (age, gender, race, educational attainment, annual household income, marital status, whether there were children in the household, and years living in the current neighborhood) were self-reported at baseline in 2011.

2.6 Statistical analysis

We constructed an index in order to measure a more holistic construct of chronic stress among participants. As cumulative stress builds over the life course, we first aimed to consider the variability of individual stressors over time. All stressor variables used numeric, count data. We used group-based trajectory modeling (GBTM) for variables that were collected over three time points or more, and ANOVA for those collected at two time points, to assess any patterns of stress over time. These measures did not vary substantially over time. We used stressor values from 2018, as these responses had been reported more recently and closest to time of cognitive testing. More details on this preliminary predictor analysis are available in the Results.

In order to check if certain stressors tended to group together, we ran an exploratory factor analysis with a varimax rotation to find an optimal number of factors. These results were checked with a confirmatory factor analysis. Environmental factors and individual stressors clustered together with little overlap. As such, we created three CSB indexes, one for neighborhood factors, one for individual stressors, and one that combined both.

To create the CSB, stressor variables were dichotomized. Two individual stressors have clinical cut points built into the measures: psychological distress measured by the K6 test, and
PTSD measured by the PCL6 test. Approximately 18% of individuals were considered clinically distressed, and approximately 16% of individuals had PTSD. As such, the remaining individual stressors (perceived stress and unfair treatment) were dichotomized and recoded by splitting participants by top 20% of scores and bottom 80%. Dichotomized individual stressors were added together to create a CSB index ranging from zero to four with higher scores indicating a larger number of individual level stressors. Figure 1a shows the score distribution for the individual CSB index: the majority of individuals did not experience any individual level stressors.

Neighborhood level factors were dichotomized by median, and likewise added together to create a neighborhood CSB index ranging from zero to four with higher scores indicating a larger number of neighborhood level stressors. The two indices were added together to form a total CSB index ranging from zero to eight with higher scores indicating a larger number of stressors in general, including both neighborhood factors and individual stress. Figure 1b and figure 1c shows the score distributions for the neighborhood CSB index and full CSB index respectively.

The association between the CSB indices and both total cognitive function and cognitive function in different domains was assessed using generalized linear models with the inclusion of covariates. Covariates include neighborhood, household income, marital status, whether or not the participant had any children, and number of years living in the neighborhood. As the sample is a self-selected subsample of a larger study, weights are included to balance sex, education, and age differences between the subsample and the original sample.
3.0 Results

The analytic cohort includes 253 participants with complete cognitive data. Table 1 presents sample characteristics of the analytic cohort split by neighborhood. Participants were primarily female (82.2%), with a mean age of 66.6 years. Age, number of years living within the neighborhood, neighborhood satisfaction, neighborhood walkability, neighborhood safety, and experiences of unfair treatment differed significantly between neighborhoods. In particular, participants living in the Hill District report higher neighborhood satisfaction, walkability, safety, and number of years living in the neighborhood. Participants in living in the Hill District also report fewer experiences of unfair treatment.

3.1 Predictor variability

Predictor variability across time was analyzed using GBTM for variables collected at three time points or more: no significant trajectories emerged, and potential higher order groupings had poor posterior probabilities indicating that responses did not change over time. ANOVA was also run, revealing few significant differences in time points for stressor variables. Figure 2 shows predictor distributions for each time point a particular variable was collected, showing little change and constant distributions from year to year.
3.2 Factor analysis

Correlations between predictors show that there are stronger positive correlations between neighborhood factors and between individual factors, with smaller correlations between the two categories (Figure 3). To test these groupings, exploratory factor analysis was performed which determined that two was the optimal number of factors and revealed that environmental factors and individual stressors group together with little overlap. Confirmatory factor analysis was also performed to test the null hypothesis that the data contains two distinct factors and showed similar results with a comparative fit index of 0.975 and a Tucker-Lewis index of 0.962. As such, separate indices were created for environmental factors and individual stressors.

3.3 Generalized linear models with indices

In regression analyses, the individual CSB index was not significantly associated with global cognition in either unadjusted or adjusted models (p=0.12 0.12). Additionally, individual CSB is not associated with immediate memory, delay memory, or visuospatial function. However, individual CSB is significantly associated with attention in the unadjusted model (β= -0.099, p= 0.04), and marginally associated in the adjusted model (β= -0.086, p= 0.08). In contrast, individual CSB is marginally associated with executive function in the unadjusted model (β= -0.079, p= 0.05), and significantly associated with executive function in the adjusted model (β= -0.087, p=0.04). Individual CSB is associated with language in both the unadjusted and adjusted models (β= -0.10, -0.11, p= 0.04, 0.03).
Neighborhood CSB index was not significantly associated with global cognition in either unadjusted or adjusted models. Likewise, neighborhood CSB is not significantly associated with any particular cognitive domain in either model. When individual and neighborhood indices are added, only association with language persists with significant associations in both the unadjusted and adjusted models ($\beta = -0.086, -0.103, p = 0.02, 0.01$).

### 3.4 Generalized linear models with stressors

When all four components of the individual CSB index are used rather than the index itself, there are likewise no significant associations between any stressor and global cognition. Perceived stress alone is marginally associated with attention in the unadjusted model ($\beta = -0.27, p = 0.05$): however, there is no significant association in the adjusted model. In models with other domains, no individual stressor reveals significant associations.
4.0 Discussion

In a cohort comprised of 253 individuals recruited from primarily African American neighborhoods in Pittsburgh, PA, self-reported individual level cumulative stress was negatively associated with certain domains of cognition: attention, executive function, and language in particular. In other words, increased individual stress is related to lower cognitive function within these domains. Results persist after adjusting of covariates such as neighborhood, household income, marital status, whether there were children in the household, and years in the neighborhood.

However, a CSB index using only neighborhood level factors did not show significant associations with cognition generally or with any cognitive domain. Likewise, a full index including both neighborhood level factors and individual stressors did not show significant associations with cognition, except with the language domain. These results are likely driven by the strong, significant effect size with individual level stressors rather than a combined effect of neighborhood effects and individual stressors together. As such, these results suggest that cumulative individual stress may contribute to poorer attention, executive function, and language function in African American adults over 50 years of age.

We are unaware of previous studies that have considered the effect of different neighborhood and individual stressors together. The current study also includes a comprehensive and rigorous cognitive battery split by domain using both theoretical and statistical considerations. Other studies have often used single tests to define specific domains or have not considered separate domains at all. Additionally, this study fills an important gap in understanding how these stressors may affect African American communities specifically, with emphasis on how one’s
environment and neighborhood can have a unique influence on what stressors individuals experience. Furthermore, existing literature is mostly cross-sectional, and potential changes in stress over time are not considered. The current study examines potential variability in stressors over up to five visits.

Effect sizes for the association between the individual CSB index and cognition are meaningful. Here, we quantify cognition is by z-score, where scores are meaned at 0 with a standard deviation of 1. As such, we interpret coefficient estimates relative of the mean and standard deviation of the sample as whole. For instance, a one unit increase in individual CSB index (as defined as the addition of another stressor), is related to a 11% standard deviation decrease in language.

Further, results show that when stressors are considered separately, there is not a significant association with cognition with any individual stressor. This indicates that cumulative stress is related to cognition in this cohort, as the combination of individual stressors in an index is significantly associated with particular domains while individual stressors themselves are not. In contrast with the current analysis, past research has found significant associations between single measures of stress and cognition is other cohorts.\textsuperscript{34,35,37,40} The current study differs from past studies in that the Think PHRESH cohort is primarily African American and includes older adults starting at 50 years old. Additionally, participants are recruited from two neighborhoods who are undergoing different stages of socioeconomic change: the Hill District has been undergoing substantial economic revitalization where Homewood has not. As such, there is unique natural variability in stressors in this otherwise fairly demographically homogenous cohort which allows us to better understand how these risk factors affect cognition in mid- to late-life African Americans specifically.
Considering cohort differences, these results are consistent with literature on weathering effects in African American participants, as chronic cumulative stress in this population, that builds from various stressors rather than acute events or one source of stress, has been linked to poorer health outcomes. Additionally, these results suggest that the force of neighborhood level factors that feed into weathering effects may not be evident by considering neighborhood level features alone. Instead, stress assessments require the measurement of self-reported stressors.

Although specific mechanisms for why cumulative stress may affect the domains of attention, executive function, and language specifically are unclear, past literature on the effect of cortisol suggests that increased cortisol can be neurotoxic to particular areas of the brain, such as the prefrontal cortex and temporal regions, and potentially increase dementia risk. These regions have been associated with attention, executive function, and language. Other studies have considered the effect of cortisol on cognitive outcomes; however, taking cortisol levels alone as a proxy for stress loses dimension as particularities about a participant’s unique context is lost, which also limits applicability to prevention efforts. The current study provides key evidence that self-reported cumulative stress, rather than acute stress events or one type of stress, impacts cognition. Clinically, this may influence screening for alterable stressors for adults reporting cognitive changes or decline. Furthermore, these results could incentivize cognitive testing in more disadvantaged neighborhoods where such stressors are more prevalent.

This study has several limitations. First, the study population is comprised of older African American participants living in a regionally select urban setting. Additionally, participants in this cohort tended to be female and also stay in their neighborhoods for a considerable amount of time (mean of 33.07 years), which may compound effects of stress. On the other hand, neighborhood level factors can also buffer against effects of stress, where, for example, strong ties to within-
neighborhood support structures and constant access to ample resources can decrease the effects of other stressors. As such, results from this analysis may not be generalizable to older adults living in substantially different settings. Second, this cohort is self-selected from a larger cohort. In this case, these participants were more likely to be female, younger, and more educated. To offset these differences, weights were added to regression models to balance these factors with the original cohort. Third, the analysis is primarily cross-sectional as only stressor and cognitive data from 2018 was considered. However, this data was selected only after analyzing stressor variability over time. Preliminary analyses showed that level of stress did not change over follow up. As such, only most relevant and complete data was used: this analysis used data collected in 2018 as it included all stressors and was collected closest in time to cognitive data.

In conclusion, this analysis used data from a sample of African American adults aged 50 years and older to assess the effect of cumulative stress on cognition. This study provides evidence that increased stress negatively affects cognition in older adults and suggests that a comprehensive, cumulative assessment of stress is vital to understand the dimensionality of racialized stress arising from individual, social, and neighborhood level factors. Clinical implications of this work include evidence for the benefit of increased cognitive screening in at risk populations and neighborhoods and potential stress screens in individuals reporting cognitive decline. Additionally, this analysis provides evidence for the public health relevance of interventions in African American neighborhoods aimed at decreasing experiences of stress. Understanding how stress impacts cognition in African American communities is key to developing relevant and effective prevention interventions.
Appendix A Tables and Figures

Figure 1: Cumulative index distributions
Table 1: Sample characteristics of the Think PHRESH cohort by neighborhood

<table>
<thead>
<tr>
<th></th>
<th>Total (n=253)</th>
<th>Hill District (n=171)</th>
<th>Homewood (n=82)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>66.60 (9.39)</td>
<td>65.84 (9.43)</td>
<td>68.20 (9.18)</td>
<td>0.06</td>
</tr>
<tr>
<td>Sex (female, %)</td>
<td>208 (82.2)</td>
<td>144 (84.2)</td>
<td>64 (78.0)</td>
<td>0.31</td>
</tr>
<tr>
<td>Household income (mean, SD)</td>
<td>21333.99 (19191.86)</td>
<td>20672.51 (19430.90)</td>
<td>22713.41 (18725.61)</td>
<td>0.43</td>
</tr>
<tr>
<td>Years of education (mean, SD)</td>
<td>12.59 (2.22)</td>
<td>12.41 (2.14)</td>
<td>12.98 (2.35)</td>
<td>0.06</td>
</tr>
<tr>
<td>Any children in the household? (n, %)</td>
<td>55 (21.7)</td>
<td>36 (21.1)</td>
<td>19 (23.2)</td>
<td>0.83</td>
</tr>
<tr>
<td>Years in nbhd (mean, SD)</td>
<td>33.07 (22.4)</td>
<td>39.00 (21.58)</td>
<td>20.70 (18.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Marital status (married, %)</td>
<td>47 (18.60)</td>
<td>30 (17.5)</td>
<td>17 (20.7)</td>
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</tr>
<tr>
<td>Nbhd satisfaction (mean, SD)</td>
<td>3.77 (1.08)</td>
<td>3.98 (0.98)</td>
<td>3.34 (1.15)</td>
<td>&lt;0.001</td>
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<tr>
<td>Nbhd walkability (mean, SD)</td>
<td>8.30 (1.96)</td>
<td>8.95 (1.84)</td>
<td>6.92 (1.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nbhd safety (mean, SD)</td>
<td>2.88 (0.90)</td>
<td>3.08 (0.86)</td>
<td>2.44 (0.85)</td>
<td>&lt;0.001</td>
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<tr>
<td>Social cohesion (mean, SD)</td>
<td>3.31 (0.75)</td>
<td>3.30 (0.74)</td>
<td>3.32 (0.76)</td>
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<tr>
<td>Perceived stress (mean, SD)</td>
<td>4.22 (3.17)</td>
<td>4.38 (3.17)</td>
<td>3.89 (3.16)</td>
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</tr>
<tr>
<td>Psychological distress (mean, SD)</td>
<td>3.88 (4.22)</td>
<td>3.68 (3.96)</td>
<td>4.28 (4.72)</td>
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<tr>
<td>Unfair treatment (mean, SD)</td>
<td>4.23 (4.38)</td>
<td>3.81 (4.36)</td>
<td>5.09 (4.31)</td>
<td>0.03</td>
</tr>
<tr>
<td>PTSD score (mean, SD)</td>
<td>10.10 (4.18)</td>
<td>10.02 (4.15)</td>
<td>10.26 (4.27)</td>
<td>0.67</td>
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</table>
Figure 2: Variable distributions across time
Figure 3: Correlations between stressors
Table 2: Associations between individual CSB index and cognition

<table>
<thead>
<tr>
<th>Outcome</th>
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<th>Adjusted</th>
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<td></td>
<td>Estimate</td>
<td>SE</td>
<td>p-value</td>
<td>Estimate</td>
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<td>3MS score</td>
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<td>-0.051</td>
</tr>
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<td>Global</td>
<td>-0.349</td>
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<td>-0.353</td>
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<tr>
<td>Attention</td>
<td>-0.099</td>
<td>0.049</td>
<td>0.04</td>
<td>-0.085</td>
</tr>
<tr>
<td>Executive</td>
<td>-0.079</td>
<td>0.040</td>
<td>0.05</td>
<td>-0.087</td>
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<tr>
<td>Language</td>
<td>-0.102</td>
<td>0.049</td>
<td>0.04</td>
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</tr>
<tr>
<td>Immediate memory</td>
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<td>0.049</td>
<td>0.42</td>
<td>-0.038</td>
</tr>
<tr>
<td>Delayed memory</td>
<td>-0.021</td>
<td>0.050</td>
<td>0.67</td>
<td>-0.017</td>
</tr>
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<td>Visuospatial</td>
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<td>0.069</td>
<td>0.85</td>
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</tbody>
</table>

*Separate model for each cognitive outcome
*Adjusted models covariates: neighborhood, household income, marital status, any children, years in the neighborhood. Cognitive outcomes have previously been adjusted for age, sex, and education.

Table 3: Associations between neighborhood CSB index and cognition

<table>
<thead>
<tr>
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<td>SE</td>
<td>p-value</td>
<td>Estimate</td>
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<td>0.057</td>
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<td>-0.071</td>
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<tr>
<td>Global</td>
<td>0.062</td>
<td>0.198</td>
<td>0.76</td>
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</tr>
<tr>
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<tr>
<td>Executive</td>
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<td>0.077</td>
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</tbody>
</table>

*Separate model for each cognitive outcome
*Adjusted models covariates: neighborhood, household income, marital status, any children, years in the neighborhood. Cognitive outcomes have previously been adjusted for age, sex, and education.

Table 4: Associations between combined index and cognition

<table>
<thead>
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<td>-0.070</td>
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<td>-0.039</td>
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<tr>
<td>Visuospatial</td>
<td>0.046</td>
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*Separate model for each cognitive outcome
*Adjusted models covariates: neighborhood, household income, marital status, any children, years in the neighborhood. Cognitive outcomes have previously been adjusted for age, sex, and education.
Table 5: Associations between individual stressors and cognition

<table>
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<td>SE</td>
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<tr>
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</table>

*Separate model for each cognitive outcome

*Adjusted models covariates: neighborhood, household income, marital status, any children, years in the neighborhood. Cognitive outcomes have previously been adjusted for age, sex, and education.
Bibliography


71. Wilkinson GS. Wide range achievement test–revision 3.


