HHS Public Access

Author manuscript

Psychoneuroendocrinology. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

Psychoneuroendocrinology. 2016 July ; 69: 90–97. doi:10.1016/j.psyneuen.2016.03.018.

Perceived neighborhood problems are associated with shorter telomere length in African American women

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Abstract

Objectives—African Americans (AA) experience higher levels of stress related to living in racially segregated and poor neighborhoods. However, little is known about the associations between perceived neighborhood environments and cellular aging among adult AA. This study examined whether perceived neighborhood environments were associated with telomere length (TL) in AA after adjustment for individual-level risk factors.

Methods—The analysis included 158 women and 75 men AA aged 30 to 55 years from the Morehouse School of Medicine Study. Relative TL (T/S ratio) was measured from peripheral blood leukocytes using quantitative real-time polymerase chain reaction. Multivariable linear regression models were used to examine the associations of perceived neighborhood social cohesion, problems, and overall unfavorable perceptions with log-TL.

Results—Women had significantly longer TL than men (0.59 vs. 0.54, p=0.012). After controlling for sociodemographic, and biomedical and psychosocial factors, a 1-SD increase in perceived neighborhood problems was associated with 7.3% shorter TL in women (Mean Difference [MD] = −0.073 (Standard Error =0.03), p = 0.012). Overall unfavorable perception of neighborhood was also associated with 5.9% shorter TL among women (MD = – 0.059(0.03), p= 0.023). Better perceived social cohesion were associated with 2.4 % longer TL, but did not reach statistical significance (MD = 0.024(0.02), p=0.218). No association was observed between perceived neighborhood environments and TL in men.

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Author Contributions: G.Y.S conceived the study concept and design and wrote the draft manuscript. G.Y.S. performed the statistical analysis. All authors of this manuscript have read and critically revised the manuscript for important intellectual content. All authors approved the final version submitted. S.K.D and G.H.G supervised the study, provided funding, administrative, technical and material support.

Conflict of Interest: None

Conclusions—Our findings suggest that perceived neighborhood environments may be predictive of cellular aging in AA women even after accounting for individual-level risk factors. Additional research with a larger sample is needed to determine whether perceived neighborhood environments are causally related to TL.

Keywords

African Americans; cellular aging; telomere length; stress; perceived neighborhood environments; psychosocial factors

Introduction

A large body of evidence suggests that neighborhood contexts are associated with a wide-range of health outcomes above and beyond individual-level risk factors and socioeconomic status (SES) (Diez Roux and Mair, 2010). However, the molecular or cellular mechanisms through which neighborhood contexts contribute to health outcomes are not well understood. Several recent studies have indicated that shorter telomere length (TL) is associated with increased risk of diabetes, hypertension, atherosclerosis, cardiovascular diseases (CVD), cancer and mortality(Cawthon et al., 2003, Blasco, 2005, Demissie et al., 2006, Salpea and Humphries, 2010, Sanders and Newman, 2013, Zee et al., 2010, Geronimus et al., 2010), although some studies have not replicated these associations (Bischoff et al., 2006, Carty et al., 2015). Therefore, TL may provide the biological link between neighborhood contexts and health outcomes.

Telomeres are nucleoprotein structures located at the ends of chromosomes, which play a vital role in providing genomic stability and maintaining chromosomal structural integrity (Blackburn, 2000). TL generally shortens progressively with every cell division and over the lifespan. A critically shortened TL triggers cellular senescence making TL a valuable biomarker for chronic stress and biological aging (Blackburn, 2000, Monaghan, 2010). Although genetic factors partially determine early life TL, evidence suggests that environmental factors may also affect TL in adulthood (Slagboom et al., 1994, Epel et al., 2004). Indeed, several studies have reported that telomere shortening is associated with various forms of chronic psychosocial stressors, such as life stress, low socioeconomic status, racial discrimination and depression (Epel et al., 2004, Simon et al., 2006, Geronimus et al., 2010, Price et al., 2013, Chae et al., 2014, Geronimus et al., 2015, Needham et al., 2015). Moreover, genetic factors and psychosocial stressors may further act synergistically to affect TL. For example, recent research found adverse social environment led to shorter TL in African American children with high risk of genetic variants in the serotonin and dopamine systems (Mitchell et al., 2014). Although the underlying mechanisms by which psychosocial stressors affect TL are not fully understood, it has been suggested that they may contribute to shorter TL by promoting oxidative stress and inflammation - two biological mechanisms that are known to cause accelerated TL shortening(Monaghan, 2010).

Aspects of neighborhood environments have also been suggested as sources of psychological and physiological stress (Ross and Mirowsky, 2001, Steptoe and Feldman, 2001, Burdette and Hill, 2008), and thus potential risk factors for cellular aging. Researchers hypothesize that residents who live in disordered neighborhood environments (e.g. problems with crime, vandalism, abandoned buildings, litter, poor quality of facilities, mistrust of neighbors) perceive their neighbors and neighborhoods less favorably and experience heightened psychological and physiological stress responses compared to residents who perceive their neighborhoods more favorably (Hill et al., 2005, Burdette and Hill, 2008). The constant exposure to a disordered neighborhood environment can lead to over-activation of multiple physiological systems, including the hypothalamic pituitary adrenal (HPA)-axis and sympathetic nervous system (SNS)(McEwen, 1998, Bird et al., 2010). Perpetual over-activation of these systems have been shown to increase allostatic load, inflammation and oxidative stress, which in turn are major cause of cellular degradation and TL shortening (Tomiyama et al., 2012, Monaghan, 2010). Additionally, residents who live in disordered neighborhood environments are more likely to engage in negative health behaviors (e.g., smoking, sedentary behaviors, alcohol drinking, and poor diet quality), which could have deleterious effects on cellular aging (Hill et al., 2005, Burdette and Hill, 2008). On the other hand, neighborhood social cohesion is hypothesized to influence psychosocial processes by generating mutual trust, meaningful social bonds among neighbors and strong social support mechanisms (Kawachi and Berkman 2000). These psychosocial resources can serve as a buffer against adverse effects of chronic stress, which may in turn decelerate cellular aging. In addition, social cohesion may also play a protective role against cellular aging by promoting rapid diffusion of health-related knowledge, increasing access to services and amenities and reinforcing social norms for positive health-related behaviors (e.g. walking or exercise, banning smoking and drinking in public) (Kawachi and Berkman 2000, Echeverría et al., 2008).

To date, there are only three empirical studies that have examined associations between perceived neighborhood environments and cellular aging. One study reported that parental perceived neighborhood disorder was associated with salivary TL in African American children (Theall et al., 2013). A study in economically advantaged older populations from New York and Los Angeles reported neighborhood perceived lower aesthetic quality, safety and social cohesion were associated with shorter leucocyte TL (Needham et al., 2014). Recent study in Dutch populations from the Netherlands also showed an association between perceived neighborhood quality and cellular aging (Park et al., 2015). To our knowledge, no study has examined the associations between perceived neighborhood environments and TL in adult African Americans from the southern United States.

More research in African Americans is especially needed given recent studies indicate that a steeper decline in TL with age in African Americans than in white (Diez Roux et al., 2009, Rewak et al., 2014). It has been suggested that cumulative exposure to multiple sources of psychosocial stressors over the lifecourse as possible contributors to faster TL shortening with age in African Americans (Diez Roux et al., 2009). While previous studies indicated that racial discrimination, perceived stress, and poverty are associated with TL among African Americans (Geronimus et al., 2010, Chae et al., 2014, Geronimus et al., 2015), the assocations between neighbrhood enviroments and TL in adult African Americans are not currently known. Researchers generally have shown that African Americans are more likely than whites or other racial groups to reside in neighborhoods with high levels of social and physical disorders often characterized by high rates of poverty, crime, noise, litter, trash, and environmental hazards (Williams and Jackson, 2005, Osypuk et al., 2009). Additionally, African Americans neighborhoods often lack the material and psychosocial resources (e.g. economic opportunities, quality health care, social network) necessary to cope with chronic stressors (Williams and Jackson, 2005). These stressful neighborhood environments can lead to physiological and psychological "wear and tear", which in turn may result in biological weathering of TL in African Americans. Therefore, understanding the relationships between perceived neighborhood environments and TL has the potential to elucidate the cellular mechanisms by which neighborhood stressors contribute to life-shortening diseases in African Americans.

In this study, we examined the associations between perceived neighborhood environments and TL in adult African Americans recruited from the South after adjusting for individual-level risk factors. We hypothesized that perceived neighborhood social cohesion would be associated with longer TL whereas perceived neighborhood problems and overall unfavorable perception of neighborhood would be associated with shorter TL. We also hypothesized that the associations between perceived neighborhood environments and TL would be attenuated after adjusting for individual-level sociodemographic variables, and CVD and psychosocial risk factors.

Materials and Methods

Population Study

Data for this study were obtained from the Minority Health Genomics and Translational Research Bio-Repository Database (MH-GRID) study, a multi-cohort case-control study of severe-controlled and resistant hypertension among African Americans aged 30 to 55 years from the Southern United States. Details of the MH-GRID study design are described in detail elsewhere (Horbal et al., 2016). In this study, analysis was focused on a subset of MH-GRID participants who were recruited from Morehouse School of Medicine (Atlanta, GA), Grady Health System (Atlanta, GA), Kaiser Permanent-Georgia (Atlanta, GA), and the Jackson-Hinds Clinic (Jackson, MS) between April 2012 and September 2013. These participants were chosen because they had data on TL and completed an extensive examination on socio-demographic, health behaviors, biomedical, psychosocial and neighborhood measures. In total, 373 participants had information on TL. After excluding missing data on socio-demographic, neighborhood measures, and biomedical risk factors as well as mismatch of self-reported sex with genotypic sex, analysis included 233 (158 women and 75 men) participants with complete covariate data. Informed consent was obtained from the participants included in the present analysis and the study was approved by the Morehouse School of Medicine, Kaiser Permanente, Grady Health System, Research Oversight Committee, and the National Institutes of Health Institutional Review Boards.

Relative Telomere Length Assay

TL was measured using genomic DNA extracted from peripheral blood leukocytes via frozen EDTA blood tubes using the EZNA blood DNA Midi Kit (Omega Bio-tek, Norcross, GA). The DNA concentration was measured using a NanoDrop Spectrophotomer (Thermo

Scientific, Wilmington, DE) and a dsDNA- intercalating dye (QuantiFluor, Promega, Madison, WI). TL measure was performed at the Cancer Genomics Research laboratory (CGR), National Cancer Institute using a technique adapted from Cawthon's quantitative real-time polymerase chain reaction (qPCR) protocol (Cawthon, 2002, Cawthon, 2009). This method measures TL as a ratio (T/S) of telomere repeat length (T) to copy number of a single copy gene, 36B4(S), within each sample.

4 ng of sample DNA, according to Quant-iT PicoGreen dsDNA quantitation (Life Technologies, Grand Island, NY), was transferred into LightCycler-compatible 384-well plates (Roche, Indianapolis, IN) and dried down. An internal standard curve (6 concentrations of pooled reference DNA samples spanning a 97.6-fold range in concentration, prepared by serial dilution) and randomly located internal QC samples utilized as calibrator samples were applied to the assay plates to guide analysis and indicate overall quality of assay performance. Additionally, an NTC was added to random well locations of 384-well plate to provide a unique fingerprint for each plate. All study and control samples were assayed in triplicate on each plate.

PCR was performed using 5 uL reaction volumes consisting of: 2.5 uL of 2X Rotor-Gene SYBR Green PCR Master Mix (QIAGEN, Germantown, MD), 2.0 uL of MBG Water, and 0.5 uL of 1 μM assay-specific mix of primers. Oligonucleotides (Integrated DNA Technologies, Coralville, IA) were manufactured in LabReady format (Normalized to 100 uM in IDTE, pH 8.0 and HPLC Purified). Primers for the telomeric PCR were *Telo_FP* [5'-CGGTTT(GTTTGG)5GTT-3'] and *Telo_RP* [5'-GGCTTG(CCTTAC)5CCT-3']. Primers for the single-copy gene (36B4) PCR were *36B4_FP* [5'-CAGCAAGTGGGAAGGTGTAATCC-3'] and *36B4_RP* [5'-CCCATTCTATCATCAACGGGTACAA-3']. 1 μM assay mixes were generated by combining 990 uL of 1X Tris-EDTA Buffer with 5 uL of forward oligo and 5 uL of reverse oligo. Thermal cycling was performed on a LightCycler 480 (Roche) where PCR conditions consisted of the following steps: Cycling for T (telomeric) PCR: 95°C hold for 5 min, denature at 98°C for 15 s, anneal at 54°C for 2 min, with fluorescence data collection, 35 cycles. Cycling for S (single-copy gene, 36B4) PCR: 98°C hold for 5 min, denature at 98°C for 15 s, anneal at 58°C for 1 min, with fluorescence data collection, 43 cycles.

Analysis of the PCR output was preformed using LightCycler software (Release 1.5.0), which used to generate the standard curve based on the maximum secondary derivative of each reaction and to determine the T and S copy numbers within each sample. The concentration of telomere (T) signal was divided by the concentration of 36B4 (S) signal to calculate T/S ratio. This raw T/S ratio was then divided by the average T/S ratio of the internal QC calibrator samples, within the same plate, to calculate the final standardized T/S ratio for each sample. In this study, the intra-class correlation coefficient (ICC) between the repeated measures was 0.89 (95% confidence interval: 0.84, 0.92) and the coefficient of variation (CV) was 5.95%. In our analysis, we used standardized log-transformed T/S ratio as an outcome of TL.

Perceived Neighborhood Environments

We used two perceived neighborhood scales that had been previously linked to stress. Perceived neighborhood social cohesion was assessed based on five items (Sampson et al., 1997) and neighborhood problems was assessed based on seven items (Ross and Mirowsky, 1999). Participants were asked to respond their level of agreement related to their neighborhood social cohesion using on a 5-point Likert scale (1=strongly disagree to 5=strongly agree) whether their neighborhood is ‘close knit’, and neighbors are willing to help each other, neighbors get along, neighbors can be trusted and neighbors share the same values. Responses to the five items were summed and divided by the total number of items to create a mean index of perceived social cohesion (Echeverría et al., 2008, Dulin-Keita et al., 2013, Martin et al., 2010). The reliability for the perceived social cohesion was acceptable (Cronbach’s alpha=0.70). Perceived neighborhood problems was assessed by asking participants using a 4-point Likert scale (1=not really a problem to 4 = very serious problem). The items included excessive noise, heavy traffic or speeding cars, lack of access to adequate food shopping, lack of parks or playgrounds, trash/litter, no sidewalks or poorly maintained sidewalks, and violence. Responses to the items were summed and divided by the total number of items in the scale to create a mean index of perceived neighborhood problems. The reliability for the perceptions of neighborhood problems was strong (Cronbach’s alpha=0.85). In addition to these two scales, we also combined the scores for perceived problems and social cohesion to create a summary index representing overall unfavorable perception of neighborhood. Perceived neighborhood social cohesion was reverse-coded before averaging so that a higher score for the summary index indicate a higher score of overall unfavorable perception of neighborhood.

Sociodemographic Characteristics

Sociodemographic factors include age (years), sex (female/male), marital status (married/ living with partner or not). Participants also reported the highest educational level completed. Education was categorized into three categories for this analysis (1) completed high school or less, (2) technical school certificate, some college, and associate degree, and (3) bachelor's degree, or graduate/professional degree. In addition, participants were asked to select their total gross family income in the past 12 months from 13 categories. Income was collapsed into 4 categories (<$20,000, $20,000–$34,999, $35,000–$74,999, or ≥$75,000) for the present analyses.

Covariates

Other covariates examined as possible confounders and/ or mediators included smoking status, alcohol consumption, body mass index (BMI), hypertension, fasting glucose (mg/dL), low density lipoprotein (LDL- mg/dL), high density lipoprotein (HDL- mg/dL) cholesterol, triglycerides (mg/dL), estimated glomerular filtration rate (eGFR) and albuminuria. Self-reported smoking status was assessed as never, former, current cigarette smoker. Self-reported alcohol consumption was also assessed as never, former, occasional and regular drinker. BMI was calculated as the measurement of weight (kg)/height $(m)^2$. Fasting glucose, LDL, HDL and triglycerides were measured using standard techniques by a commercial laboratory (Quest Diagnostics, Atlanta, and GA). Hypertension was defined as a systolic blood pressure of ≥140 mm Hg and ≤180 mm Hg, diastolic blood pressure of ≥90 mm Hg and ≤110 mm Hg, or the use of ≥ 2 medications for blood pressure for at least the last 3 months. eGFR was calculated according to the Chronic Kidney Disease Epidemiology Collaboration equation using age, sex, race, and serum creatinine concentration. Albuminuria was assessed as the urinary albumin-to-creatinine ratio. Smoking, alcohol, and hypertension status were used as categorical variables; and BMI, glucose, LDL, HDL, triglycerides, eGFR, and ACR were used as continuous variables. In addition, psychosocial factors were assessed using standardized questionnaires. Depression was assessed based on a 16-item scale developed by the Center for Epidemiology Studies Depression scale (CES-D) (Radloff, 1977), and perceived stress was assessed using the 14-item Cohen's scale(Cohen et al., 1983). Depression and perceived stress were used as continuous variables.

Statistical analysis

We first examined the distribution of selected individual-level characteristics and perceived neighborhood environments by sex. Differences between women and men were investigated using *t*-tests for the continuous covariates and chi-square tests for the categorical variables.

TL (T/S ratio) was log-transformed to improve the normality of the distribution before the analysis. Multivariable linear regression models were used to estimate mean differences in log-TL associated with a standard deviation increase in perceived neighborhood environments before and after adjustment for sets of covariates. Neighborhood predictors were transformed into SD units to allow comparison across the different measures. Perceived neighborhood environments were included as continuous variables because descriptive analyses did not show evidence of a threshold effect. Each neighborhood predictor was investigated separately in multivariable regression models. We fitted sequential models for each neighborhood predictor: Model 1 adjusted for socio-demographic factors, including age, marital status, education, and income. Model 2 further adjusted for CVD risk factors, including smoking, alcohol consumption, BMI, fasting glucose, hypertension, LDL, HDL, triglycerides, ACR, and eGFR. Model 3 additionally adjusted for depression and perceived stress, which may serve as potential mediators of the neighborhood-TL association. In order to investigate the independent effects of perceived social cohesion and neighborhood problems, we also fitted the same sequence of models by entering the two neighborhood predictors simultaneously in the same model. We also tested for interactions between perceived neighborhood variables and gender and hypertension. We found statistically significant interactions between gender and perceived neighborhood problems (p value for interaction = 0.050), so all analyses were stratified by gender. However, we found no evidence of interaction between neighborhood variables and hypertension (all p values for interactions were > 0.05). Residual diagnostics inspection showed that the models met the assumptions of linear regression. Moreover, the models were checked for potential outliers using regression diagnostics. The models were also checked for multicollinearity and found no evidence of variance inflation (VIF) more than 5. All analyses were conducted using SAS software (SAS Institute, Cary, NC).

Results

Table 1 shows the distribution of socio-demographic, CVD risk factors and perceived neighborhood environments by sex. Women comprised 68% of the sample and were similar in age with men. Most men were unmarried/ living with no partner, and had a high school education or less, and reported lower annual income than women. TL varied by sex, as women had significantly longer mean TL of 0.59 compared with 0.54 for men (p=0.012). Men were also more likely to smoke and consume alcohol, but had lower mean BMI and hypertension rates than women. There were no significant gender differences with respect to lipid profiles, fasting glucose, depression and stress. However, women were more likely than men to report higher perceived neighborhood problems (mean score 3.4 vs. 3.0) and lower perceived neighborhood social cohesion (2.6 vs. 2.7). Overall, women perceived their neighborhood more unfavorably than men (3.4 vs. 3.1). Bivariate relationships generally show low to modest correlations between perceived neighborhood environments and covariates (supplemental Table 1).

Table 2 shows sex–stratified adjusted mean differences of TL associated with perceived neighborhood environments. Estimates correspond to mean differences in log-T/S ratio of TL per 1-standard deviation (SD) increase in perceived neighborhood environments. Among women, 1-SD increase in perceived neighborhood social cohesion was associated with 1.7% longer TL after adjusting for sociodemographic factors (age, marital status, education, and income), but the association did not reach statistical significance (model 1: mean difference =.017, standard error (SE) =.02, p =0.365). Further adjustment for CVD risk factors (smoking, alcohol use, BMI, hypertension, glucose, LDL, HDL, triglycerides, ACR, and eGFR) (model 2: mean difference =.019, SE = .02, p=0321) and psychosocial factors (depression and perceived stress) (model 3: mean difference =.024, SE = .02, p=0218) did not substantially modify the association between social cohesion and TL.

Perceived neighborhood problems were inversely associated with TL among women. A 1-SD increase in perceived neighborhood problems was marginally associated with 4. 9% shorter TL among women after adjusting for sociodemographic factors (model 1: mean difference in TL = −.049, SE = .02, p=0.052). After adjustment for CVD risk factors, a 1-SD increase in perceived neighborhood problems was significantly associated with 5.6% of shorter TL (model 2: mean difference =−.056, SE=03, p=0.038). Further adjustment for depression and perceived stress, the association became significantly stronger (model 3: mean difference =−.073, SE=.03, p=0.012). In addition, overall unfavorable perception of neighborhood was significantly associated with 5.9% of shorter TL among women in a fully adjusted model (mean difference =−.050, SE =.02, p=0.023). When perceived social cohesion and problems were examined simultaneously in relation to TL among women (Table 3), 1-SD increase in perceived neighborhood problems was still associated with 6.9% shorter TL independent of social cohesion in a fully adjusted model 3 (mean difference = −.069, SE =.03, p=0.021). Among men, no association was found between perceived neighborhood environments and TL in any of the models. Overall, perceived neighborhood environments were more strongly associated with TL in African American women than in men.

Discussion

In this study, we examined the associations between perceived neighborhood environments and cellular aging in African Americans from the South. Our results suggest that higher perceived neighborhood problems were associated with 7.3% shorter TL among African American women. Furthermore, women with higher overall unfavorable perception of neighborhood had 5.9% shorter TL. These associations were generally robust even after adjustment for key confounders and hypothesized mediators of perceived stress and depression. We also observed that women with better perceived neighborhood social cohesion had longer TL, but the association was not statistically significant. However, there was no evidence of association between perceived neighborhood environments and TL in African American men.

Thus far there have been only three studies relating neighborhood environments to TL and they were limited to African American children, economically advantaged elderly populations or white populations. In a study of 99 African American children aged between 4 and 14 from New Orleans, Louisiana, Theall and colleagues found that children living in greater level of neighborhood disorder by the mother's appraisal had lower salivary TL than those who did not (Theall et al., 2013). The Multi-Ethnic Study of Atherosclerosis (MESA) has shown that perceived neighborhood environments related to aesthetic quality, safety, and social cohesion were associated with longer leukocyte TL in a multi-ethnic US sample aged between 45 and 84 (Needham et al., 2014). A recent study in a Dutch population from the Netherlands Study of Depression and Anxiety showed that perception of poor neighborhood quality was associated with a 174 base pair shorter TL (Park et al., 2015). Our study adds and extends to this limited literature by being the first to explore the associations between TL and perceived neighborhood environments in adult African Americans who live in more stressful neighborhood environments, a research topic previously investigated in children and white populations. Our findings suggest that neighborhood problems are associated with 7.3% shorter TL in African American women, even after taking potential confounders and/or meditators into account. In addition, the point estimate continued to suggest that African Americans women living in problematic neighborhoods were associated with 6.9% shorter TL, even after adjusting for perceived social cohesion. In contrast to the MESA study, we did not find significant association between perceived social cohesion and TL, although the direction of the association was in the expected direction as that of the MESA study. Additional studies involving longitudinal data are needed to determine whether neighborhood environments are causally related to TL in African Americans. Future studies should also consider additional dimensions of neighborhood social and physical environments, including objective measures to improve our understanding how different aspects of neighborhood environments contribute to cellular aging.

To the best of our knowledge, our study is the first to report sex differences in the associations between perceived neighborhood environments and cellular aging. However, our findings are in line with one previous study that has shown associations of TL with perceived stress and poverty in 117 African American women (Geronimus et al., 2010). In our study, shorter TL was strongly associated with neighborhood problems in African American women, but not in African American men. The reasons for the observed differences remain unclear. However, prior work has indicated that women and men differ in their perceptions, exposure, vulnerability and coping degree to the various aspects of neighborhood environments (Stafford et al., 2005), which could be one of the reasons for the observed gender differences in associations with TL. Women are especially more vulnerable than men to certain aspects of neighborhood environments due to their social roles whereas men may be more resilient or may have more resources to cope with neighborhood stressors than women (Stafford et al., 2005). Alternatively, differences in hormonal exposure related to menopausal status may also explain the observed associations among women. It has been suggested that not only is TL longer in women than in men, but also telomere attrition may vary by menopausal status caused by the effects of estrogen (Dalgård et al., 2015). Finally, the lack of association in men could simply be due to smaller sample sizes in our study. Although our results provide preliminary evidence of sex-specific difference in the associations of perceived neighborhood environments and TL, future studies should confirm these results in larger sample and clarify whether sex, menopausal status and sex-hormones are involved in modifying the relationships between perceived neighborhood environments and cellular aging.

The mechanisms by which neighborhood problems affect TL are not completely understood. However, one potential explanation for the observed associations is through psychological stress. Because of residential segregation, African Americans are more likely to live in disadvantaged neighborhoods characterized by higher rates of disorder, poverty, problems and violence, which leads to a host of mental and emotional problems, such as hopelessness, perceived stress, anxiety, and depression (Hill et al., 2005, Schulz et al., 2006, Gary et al., 2007). These psychological stressors have been linked to oxidative stress and shorter TL (Epel et al., 2004, Salim, 2014, Needham et al., 2015). In our study, however, adjusting for perceived stress and depression strengthened the association between perceived neighborhood problems and TL. This is consistent with one study that reported the association between poor neighborhood quality and shorter TL remained significant after adjusting for depression and anxiety, concluding that neighborhood quality affects TL above and beyond psychological stress (Park et al., 2015). Although we did not specifically investigate the role of HPA-axis as mediators in our study, perceived neighborhood problems may contribute to cellular aging through their effect on HPA-axis, including allostatic load, inflammatory mechanisms and oxidative stress. There is evidence that perceived neighborhood environments (such as problems, disorder and lack of social cohesion) are significantly associated with higher inflammation and oxidative stress (Nazmi et al., 2010, Schulz et al., 2012). Indeed, several studies have demonstrated that increased inflammations and oxidative stress are major risk factors of telomere shortening (O'Donovan et al., 2011, Tomiyama et al., 2012). Lastly, perceived neighborhood problems may indirectly affect TL by promoting negative health behaviors, such as smoking, lack of physical activity, and poor diet, which could potentially lead to cellular aging(Puterman et al., 2015). It is also important to note that TL is strongly influenced by genetic factors therefore it is possible that genetic factors could also modulate the associations of neighborhood environments with TL (Mitchell et al., 2014). Additional studies are warranted to elucidate the underlying mechanisms of the associations between neighborhood environments and TL. In addition, it would be also important future studies to consider the role of genetic variants in modulating the associations of neighborhood environments with TL.

An important strength of our study is the assessment of specific features of neighborhood environments with TL in a high- risk population of African Americans. To our knowledge, we are the first to report the associations between perceived neighborhood environments and TL in African American women, thus our findings contribute new evidence to the limited knowledge in this research topic. Moreover, our study adjusted for a large set of important covariates, including sociodemographic factors, health behaviors, CVD risk factors and psychosocial factors, which minimized the influence of confounding. Additionally, the use of reliable and well-validated measure of TL is another important strength of this study. However, our study has several limitations that must be considered when interpreting the results. The primary limitation of the study is that relatively small sample, especially among men may have limited our ability to draw firm conclusions. Thus, more studies involving large representative samples are necessary to clarify the relationships between neighborhood environments and TL. The cross-sectional nature of our study also precludes drawing causal inferences. Therefore, longitudinal studies are needed to determine whether the observed associations are causal and if so to identify the specific mechanisms involved. Additionally, our findings are based on perceived neighborhood measures; we did not have objective measures of neighborhood environments, which might lead to different relationships with TL. Another limitation is that although we were able to adjust for a comprehensive set of covariates in our caution to avoid residual confounding, over-adjustment may be biasing our findings. It may also possible that other unmeasured confounding may still exist resulting in “omitted variable bias” (e.g., menopausal status, sex hormones, diet, physical activity, and other age-related chronic diseases). Further, TL measure using Cawthon’s qPCR technique is subject to measurement errors thus may mask true associations between perceived neighborhood environments and TL, although this is less likely since our TL measure had higher accuracy with small coefficient of variations. Lastly, our findings are based on middle-aged African Americans from the South who had higher rates of severe hypertension; therefore, the findings may not be generalizable to older or other African Americans subgroups in other regions of the US.

In conclusion, perceived neighborhood problems are associated with shorter TL among African American women above and beyond individual-risk factors and social cohesion. Thus, our findings contribute further evidence to the limited literature that neighborhood problems as a source of chronic stress may lead to TL shortening. Although longitudinal studies are needed to better understand how the different aspects of neighborhood environments may affect TL, our results provide preliminary evidence that neighborhood environments may be a useful intervention target for reducing premature aging, age-related diseases and mortality in African Americans, particularly in African American women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research is supported by Intramural Program of National Human Genomics Institute, National Institutes of Health. The MH-GRID study was supported by the National Institute on Minority Health and Health Disparities (1RC4MD005964-01). We also thank Cancer Genomics Research laboratory (CGR) for performing telomere assay for our study and we also wish to thank Casey Dagnall for her helpful comments on telomere measures.

Role of the funding sources:

The funders had no role in the study design, analysis of data, interpretation of findings, or the writing of the manuscript. The findings and conclusions expressed in this article are those of the authors and do not necessarily represent the views of the National Institutes of Health (NIH) or the Department of Health and Human Services (DHHS).

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Highlights

- African Americans experience greater levels of neighborhood-related stress.
- We examined the relation between neighborhood environments and Telomere length (TL).
- Perceived neighborhood problems were associated with shorter TL in women.
- This association was independent of individual-level risk factors and social cohesion.
- Neighborhood environments appear to contribute to cellular aging in African American women.

Table 1

Distribution of selected individual-level characteristics and perceived neighborhood environments by sex in African Americans.

Characteristic	Women (N=158)	Men (75)	*p value
TL (T/S ratio), mean (SD)	0.59 (0.14)	0.54(0.12)	0.012
Age (years), mean (SD)	45.1(7.1)	46.4(6.8)	0.184
Marital status, % (married/ living with partner)	31.7	18.7	0.038
Education, %			0.002
High school or less	24.1	44..0	
Some college/associate degree	52.3	32.0	
College graduate	24.7	24.9	
Annual family income, %			
<$20,000	36.7	66.7	<.001
$20,000 –$34,999	17.1	13.3	
$35,000 –$74,999	31.7	5.3	
>$75,000	14..6	14.7	
Smoking status, %			<.001
Never	73.4	48.0	
Former	7.6	6.7	
Current	19.0	45.3	
Alcohol consumption, %			0.01
Never	26.0	4.7	
Former	16.5	28.0	
Occasional	33.5	21.3	
Regular	24.1	36.0	
Body mass index (kg/m^2), mean (SD)	35.2(7.7)	28.5(6.5)	<.001
Fasting glucose (mg/dL), mean (SD)	91.3 (13.2)	90.7(9.92)	0.716
Hypertension, %	75.3	50.7	<.001
LDL cholesterol (mg/dL), mean (SD)	110.2 (32.6)	111.0(29.9)	0.868
HDL cholesterol (mg/dL), mean (SD)	58.0(15.2)	59.7(17.3)	0.443
Triglyceride, mean (SD)	92.2 (41.8)	90.5(42.7)	0.778
eGFR, mean (SD)	100.0(19.0)	96.9(22.9)	0.052
ACR, mean (SD)	8.0(17.6)	7.6(10.6)	0.871
CES-D, mean (SD)	12.0(10.0)	13.0(9.7)	0.398
Perceived stress, mean (SD)	22.3(8.5)	22.1(9.1)	0.802
Perceived social cohesion, mean (SD)	2.6(0.8)	2.7(0.7)	0.130
Perceived neighborhood problems, mean (SD)	3.4(0.6)	3.0(0.8)	<.001
Overall unfavorable perception of neighborhood, mean (SD)	3.4(0.5)	3.1(0.6)	<.001

Abbreviation: TL, Telomere length; SD, standard deviation; LDL, low-density lipoprotein; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; ACR, albumin to creatinine ratio; CES-D, center for epidemiology studies depression scale.

* p value derived from student t-test for continuous variables and chi-square test for categorical variables.

Table 2

Adjusted mean difference in log telomere length (T/S ratio) corresponding to a one standard deviation increase in perceived neighborhood environments by sex in African Americans.*

Women (N=158)						
	Social Cohesion	***p* value**	**Neighborhood Problems**	***p* value**	**Unfavorable Neighborhood**	***p* value**
Model 1	.017 ± .02	0.365	−.049 ± .03	0.052	−.039 ± .02	0.090
Model 2	.019 ± .02	0.321	−.056 ± .03	0.038	−.044 ± .02	0.067
Model 3	.024 ± .02	0.218	−.073 ± .03	0.012	−.059 ± .03	0.023
Men (N=75)						
	Social Cohesion	*p* value	Neighborhood Problems	*p* value	Unfavorable Neighborhood	*p* value
Model 1	.009 ± .03	0.749	.004 ± .03	0.934	−.002 ± .03	0.951
Model 2	.012 ± .03	0.7203	.003 ± .03	0.909	−.004 ± .03	0.912
Model 3	.002 ± .03	0.843	.015 ± .03	0.620	.008 ± .03	0.794

Perceived neighborhood variables were entered into the models individually

*T/S was log transformed and all estimates were scaled to a one standard deviation increase in the perceived neighborhood variables.

Model 1 adjusted for sociodemographic variables (age, marital status, household income, education)

Model 2 adjusted for CVD risk factors (smoking, alcohol use, body mass index, hypertension, fasting glucose, LDL and HDL cholesterol, eGFR, ACR), in addition to the factors in model1

Model 3 adjusted for psychosocial factors (CES-D and perceived stress), in addition to the factors in model 2

Table 3

Adjusted mean difference in log telomere length (T/S ratio) corresponding to a one standard deviation increase in perceived neighborhood environments in African American women.*

	Model 1	***p* value**	**Model 2**	***p* value**	**Model 3**	***p* value**
Social Cohesion	.007 ± .02	0.719	.008± .02	0.678	.012 ± .02	0.557
Neighborhood Problems	−.047 ± .03	0.080	−.053 ± .03	0.063	−.069 ± .03	0.021

Perceived neighborhood social cohesion and problems were entered into the models simultaneously

*T/S was log transformed and all estimates were scaled to a one standard deviation increase in the perceived neighborhood variables.

Model 1 adjusted for sociodemographic variables (age, marital status, household income, education)

Model 2 adjusted for CVD risk factors (smoking, alcohol use, body mass index, hypertension, fasting glucose, LDL and HDL cholesterol, eGFR, ACR), in addition to the factors in model1

Model 3 adjusted for psychosocial factors (CES-D and perceived stress), in addition to the factors in model 2