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Race-Related Health Disparities and Biological Aging: Does Rate of Telomere Shortening Differ Across Blacks and Whites?

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Summary

Recent work suggests that leukocyte telomere length (LTL), a marker of cellular aging, is sensitive to effects of social stress and may also provide early indication of premature aging. Using data from a birth cohort with LTL information at birth and in middle adulthood we examined a potential source of race-based health disparity by testing the hypothesis that Blacks would demonstrate a faster rate of telomere shortening than Whites. Linear regression analyses were conducted and adjusted for pack years, BMI, education and social factors, diet, exercise, marital status, and age. At birth black individuals had LTLs that were longer, on average, than their White counterparts ($b = 3.85$, $p < 0.01$). However, rate of shortening was greater for Blacks, who showed a larger difference in length between birth and adulthood ($b = 5.10$, $p = 0.01$) as compared with Whites, resulting in smaller racial differences in absolute adult LTL.

Keywords

Telomere; social stress; race; human; telomere shortening; prospective follow-up; social disparities in health

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Conflict of Interest

All authors declare that they have no conflicts of interest.

Racial disparities in health have been well documented in the U.S. Racial disparities in health have been well documented in the U.S. with lower life expectancy, earlier onset of chronic diseases, and greater disability among Blacks relative to Whites (Murray et al., 2006; Williams & Mohammed, 2009; Wyatt et al., 2003). One explanation for these disparities is the “weathering” hypothesis put forth by Geronimus et al. (2006), which suggests that U.S. Blacks experience a faster rate of biological aging due to higher psychosocial stress levels and relative lack of resources. These “weathering” effects that lead to the observed higher rates of chronic illness and lowered life expectancy manifest in physical deterioration at earlier ages (Geronimus, Bound, Waidmann, Colen, & Steffick, 2001). Health-related effects of minority social status may therefore be evident well before development of significant chronic diseases.

Discussions of race-based disparities in aging and health frequently focus on measurement of extant disease and biological markers of health conditions (e.g., hypertension, low level inflammation) on the pathway to chronic health disorders. However, a number of recent studies have suggested that leukocyte telomere length (LTL), a marker of cellular aging, may be sensitive to effects of social stress (Cherkas et al., 2006; Epel et al., 2004; Epel et al., 2006; Simon et al., 2006) and also provide early indication of premature aging. Telomeres are base pair repeats located at the ends of chromosomes that serve to buffer and protect genetic information. With each cell replication, the number of base pairs in the telomeres at the distal ends of the chromosomes decreases (De Vivo et al., 2009). Telomeres shorten with age; for any chronological age, shorter LTL (measured by the number of base pairs at a given point in time) has been linked with premature mortality (R.M. Cawthon, Smith, O'Brien, Sivatchenko, & Kerber, 2003; Harris et al., 2006) and earlier development of chronic disease (Serrano & Andres, 2004; Wong & Collins, 2003), although the specific relationship between LTL and life expectancy has not been determined. Thus, examining LTL may allow for an examination of how health disparities influence health even prior to development of chronic disease.

Telomere length has a relatively short history of use as a marker for biological aging in studies of race-based health disparities. Given disproportionately high levels of poor health amongst Blacks, the prevailing expectation is that Blacks should have shorter telomeres relative to Whites. Surprisingly, most recent studies examining LTL indicate the opposite, suggesting that on average, Blacks have longer telomeres (Chen et al., 2011; Diaz, Mainous, Player, & Everett, 2009; Fitzpatrick et al., 2011; Hunt et al., 2008; Zhu et al., 2011). For example, a cross-sectional analysis of 2,453 adults found significantly longer LTLs among Blacks (female mean age 54.0±10.9 years, male mean age 52.4±10.6 years) compared with Whites (female mean age 58.5±13.1 years, male mean age 57.3±13.6 years) (Hunt et al., 2008), and similar results were obtained from a study of 667 adolescents (Zhu et al., 2011). Most recently, a cross-sectional study of 2,599 high functioning Black and White older adults reported shorter LTLs among older individuals with only a high school education versus those with post-high school education; effects were significantly stronger in Blacks versus Whites, and although Blacks had longer LTLs than Whites regardless of educational attainment, the difference was most pronounced among those with post-high school education (Adler et al., 2012).

However, LTL is not static across the life course and few studies have examined change in LTL over time. Considering the relationship between LTLs and race/ethnicity at more than one point in time either within or across individuals may help to understand cross-sectional differences reported between Blacks and Whites. For example, one study found no differences in LTL between Black and White newborns (Okuda et al., 2002). This has led some investigators to speculate that there is a slower rate of telomere shortening among Blacks between birth and early adulthood given earlier findings of longer LTL among Black adults (Adler et al., 2012; Hunt et al., 2008). They have further suggested that a faster rate of telomere length shortening only becomes evident at older ages (Hunt et al., 2008). Consistent with this, one national study of older U.S. adults (mean age over 60 years) found Blacks had shorter telomeres than Whites (Roux et al., 2009).

Contrary to the findings by Roux and colleagues, and in keeping with at least five studies that have shown longer LTLs for Blacks in mid-adulthood, two other studies of elderly adults found that Black Americans continued to have longer telomeres into late adulthood (Adler et al., 2012; Fitzpatrick et al., 2011). Because most findings are based on cross-sectional data, we cannot determine whether the discrepancies at older and younger ages are due to time-dependent processes or simply to variation between study samples. Thus, it is difficult to assess definitively whether a faster rate of telomere shortening in Blacks versus Whites occurs over time and becomes evident in later adulthood. We know of only one longitudinal study that has been conducted and considered changes in LTL at three time points across 12 years in middle adulthood. This study noted that LTL shortened over time among both Blacks and Whites but Blacks had consistently longer LTLs and a faster rate of shortening compared to Whites (Chen et al., 2011). We sought to extend previous research by examining change in LTL among self-identified Blacks and Whites within a birth cohort with telomere length information at birth and in middle adulthood. First, we tested whether LTL differed across racial/ethnic groups at birth or in middle adulthood. We expected to see no difference in LTL at birth in Blacks versus Whites and expected that Whites would have longer LTL in middle adulthood. Second, we tested whether change in LTL differed across racial group. We hypothesized that Blacks would demonstrate more telomere shortening than would Whites. Following previous work suggesting that a variety of psychological, social, and physiological factors can influence LTL changes (Adler et al., 2012; Cherkas et al., 2006; Epel et al., 2006; Valdes et al., 2005) we adjusted for demographic factors, health behaviors, and body mass index (BMI).

METHODS

Experimental Procedures

Sample—Study participants were from the New England Family Study (NEFS), which is comprised of 17,921 offspring of pregnant women enrolled into the Collaborative Perinatal Project (CPP) at the Providence, Rhode Island and Boston, Massachusetts sites (United States) between 1959 and 1974 (Niswander & Gordon, 1972). Cord blood samples, information on offspring birth outcomes and subsequent growth and development were obtained several times during the first year of life, and again at ages four and seven years. A sub-study of the NEFS, the EdHealth Study, was comprised of 914 participants selected with

preference for racial/ethnic minorities, low or high educational attainment, and assessed during 2005-2007. Of the 914 participants selected, 898 were eligible (e.g. living, not incarcerated), and 618 participated. EdHealth Study participants were interviewed in their home using a two-part protocol involving 1) a clinic-based assessment including anthropometric assessment and blood draw; and 2) a cognitive/interview assessment. Of 618 participants, 430 provided a blood sample. The study protocol was reviewed by the IRB of the Harvard School of Public Health; permission to assay the cord blood samples was granted by the Division of Epidemiology, Statistics, and Prevention Research (DESPR) at the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), NIH. Consent to use adult blood samples for future study was obtained from participants during the adult interview.

From the 430 EdHealth participants with blood samples, a subset was identified to investigate effects of social disadvantage on health. Participant inclusion for this substudy is detailed in Figure 1. Of the 430 participants, 378 had sufficient DNA volume for telomere assay, from which adult LTL was assessed. We excluded 4 participants with missing race/ethnicity data, and 15 participants that identified as Hispanic or “other race.” After exclusions, 359 individuals were available for analyses with adult LTL.

Infant LTL assays were conducted among a subset (n = 150) of these individuals, selected based on several criteria, including availability of both adult and infant blood samples, availability of measures of social disadvantage and psychosocial stress, and not having a sibling in the sample (siblings excluded to ensure independent observations). We compared participants in this sub-sample against the initial EdHealth sample (n = 618). They did not differ significantly on any demographic factors considered, including childhood socioeconomic status (SES), adulthood educational attainment, gender, or race/ethnicity. The 150-person sub-sample was an average of 1.7 years younger than the remainder of the EdHealth participants ($p < 0.001$). Considering the long-running nature of the parent study and the duration of time for which samples have been stored, there was no evidence to suggest that availability of infant blood samples was systematically patterned or due to factors beyond chance. Due to sample extraction problems (n=3), infant LTL measurements were only available for 147 individuals, and we further excluded individuals who identified as Hispanic or “other” racial/ethnic group (n=4), leaving a total of 143 Blacks and Whites with infant LTL measured. Tests that examined only adult LTL as the outcome included 359 participants but all other analyses used the smaller sample of 143 participants.

Measures

Leukocyte telomere length: Banked infant cord serum was initially frozen and maintained at a National Institute of Health storage facility (National Collaborative Perinatal Project, 1964). Adult blood samples were frozen and maintained in cryogenic storage facilities. Genomic DNA was extracted from infant cord serum and adult buffy coat samples using the QIAamp DNA Blood kit (QIAGEN, Valencia, CA). PicoGreen DNA quantitation was performed using a Molecular Devices 96-well spectrophotometer. Samples with sufficient genomic DNA were subsequently dried down and resuspended. The ratio of telomere repeat copy number to a single gene copy number (T/S) was determined by a previously described

high-throughput version (Wang et al., 2008) of the quantitative PCR-based telomere assay (R. M. Cawthon, 2002) run on the Applied Biosystems 7900HT PCR System (Foster City, CA). For each sample, the telomere and single-copy gene (36B4) reactions were performed in triplicate. The T/S ratio for each sample was calculated by subtracting the average 36B4 Ct value from the average telomere Ct value. As the infant and adult samples were assayed on separate occasions, the calibrator DNA to control for plate-to-plate variation differed. To retain our ability to directly compare infant and telomere values, we did not correct for the telomere values of the calibrator DNA, and used the uncorrected exponentiated T/S measure in analyses. Quality control samples were included to assess variability of threshold cycle (Ct) values and the exponentiated T/S ratio. We calculated coefficient of variation (CV) values for the birth and adult samples, first estimating average telomere Ct CV values and then CV values for the single gene Ct. Average telomere Ct CV value for the adult samples was 0.86 and the single gene Ct CV value was 0.62. For the birth telomere CV values, the value for the telomere Ct CV was 0.80 and the single gene Ct CV was 0.75. CV values for corrected and uncorrected exponentiated T/S measures of the adult samples were minimally different (uncorrected 8.78% vs corrected 8.75%). All birth samples were assayed on a single plate.

Covariates: Demographics included adult age, gender, self-reported race/ethnicity (White, Black), marital status, and educational attainment reported during the adult interview. Adult marital status was assessed by the question, “Are you married or living with a partner?” (yes/no). Educational attainment was measured in a series of categorical questions (e.g. Yes/No questions for grade completion prior to high school graduation, Yes/No high school graduation, Yes/No GED, categorical selection of school completed post-high school) from which we derived a measure of the total number of years of education used as a continuous variable in our analyses. Other covariates included interview site at enrollment; household income level at the time of the participant's birth (reported in U.S. dollars); parent education reported as highest level of education (in total years) by either parent at time of participant's birth.

Adulthood lifestyle factors included smoking pack years, and body mass index (BMI). Pack years were assessed by self-report items asking participants if they were ever daily or weekly cigarette smokers, number of years of smoking, and number of packs smoked daily during heaviest smoking phase. From these variables, we constructed a continuous measure of smoking pack years, ranging from 0 to 66. Participants’ height and weight were measured by research assistants at the study site, and adult BMI was calculated as the ratio of weight in kilograms to the square of height in meters (kg/m^2). Consumption of western diet was defined as consuming high levels of pork/lamb products, fish, whole milk, processed meat products, potatoes and vegetables (score constructed as a z score with ranges from −0.1 to 18.3 where higher positive score indicates greater consumption of Western diet). Levels of exercise were measured by responses indicating the number of hours/week spent in moderate and vigorous physical activity.

Statistical Analyses: Because the distribution of the adult LTLs was significantly positively skewed, prior to analysis adult LTL scores were Winsorized (Dixon & Yuen, 1974), and we

replaced the highest outlier values with the values of the 95th percentile, and lowest outlier values with the values of the 5th percentile. Birth LTLs were not significantly skewed and thus were not adjusted. We considered the use of log transformations on all outcome variables. As the same pattern of results resulted as with using untransformed outcome variables, we report findings with untransformed variables for ease of interpretation.

We used analysis of variance (ANOVA) and chi-squared tests to examine whether covariate distributions differed across each race-gender group. We also conducted t-tests and ANOVAs to assess associations between covariates and LTL. Finally, we conducted a series of linear regressions to test the relationship between race/ethnicity and LTL. When considering adult LTL, model 1 included race/ethnicity, interview site, adult age at time of follow-up, and gender; model 2 adjusted for covariates in model 1 as well as parent education at birth, parent income at birth, adult educational attainment and adult marital status; model 3 adjusted for all covariates in Model 2 as well as BMI, smoking pack years, Western diet consumption score, and physical activity. When considering birth LTL we ran two models: model 1 included race/ethnicity, gender and interview site, and model 2 adjusted for covariates in model 1 as well as parent education at birth and parent income at birth. Because the sample of 359 individuals with valid adult LTL assay results included siblings, regressions for the adult telomere measure only were conducted using PROC GENMOD, with siblings treated as clusters in the analysis. Due to missing data for covariates, the total number of participants contributing information to each model varied slightly, and our fully-adjusted model was missing 14.8% of participants (n=306) for adult model, 3.5% (n=138) for birth LTL model, and 14.0% of participants (n=123) for telomere difference model and telomere rate of change model. However, we performed a complete case analysis wherein we ran each model using the smallest participant sample size, and did not observe results that differed significantly from the ones we report here. In addition, we examined the number of individuals with missing covariates across each race and gender group, as well as evaluating missing telomere data by site, adult educational attainment, parental education and parental income at birth. We did not find any patterns in missingness for any group, with the exception of the western diet covariate. Black women were missing significantly more of the western diet variable, but we suspect this difference is only significant because of overall small sample size for Black participants; we do not believe this difference marks a significant difference in data collection or reporting for this variable.

To assess whether amount of shortening differs across race/ethnicity, additional analyses considered the difference between birth and adult LTL. For these analyses, we created a difference score by subtracting adult T/S from infant T/S (which are generally longer than adult telomere length), so that a larger difference score represents faster shortening in LTL from birth to adulthood. Because years of follow-up were equivalent between participants, the difference score serves as a proxy for rate of telomere length decrease over time, which renders this measure comparable to the rate measures used in previous research on telomere length changes over time (Chen et al., 2011; Ehrlenbach et al., 2009; Zhu et al., 2011). However, to determine whether race-based influences in telomere length shortening were important above initial differences in length at birth, we also constructed a telomere length rate of change score by subtracting adult T/S from infant T/S, then dividing by infant T/S. We then used a set of three linear regression models identical to those described above for

adult LTL to test whether the difference score or the rate of change score was associated with race/ethnicity. Further, we tested the relationship between birth LTL and the adult LTL outcome, and the relationship between birth LTL and the LTL difference score outcome, in linear regressions adjusted for age. Finally, we tested for possible race/ethnicity-by-gender interaction effects on LTL in adulthood, LTL difference score and LTL rate of change score by creating an interaction term and including it in the linear regression models along with the main effects.

RESULTS

Preliminary Analyses

Table 1 describes the demographics and distribution of covariates in our sample. The sample of 359 individuals with adult telomere measurements was 16% Black and 58% female. There was little age heterogeneity at the time of adult follow-up with all participants in their early 40s. Black men had significantly higher levels of vigorous physical activity compared to White and Black women, but were comparable to White men. Parent income at birth was significantly lower among Black versus White individuals. Black women were significantly less likely to be married or have a long-term partner in adulthood, and Black men attained significantly less education than did White women or men. White men had significantly higher BMI than White women, and Black women had significantly higher BMI compared to White women. None of the covariates were significantly associated with LTL. Although the smaller sample size changed the relationship between covariates slightly, we found similar patterns in the relationship across covariates in the birth telomere sub-sample.

In models with LTL at birth as the primary predictor, adjusted for age, birth LTL was not associated with adult LTL (0.01 ± 0.03, $p = 0.66$), but birth telomere length was strongly associated with the telomere difference outcome such that greater initial length lead to increased net difference over time ($b = 0.99$, SE = 0.03, $p < 0.0001$). We also performed sensitivity analyses which considered the potential role of chronic disease and maternal health indicators at participant's birth, but found no relationship of LTL with these factors or altered effects on the race-LTL relationship (see Supplement).

Telomere Length and Race/Ethnicity

As represented in Table 2 and Table 3, at birth and in adulthood, LTL was significantly associated with race/ethnicity. Compared with Whites, Blacks had longer LTLs at birth in the minimally-adjusted model ($b = 4.21$, SE = 1.34, $p < 0.01$). Gender was not associated with birth LTL. Minimally-adjusted models (model 1) and those additionally adjusting for parent education at birth, parent income at birth, adult educational attainment and adult marital status (model 2) suggested that Black participants also had longer LTLs in adulthood (*Model 1* $b = 1.0$, SE = 0.41, $p = 0.01$*; Model 2* $b = 1.0$, SE = 0.45, $p = 0.02$), and the effects remain significant after adjustment for additional covariates including BMI, pack years, Western diet score, and weekly hours of moderate and vigorous physical activity (*Model 3* $b = 1.07$, SE = 0.49, $p = 0.03$).

Analyses also indicated greater telomere shortening among Blacks from birth to adulthood compared with Whites, and the relationship became more pronounced when all covariates were included (*Model 1 b* = 3.63, SE = 1.45, $p = 0.01$; *Model 2 b* = 3.56, SE = 1.57, $p = 0.03$; *Model 3 b* = 5.10, SE = 1.89, $p = 0.01$). In rate of change analyses, Blacks continued to demonstrate a higher rate of telomere shortening, but the significance of the effects was somewhat attenuated (*Model 1 b* = 0.12, SE = 0.07, $p = 0.10$; *Model 2 b* = 0.12, SE = 0.08, $p = 0.11$; *Model 3 b* = 0.15, SE = 0.09, $p = 0.10$).

Telomere Length, Race/Ethnicity and Gender

Stratified analyses were conducted to assess whether relationships between race/ethnicity and LTL were similar for men and women (Tables 2, 3). Among men, race was significantly associated with adult LTL in Model 2 (*Model 2 b* = 1.97, SE = 0.95, $p = 0.04$), but this finding was not maintained after adjusting for additional covariates. Additionally, race/ethnicity was not significantly associated with birth LTL, birth-to-adulthood LTL changes or telomere rate of change among men. However, among women, race/ethnicity was significantly associated with LTL across time points. Black women had significantly longer LTL than White women at birth (fully adjusted *Model 2 b* = 5.92, SE = 1.76, $p = 0.001$). Findings were also evident for LTL in adulthood but associations were reduced in the fully adjusted model (*Model 1 b* = 1.45, SE = 0.54, $p = 0.01$; *Model 2 b* = 1.34, SE = 0.58, $p = 0.02$; *Model 3 b* = 1.17, SE = 0.70, $p = 0.10$). Models of change in LTL indicated Black women had a significantly *greater* reduction in telomere length between birth and adulthood relative to White women (*Model 1 b* = 5.16, SE = 1.80, $p = 0.01$; *Model 2 b* = 5.35, SE = 2.04, $p = 0.01$; *Model 3 b* = 7.40, SE = 2.48, $p < 0.01$). Black women also experienced higher rate of change in LTL between birth and adulthood (*Model 1 b* = 0.20, SE = 0.09, $p = 0.03$; *Model 2 b* = 0.20, SE = 0.09, $p = 0.04$; *Model 3 b* = 0.26, SE = 0.12, $p = 0.03$). A formal test of the interaction between race/ethnicity and gender was not significant for adult LTL, LTL difference scores or telomere rate of change scores, but was marginally significant for birth LTL scores after adjusting for parent education at birth and parent income at birth ($b = -5.03$, SE = 2.87, $p = 0.08$).

DISCUSSION

This is the first study to look at change in LTL over 40 years across race/ethnicity and gender groups. Our results are consistent with other studies considering the association between race/ethnicity and telomere length, but extend previous results by looking at change in telomere length over time across race/ethnic and gender groups. For example, the Bogalusa Heart Study and NHLBI study found longer LTL in middle-aged adults among U.S. Blacks compared to Whites, although this was not true among older adults (Chen et al., 2009; Hunt et al., 2008). In addition, these studies reported a steeper rate of decrease in telomere length among Blacks compared with Whites with older ages, extrapolated from cross-sectional data. This is congruent with our finding that Blacks have greater reduction in LTL between birth and adulthood relative to Whites.

Moreover, in the cross-sectional data available from the joint Bogalusa/NHLBI comparison, LTLs were longer among Blacks versus Whites when measured among those who were 20

years old, appeared more similar in length among those who were 50-60 years old, and then were shorter in Blacks than Whites among those older than 80 years (Hunt et al., 2008). Our findings of longer LTL at birth among Blacks with greater shortening in adulthood mirror patterns found in the combined cross-sectional data, but our use of a longitudinal dataset provides additional support for the validity of this pattern. Such findings help eliminate concerns that the age-related differences previously reported were merely an artifact of variation in prior study samples.

The pronounced race/ethnicity, differences in LTL found among women in our sample of middle-aged adults are similar to findings reported in other recent data. For example, in a cross-sectional study, Geronimus and colleagues (2010) examined 110 Black and 105 White women between the ages of 42 and 52 at baseline, who were participating in the Study of Women's Health Across the Nation (SWAN). After adjusting for poverty, smoking status, abdominal adiposity, and perceived stress, LTLs among Black and White women did not differ in adulthood until later middle age (ages 49-55 years) when Black women began to evidence significantly shorter telomeres than White women. Similarly, Okuda et al. (2002) examined telomere length amongst infants of different ethnic backgrounds (including Black, White, Hispanic, and other), and found that Black infants displayed longer telomere lengths in white blood cells and umbilical artery cells as compared to White infants, although these differences were not statistically significant. Our ability to consider LTL changes over time in Black men was limited by the small sample of Black men with LTL measures available at birth, and examination of these patterns is needed within a larger sample to determine if they hold for men. However, more generally our findings are highly consistent with prior cross-sectional findings of race/ethnicity differences in LTLs at different points in the life course. Moreover, many highly informative and well-regarded studies of LTL have been conducted with small samples ranging from 15 to 43 in each study group (Epel et al., 2004; Garcia-Rizo et al., 2012; Hoge et al., 2013; O'Donovan et al., 2011; Tyrka et al., 2010). Thus, while our sample is small, given the findings are in line with those from larger scale studies and offer the insight of approximately 40 years of follow-up, such findings are important and suggest the issue bears further investigation.

To explain initial longer telomere length observed in Blacks, several researchers have noted that white blood cell admixture differs by race (Lim, Cembrowski, Cembrowski, & Clarke, 2010),. Zhu and colleagues found that Black individuals have longer LTL in adolescence, and Hunt and colleagues present cross-sectional data that suggested LTL was longer in Blacks vs. Whites in young adulthood. As explanation, both sets of authors speculate that the lower rate of replications in hematopoietic stem cells and progenitor cells in Blacks may lead to longer telomere length in the early years of life (Hunt et al., 2008; Zhu et al., 2011). It is possible that similar processes could be present during prenatal development, leading to longer telomere length at birth for Black individuals. However, the admixture profile of white blood cells in our sample is unknown, so these factors cannot be measured in our data.

We found a strong relationship between longer telomere length at birth and change in telomere length from birth to adulthood, which is consistent with other work demonstrating that baseline length is the greatest predictor of the rate of telomere length decrease over time (Abraham Aviv et al., 2009; Nordfjäll et al., 2009). In addition, we found that initial length

did not serve as a predictor of adult length. The mechanism for this is unclear, but suggests a strong role for biological processes in the determination of shortening over time. However, despite the demonstration that early length is strongly associated with rate of shortening over time, our analyses indicated an effect of race which persisted after accounting for longer initial length in the outcome. Although these effects were less strong relative to the difference score analyses, stronger evidence for this relationship may be detectable in a larger sample.

Previous work has indicated that middle adulthood may represent a time during which telomere length differences between Blacks and Whites narrows, wherein Blacks have longer telomeres early in life, but their rate of telomere length shortening is faster compared with Whites (for reasons yet to be determined) (Chen et al., 2011; Hunt et al., 2008). We speculate that this period of narrowing may eventually lead elderly Blacks to have shorter telomere lengths compared to Whites. Thus, in older age, the shorter telomere length among Blacks may serve as a marker of increased risk for chronic disease and premature mortality. Our finding of greater shortening in LTL among Blacks between birth and adulthood may be consistent with the idea of greater “weathering” among Blacks versus Whites. In particular, the results of our rate of change analyses suggest that there may be a role played by race-related social factors in telomere length decrease over time. Social stress often clusters with other potentially harmful exposures including toxic physical (e.g., air pollution) and social environment (e.g., chaotic neighborhoods) (Clougherty et al., 2007). Thus, Blacks may age more rapidly in part because the experience of race-based discrimination in the U.S. leads to inadequate access to physical resources and because it is biologically taxing. In this way, experiences of discrimination and their associated coping strategies become reflected in the rate of cellular aging.

Somewhat surprisingly, in our study, beside race/ethnicity no other factors measured in either childhood or adulthood (including educational attainment, pack years, and BMI) were associated with change in LTL between birth and adulthood. It is possible that our study sample was too small to see these relationships; as Aviv and colleagues note, often large samples of participants are needed to see health and telomere effects in observational samples (A. Aviv, Valdes, & Spector, 2006). Moreover, unlike some previous findings that men have a faster rate of shortening than women, we did not find differences in telomere shortening between White men and women in our sample (Barrett & Richardson, 2011). In some models, our effect size decreased with increased numbers of covariates added to the model, but because we observed no links between any of our covariates and LTL, we believe this reduction is due to confounding between race and socioeconomic variables for which we were unable to completely adjust.

This study has several limitations. Our Black sample is small, which may increase the possibility that results were due to chance. Changes and patterns in telomere length may vary over childhood and later adulthood (Iwama et al., 1998). With measurements of telomere length only at birth and mid-adulthood, we may miss patterning in the changes that occur between those two times. Repeated measures over time and at other life stages would provide more detailed information and insight into when disparities in LTLs begin to be evident. Prior work has suggested some differences in total cell counts or proportion of cells

by race/ethnicity (Bain, 1996; Freedman et al., 1997; Grann et al., 2008; Lim et al., 2010). Information about leukocyte fractionation is not available for our samples, thus we were unable to directly assess whether this might account for some of our findings. However, other work has considered this issue in some detail and found little evidence to suggest that this could account for all racial/ethnic differences observed in telomere length (Hunt et al., 2008). In addition, although telomerase activity also gives important information about cellular aging, we were unable to perform this assay with blood samples that were available in this cohort. We were also unable to adjust for other exposures that may help account for racial differences in telomere length, such as history of child maltreatment (Tyrka et al., 2010) as they were not included in the original NCPP study. A final limitation was the necessity of measuring adult and birth telomere length at the same lab site, but at different time points. Although this may have introduced possible batch effects into our sample, this would have not have influenced race relationships within each age group; as these relationships remain consistent at both time points, this reduces concern about such effects in our models.

This study also has a number of strengths. Telomere length and changes in telomere length were assessed in a well-characterized and reasonably diverse cohort. Measures of potential confounders were available at two time points, birth and adulthood, and birth measures were prospectively assessed. Although one prior study has longitudinally examined the relationship between racial groups and telomere length change over a 12-year period in mid-adulthood (Chen et al., 2011), our birth samples allowed us to see how LTLs change over a significant period of the lifespan. Thus, to our knowledge this is the first study that can assess change in LTL between birth and adulthood. In addition, the extensive questionnaire data collected for this cohort at birth and follow-up allows us to place the results of this study inside a body of evidence which examines many other health and lifestyle characteristics.

Several notable findings emerge from this study. First, while Blacks had significantly longer LTL at birth compared with Whites, adult LTL did not differ as consistently. Second, between birth and adulthood, greater telomere shortening occurred among Blacks relative to Whites, with the findings most pronounced among Black women. We might speculate that with more years of follow-up differences would show more dramatic changes, and ultimately Blacks would have shorter telomeres than Whites. In fact, few studies to date have considered whether it is shorter telomere length per se that increases risk of chronic disease and premature mortality or if the rate of change itself is relevant. However, examination of factors that influence cellular aging and when they occur during the life course may provide important insight into the origins of social disparities in health. Such research may suggest whether there is a sensitive period during which certain exposures may be particularly potent with regard to telomere shortening. A greater understanding of the biology that may underlie social disparities in health will facilitate identification of prevention or intervention strategies for reducing these disparities.

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Highlights

!! We examined change in leukocyte telomere length (LTL) and its link with race

!! We used a unique data set containing data on LTL at birth and in mid-adulthood

!! Given links between LTL and disease, variation may point to racial health disparity

!! We propose Black individuals will have shorter LTL due to race-based social stress

!! Blacks begin with longer LTL than Whites, but undergo more rapid shortening

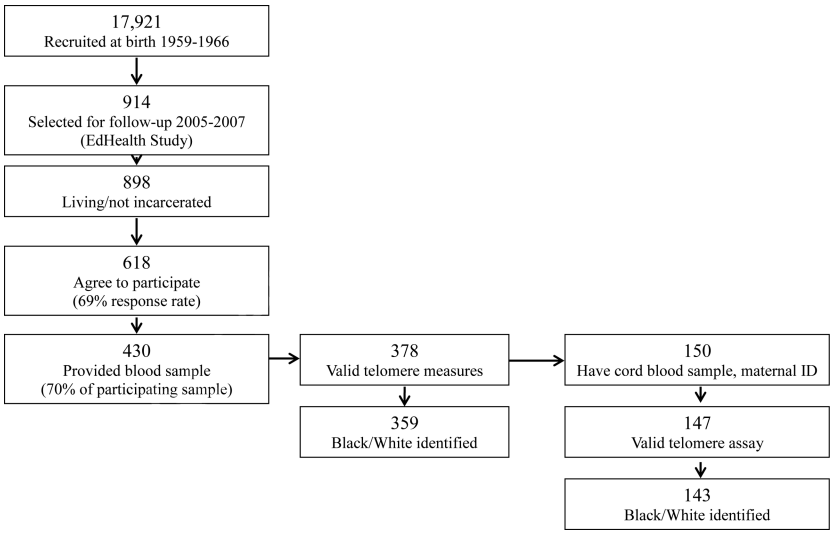

Figure 1.
Participant Flow Chart

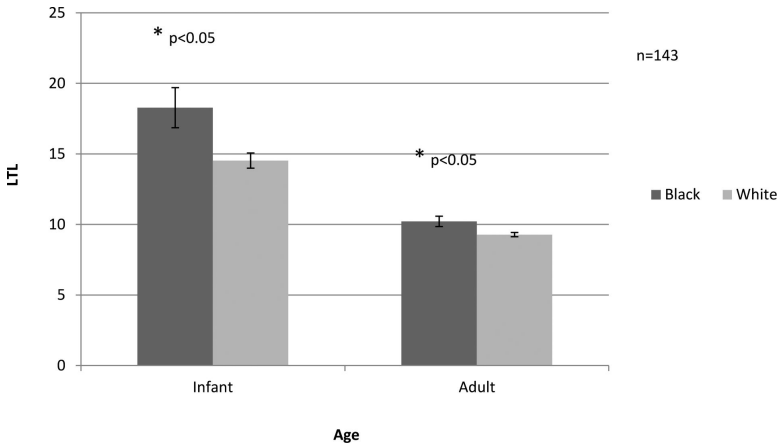

Figure 2.
Adult and infant LTLs – unadjusted

Table 1

General characteristics of study participants: Full group (n = 359) and birth telomere subsample (n =143)

	White		Black	
	Women	**Men**	**Women**	**Men**
N Full sample	n = 174	n =126	n = 36	n = 23
N Birth telomere sub-sample	n = 71	n = 45	n = 19	n = 8
Covariates – Childhood				
Parent income at birth ($)				
Full sample	5,089 ± 2,011^{A}	4,985 ± 1,991^{A}	3,388 ± 1,542^{B}	3,614 ± 1,915^{B}
Birth telomere sub-sample	5,062 ± 2,118^{A}	4,441 ± 1,956^{AB}	3,567 ± 1,705^{B}	3,975 ± 1,756^{AB}
Parent education at birth (years)				
Full sample	11.9 ± 2.4	12.1 ± 2.6	10.9 ± 1.9	11.3 ± 2.2
Birth telomere sub-sample	11.7 ± 2.9	12.0 ± 2.5	11.2 ± 2.2	11.6 ± 0.5
Covariates - Adulthood				
Age at follow-up (years)				
Full Sample	42.0 ± 1.7	42.3 ± 1.9	42.4 ± 2.0	42.6 ± 1.6
Birth telomere sub-sample	41.1 ± 1.2	41.4 ± 1.3	41.2 ± 1.4	41.0 ± 1.3
Adult education (years)				
Full Sample	13.8 ± 2.5^{A}	13.8 ± 2.7^{A}	13.2 ± 2.7^{AB}	12.1 ± 3.3^{B}
Birth telomere sub-sample	13.7 ± 2.6^{A}	13.6 ± 2.7^{A}	13.3 ± 2.5^{AB}	10.5 ± 4.2^{B}
Smoking Pack Years				
Full Sample	4.3 ± 7.5	4.9 ± 9.5	4.0 ± 7.5	1.6 ± 3.2
Birth telomere sub-sample	4.4 ± 7.4	5.4 ± 8.5	3.0 ± 5.6	0.2 ± 0.5
Married/living with partner (yes)				
Full Sample	75%^{A}	74%^{A}	42%^{B}	70%^{AB}
Birth telomere sub-sample	79%^{A}	62%^{AB}	42%^{B}	75%^{AB}
Boston Interview Site (yes)				
Full Sample	61%^{A}	56%^{AB}	14%^{B}	30%^{AB}
Birth telomere sub-sample	58%^{A}	53%^{AB}	21%^{B}	38%^{AB}
BMI (kg/m^2)				
Full Sample	27.8 ± 7.7^{A}	30.6 ± 7.3^{B}	31.7 ± 6.2^{B}	31.6 ± 9.8^{AB}
Birth telomere sub-sample	27.7 ± 9.2	30.2 ± 6.4	30.8 ± 5.6	34.6 ± 12.0
Hours/week moderate physical activity				
Full Sample	12.5 ± 16.6	12.0 ± 16.0	6.8 ± 7.8	15.0 ± 18.5
Birth telomere sub-sample	14.0 ± 16.2	12.3 ± 16.6	6.6 ± 7.3	16.7 ± 22.3
Hours/week vigorous physical activity				
Full Sample	3.1 ± 5.4^{A}	7.4 ± 2.3^{AB}	5.4 ± 14.3^{A}	11.7 ± 19.9^{B}
Birth telomere sub-sample	3.3 ± 3.9^{A}	7.9 ± 13.5^{AB}	8.0 ± 19.2^{AB}	18.0 ± 25.0^{B}

	White		Black	
	Women	**Men**	**Women**	**Men**
Western diet score				
Full sample	−0.01 ± 1.5	0.10 ± 0.5	0.06 ± 0.6	0.04 ± 0.6
Birth telomere sub-sample	−0.08 ± 0.6	0.12 ± 0.4	−0.15 ± 0.5	0.10 ± 0.5
Leukocyte Telomere Length (LTL)				
At birth				
Birth telomere sub-sample	14.5 ± 5.8^{A}	14.5 ± 5.9^{A}	19.7 ± 7.6^{B}	14.8 ± 5.8^{AB}
In adulthood				
Full Sample	9.3 ± 2.6^{A}	9.2 ± 2.6^{A}	10.6 ± 3.1^{B}	9.7 ± 2.4^{AB}
Birth telomere sub-sample	9.1 ± 2.3	9.1 ± 2.7	10.0 ± 3.0	8.9 ± 2.2
LTL differences (birth - adult)				
Birth telomere sub-sample	5.5 ± 6.3	5.5 ± 6.4	9.8 ± 8.0	6.0 ± 6.5
LTL rate of change				
Birth telomere sub-sample	0.27 ± 0.34	0.29 ± 0.32	0.43 ± 0.27	0.26 ± 0.49

Mean and standard deviation values reported for all variables unless otherwise indicated.

^{A}denote significant differences in the covariates across race/gender groups, tested by ANOVA or chi-squared tests. Sub-groups with different letter denotations are significantly different from one another, while sub-groups marked by the same letter (or left blank) are not significantly different. Sub-groups with two letters are not significantly different from either group.

^{B}denote significant differences in the covariates across race/gender groups, tested by ANOVA or chi-squared tests. Sub-groups with different letter denotations are significantly different from one another, while sub-groups marked by the same letter (or left blank) are not significantly different. Sub-groups with two letters are not significantly different from either group.

Table 2

Association of birth leukocyte telomere length and race (n=143)

	Model 1	Model 2
Birth LTL in full sample (n=143)		
Black race	4.21 ± 1.34, p=0.002‡	3.85 ± 1.40, p=0.007‡
Birth LTL in men (n=53)		
Black race	0.45 ± 2.30, p=0.85	0.32 ± 2.36, p=0.89
Birth LTL in women (n=90)		
Black race	6.13 ± 1.65, p<0.001‡	5.92 ± 1.76, p=0.001‡

Model 1 –adjusted by race, gender and research site

Model 2 - Model 1 plus parental income at birth, parental education at birth

Note: Gender stratified analyses not adjusted by gender

‡Significant relationship, p<0.05

Table 3

Association of Black race/ethnicity with adult leukocyte telomere length, changes in leukocyte telomere length, and gender

	Model 1	Model 2	Model 3
Full Sample			
Adult LTL (n=359)	1.00 ± 0.41, p=0.01‡	1.00 ± 0.45, p=0.02‡	1.07 ± 0.49, p=0.03‡
Birth-Adult LTL Difference (n=143)	3.63 ± 1.45, p=0.01‡	3.56 ± 1.57, p=0.03‡	5.10 ± 1.89, p=0.01‡
Birth-Adult LTL Rate of Change (n=143)	0.12 ± 0.07, p=0.10	0.12 ± 0.08, p=0.11	0.15 ± 0.09, p=0.10
Men Only			
Adult LTL (n=149)	0.44 ± 0.59, p=0.45	1.97 ± 0.95, p=0.04‡	0.84 ± 0.72, p=0.24
Birth-Adult LTL Difference (n=53)	0.79 ± 2.51, p=0.75	1.54 ± 2.84, p=0.59	2.70 ± 3.92, p=0.50
Birth-Adult LTL Rate of Change (n=53)	−0.02 ± 0.14, p=0.86	0.09 ± 0.14, p=0.53	0.11 ± 0.20, p=0.59
Women Only			
Adult LTL (n=210)	1.45 ± 0.54, p=0.01‡	1.34 ± 0.58, p=0.02‡	1.17 ± 0.70, p=0.10
Birth-Adult LTL Difference (n=90)	5.16 ± 1.80, p=0.01‡	5.35 ± 2.04, p=0.01‡	7.40 ± 2.48, p<0.01‡
Birth-Adult LTL Rate of Change (n=90)	0.20 ± 0.09, p=0.03‡	0.20 ± .09, p=0.04‡	0.26 ± 0.12, p=0.03‡

Model 1 - adjusted by race, age at follow-up, gender, research site

Model 2 – Model 1 plus parental income at birth, parental education at birth, marital status and adult educational attainment

Model 3 – Model 2 plus BMI, smoking pack years, western diet consumption, moderate physical activity and vigorous physical activity

Note: Gender stratified analyses not adjusted by gender, all parameter estimates are for Black race

‡Significant relationship, p<0.05