Neighborhood disorder and telomeres: Connecting children's exposure to community level stress and cellular response

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ABSTRACT

Our objective was to explore the utility of salivary telomere length (sTL) as an early indicator of neighborhood-level social environmental risk during child development. We therefore tested the hypothesis that sTL would be associated with markers of social stress exposure in children. Children age 4–14 from 87 neighborhoods were recruited through five urban schools in New Orleans, Louisiana, U.S. Data were collected at the level of the child, family/household, and neighborhood. DNA was obtained from saliva using commercially available kits and sTL was determined for 104 children using quantitative PCR. Analysis was performed on 99 children who had complete data including sTL, social environmental stress, and additional covariates. The mean sTL value was 7.4 T/S (telomere signal/single-copy signal) ratio units (± 2.4, range = 2.5–18.0), and 4.7% of the variance in sTL was attributed to differences across neighborhoods. Children living in neighborhoods characterized by high disorder had an sTL value 3.2 units lower than children not living in high disordered environments ($p < 0.05$) and their odds of having low relative sTL (defined as <1 standard deviation below standardized Z-score mean) values was 3.43 times that of children not living in high disorder environments (adjusted OR = 3.43, 95% CI = 1.22, 9.62). Our findings are consistent with previous studies in adults demonstrating a strong link between psychosocial stress and sTL obtained from peripheral blood, consistent with previous studies in youth demonstrating an association between early life stress and sTL obtained from buccal cell DNA and offer increased support for the hypothesis that sTL represents a non-invasive biological indicator of psychosocial stress exposure (i.e., neighborhood disorder) able to reflect differences in stress exposure levels even in young children.

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Introduction

The American Academy of Pediatrics recently emphasized the need to increase the understanding of the early roots of health disparities. They proposed the incorporation of an eco-biodevelopmental (EBD) framework that underscores the need to identify the biological indicators of exposure to early adversity, track these indicators across development, and use these indicators to unravel the underlying mechanisms, improve health outcomes, and minimize health disparities (Committee on Psychosocial Aspects of Child and Family Health, Committee on Early Childhood Adoption and Dependent Care, Section on Developmental and Behavioral Pediatrics, & American Academy of Pediatrics, 2012). This extension of the allostasis framework, and other more recent models, including the adaptive calibration model, together with the need to define the biological changes associated with potentially "toxic" early life stress requires the development of novel biomarkers that: reflect salient environments (Essex et al., 2011), are sensitive to changes across developmental time points (Buss, Davis, & Kiel, 2011), validated in individuals of all ages including young children, and, ideally, obtainable via non-invasive methods (Bush, Obradovic, Adler, & Boyce, 2011; Buss et al., 2011; Essex et al., 2011).

Telomeres represent one novel biomarker as they are (a) responsive to environmental changes and stressors, (b) have diverse effects in different organ systems, and (c) may be integral in the process by which an individual is able to calibrate their physiologic response to their social and physical environments (Lupien et al., 2006; Skinner, Shirtcliff, Haggerty, Coe, & Catalano, 2011). These are critical criteria for measures of the stress response system

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(Del Giudice, Ellis, & Shirtcliff, 2011) and indices of allostasis (McEwen, 2006). Allostasis is a model of physiologic regulation, whereby the goal of regulation is not constancy but fitness and change under natural selection to ensure regulation as opposed to an alternate model—homeostasis—where preserving constant conditions is the goal. Telomeres are specialized nucleoprotein complexes located at the termini of chromosomes that prevent genomic instability and ensure complete chromosomal replication. Telomere size normally decreases with cellular replication. Once a critically short length is reached cellular senescence is triggered. However, telomeres are dynamic structures and additional processes can result in more rapid changes in both their length and distribution (Li & Lustig, 1996). Accelerated loss of telomere length from DNA extracted from whole blood (leukocyte TL, LTL) has been associated with multiple negative health outcomes across the lifespan, including cardiovascular disease, dementia, diabetes, and cognitive decline (Fitzpatrick et al., 2007; Martin-Ruiz et al., 2006). Environmental factors that have been associated with alterations of LTL include cigarette smoking (Valdes et al., 2005), radiation (Derradiji et al., 2008), oxidative stress (Bull & Fenech, 2008; Zglinicki, 2002), and, most recently, psychological stress exposure, including a history of early maltreatment, mood disorders, perceived stress, and stress related to high intensity care-giving (Kananen et al., 2010; Lung, Chen, & Shu, 2007; Sapolsky, 2004; Simon et al., 2006; Tyrka et al., 2009). Hypothalamic–pituitary axis (HPA) dysregulation and oxidative stress have also been associated with damage to telomere DNA and decrease TL (Choi, Fauce, & Effros, 2008; Sapolsky, 2004).

Previously, we have shown an association between cumulative exposure to early severe social deprivation as a result of institutional rearing and TL in children derived from buccal epithelial cells (Drury et al., 2011). Additionally, cross-sectional and longitudinal work by others has linked other measures of exposures to altered TL, specifically socioeconomic conditions and violence exposure (Hastings et al., 2011; Needham, Fernandez, Lin, Epel, & Blackburn, 2012; Shalev et al., 2012). While most studies have utilized DNA from whole blood, which contain predominately a mixed cell population of lymphocytes, previous studies in children have also utilized buccal epithelial cells. Saliva contains both lymphocytes and buccal epithelial cells, and thus has similarities, and differences, to both of the previously utilized sources of DNA in telomere studies. Although significant future research remains to be done examining the correlation between TL obtained from peripheral and tissue samples the establishment of TL measured from non-invasive sources as a feasible biological indicator of cumulative stress exposure, applicable even in young children (Drury et al., 2011; Kroenke et al., 2011), would significantly advance the field. Accelerated TL loss, and potentially other alterations in telomere dynamics triggered by cellular stress pathways, may link early adversity to life-long poor health outcomes (Adams & White, 2004; Geronimus, Hicken, & Keene, 2006).

Together these previous studies offer significant evidence supporting the hypothesis that TL reflects exposure at the individual level. However, no previous study has examined whether TL is associated with neighborhood risk above and beyond household and individual exposure risk. Although environmental conditions such as physical and psychosocial stress are believed to play an important role in producing and maintaining health disparities (Lee, 2002; Yen & Syme, 1999), differential exposure to negative environmental conditions among many low socioeconomic and minority populations may accentuate the negative impact (LaVeist & Wallace, 2000; Massey, 2001). Lower neighborhood socioeconomic position in the U.S. has been associated with significantly greater allostatic load (i.e., the cumulative wear-and-tear on physiological processes due to recurrent or chronic stress (McEwen, 1998)), independent of individual-level socioeconomic status (SES) (Bird et al., 2010; King, Morenoff, & House, 2011), with the strongest association observed among African Americans (Merkin et al., 2009). Stemming in part from disparities in neighborhood-level factors (Lupien et al., 2006), African Americans have been found to have more dysregulation in the hypothalamic–pituitary axis (HPA) compared to Whites (Chong, Uhart, McCaul, Johnson, & Wand, 2008; Skinner et al., 2011). Although most studies to date have focused primarily on neighborhood SES and similar constructs like socioeconomic position (SEP), additional distinct neighborhood conditions such as neighborhood social and physical disorder (Sampson & Morenoff, 2004) such as lawlessness, crime, abandoned buildings, would be predicted to further impact an individual's stress response system and may be one pathway through which SEP at the community level "gets under the skin". Neighborhood disorder is distinct from SEP and may represent indicators of neighborhood disinvestment that are beyond the control of the individual and may be one consequence of lower SEP in a neighborhood (Sampson & Morenoff, 2004). Furthermore, we examine both objective and subjective neighborhood environments and subjective disorder, in particular. Research has demonstrated a discrepancy between observed indicators of neighborhood environments and residents' perceptions or self-reports of those environments (Caughy, O'Campo, & Patterson, 2001; Lin & Moudon, 2010; Sampson & Raudenbush, 2004) and there is evidence to suggest that perceptions of neighborhood environments are shaped by both observed characteristics (e.g., observed neighborhood conditions) as well as subjective experiences associated with race, ethnicity and SEP (Krysan, 2002; Krysan & Farley, 2002; Sampson & Raudenbush, 2004).

We previously have demonstrated the impact of the cumulative neighborhood environmental risk, above and beyond household level exposures, on allostatic load among adolescents in the U.S. (Theall, Drury, & Shirtcliff, in press). To provide increased support for sTL as a biological indicator of stress exposure, defined at the level of the individual, household and community, we sought to connect these programs of research by testing the hypothesis that sTL represents a proximate biological indicator of adverse neighborhood conditions in a group of African-American children in the U.S. This would be the first study, to date, associating a cellular marker of stress exposure and aging with community level factors.

Materials and methods

Subjects

Children (one per household) and their families were recruited via active consent from January–May 2010 through five local public elementary and middle schools in an urban community in New Orleans, Louisiana as part of a larger study to examine neighborhood influences on childhood health disparities (Fig. 1, highlighted area). 87 Different residential census tracts were represented. A total of 199 children, ages 4–14 years, were enrolled; sTL was available for 104 African-American children, whose parents consented to saliva sampling, and 99 children were included in final modeling once all covariates were considered. Children without sTL data, or with incomplete data, did not differ significantly ($p > 0.05$) from children included in the final analysis on any measures. Data about the child were collected from parental caregivers about multiple levels of his/her social ecology (i.e., household and neighborhood).

This study was approved by the Tulane and Louisiana State University Institutional Review Boards. Written informed consent was obtained from caregivers and assent for children over age eight.