Health & Place 28 (2014) 167–172

Contents lists available at ScienceDirect

Health & Place

journal homepage: www.elsevier.com/locate/healthplace

Neighborhood characteristics and leukocyte telomere length: The Multi-Ethnic Study of Atherosclerosis

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ARTICLE INFO

Article history:
Received 7 November 2013
Received in revised form
1 April 2014
Accepted 26 April 2014

Keywords:
Neighborhood socioeconomic disadvantage
Neighborhood social environment
Telomere length
Cell aging

ABSTRACT

Telomeres are the protective caps at the ends of eukaryotic chromosomes. Telomeres get shorter each time a cell divides, and critically shortened telomeres trigger cellular senescence. Thus, telomere length is hypothesized to be a biological marker of aging. The purpose of this study was to examine the association between neighborhood characteristics and leukocyte telomere length. Using data from a subsample ($n=978$) of the Multi-Ethnic Study of Atherosclerosis, a population-based study of women and men aged 45–84, we found that neighborhood social environment (but not neighborhood socioeconomic disadvantage) was associated with telomere length. Respondents who lived in neighborhoods characterized by lower aesthetic quality, safety, and social cohesion had shorter telomeres than those who lived in neighborhoods with a more salutary social environment, even after adjusting for individual-level socioeconomic status and biomedical and lifestyle factors related to telomere length. Telomere length may be one biological mechanism by which neighborhood characteristics influence an individual's risk of disease and death.

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1. Introduction

People who live in socioeconomically disadvantaged neighborhoods tend to have greater morbidity (Diez Roux and Mair, 2010) and mortality (Meijer et al., 2012) than those who live in more advantaged neighborhoods, even after controlling for individual-level socioeconomic status (SES). Previous research suggests that this may be due, in part, to differences in physical and social features of neighborhoods, such as aesthetic quality, safety, and social cohesion, that shape exposure and vulnerability to stress (Diez Roux and Mair, 2010; Hill et al., 2005; Ross and Mirowsky, 2001). Several theoretical models propose that the chronic stress associated with social disadvantage contributes to wear and tear on the body, which accelerates the rate of decline in physiological functioning (Geronimus et al., 2006; McEwen, 1998).

Leukocyte telomere length (LTL) has recently emerged as a potential biomarker of cell aging (Der et al., 2012) and exposure to chronic stress (Epel, 2009). Telomeres cap the ends of chromosomes and promote chromosomal stability. Telomere shortening, which tends to occur with advancing chronological age (Aubert and Lansdorp, 2008; Frenck et al., 1998; Iwama et al., 1998), triggers cellular senescence (Blasco, 2005; Hayflick, 1965), a component of biological aging (Campisi and d'Adda di Fagagna, 2007). In support of the role of telomere length in aging and disease, a number of studies have found that shorter telomere length is associated with increased morbidity (e.g., Demissie et al., 2006; Fitzpatrick et al., 2007; Samani et al., 2001; Zee et al., 2010) and mortality (e.g., Bakaysa et al., 2007; Cawthon et al., 2003; Fitzpatrick et al., 2011; Weischer et al., 2012), independent of chronological age.

A growing body of evidence suggests that exposure to stressful life circumstances is associated with shorter telomere length (Damjanovic et al., 2007; Drury et al., 2011; Epel et al., 2004; Kananen et al., 2010; Tyrka et al., 2010). However, we are aware of only one previous study that investigated whether exposure to neighborhood stressors is associated with telomere length. In a small sample ($n=99$) of African–American children in New Orleans, Theall et al. (2013) found that neighborhood socioeconomic disadvantage and neighborhood disorder were associated with shorter telomeres. Observing a link between neighborhood stressors and telomere length would suggest that the chronic stress associated with neighborhood conditions has measurable biological consequences with possible implications for a range of health outcomes. In this study, we used data from the Multi-Ethnic Study of Atherosclerosis (MESA) to examine the association

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http://dx.doi.org/10.1016/j.healthplace.2014.04.009
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between neighborhood conditions and telomere length in a population-based sample of US adults.

1.1. Hypotheses

We hypothesized that (1) individuals living in socioeconomically disadvantaged neighborhoods would have shorter telomeres than those living in more advantaged neighborhoods and (2) individuals living in neighborhoods with poorer social environments, as indicated by lower aesthetic quality, safety, and social cohesion, would have shorter telomeres than those living in neighborhoods with more salutary social environments.

2. Data and methods

2.1. Data

The Multi-Ethnic Study of Atherosclerosis (MESA) is a population-based longitudinal study designed to identify risk factors for the progression of subclinical cardiovascular disease (CVD) (Bild et al., 2002). Between July 2000 and August 2002, 6814 white, African–American, Hispanic, and Chinese–American women and men aged 45–84 without clinically apparent CVD were recruited from six regions in the US, including Forsyth County, NC; Northern Manhattan and the Bronx, NY; Baltimore City and Baltimore County, MD; St. Paul, MN; Chicago, IL; and Los Angeles County, CA. Each Field Center recruited from locally available sources, which included lists of residents, lists of dwellings, and telephone exchanges, with the goal of obtaining balanced recruitment across strata defined by gender, race/ethnicity, and age. Additional information on study recruitment has been published elsewhere (Bild et al., 2002). Paper-based questionnaires were interviewer-administered. Field Center staff were responsible for data entry, and data are stored electronically at the MESA Coordinating Center at the University of Washington. Telomeres were assessed on a subsample of 978 white, African–American, and Hispanic MESA participants aged 45–84 years from the New York and Los Angeles sites who agreed to participate in an ancillary study examining the effects of stress on cardiovascular outcomes (the MESA Stress Study). Participants were enrolled in the order in which they attended the MESA exam, until approximately 500 participants were enrolled at each site. This resulted in an approximately random sample of white, African–American, and Hispanic participants from the New York and Los Angeles sites. This study was approved by the Institutional Review Boards of all MESA Field Centers and the MESA Coordinating Center.

2.2. Measures

2.2.1. Dependent variable

Telomere length was measured from baseline blood samples by quantitative PCR (Q-PCR) (Cawthon, 2002). Blood was collected by venipuncture and stored at -80° at the University of Vermont and the University of Minnesota. Each sample was amplified for telomeric DNA and for 36B4, a single-copy control gene that provided an internal control to normalize the starting amount of DNA. A four-point standard curve (2-fold serial dilutions from 10 to 1.25 ng DNA) was used to transform cycle threshold into nanograms of DNA. Baseline background subtraction was performed by aligning amplification plots to a baseline height of 2% in the first 5 cycles. The cycle threshold was set at 20% of maximum product. All samples were run in triplicate and the median was used for calculations. The amount of telomeric DNA (T) was divided by the amount of single-copy control gene DNA (S), producing a relative measurement of the telomere length (T/S ratio). Two control samples were run in each experiment to allow for normalization between experiments and periodical reproducibility experiments were performed to guarantee correct measurements. The intra- and inter-assay variability (coefficient of variation) for Q-PCR was 6 and 7%, respectively.

2.2.2. Independent variables

Neighborhood socioeconomic disadvantage scores for each neighborhood were created based on a principal components analysis of 16 census-tract level variables from the 2000 US Census. These variables reflect dimensions of education, occupation, income and wealth, poverty, employment, and housing. The neighborhood SES score is the weighted sum of the following six standardized variables, which accounted for 49% of the variance and loaded on the first factor: percent in census tract with a bachelor's degree; percent with a managerial/professional occupation; percent with a high school education; median home value; median household income; and percent with household income greater than $50,000 per year. Higher values on the scale indicate greater neighborhood socioeconomic disadvantage.

Neighborhood social environment is the sum of standardized conditional empirical Bayes estimate (CEB) scales for aesthetic quality, safety, and social cohesion. Information on neighborhood characteristics was obtained from questionnaires administered to MESA participants and to an auxiliary sample of other neighborhood residents in the New York site (Mujahid et al., 2007). Responses were aggregated across respondents in census tracts to create neighborhood-level measures of aesthetic quality, safety, and social cohesion. The CEB estimates are more reliable than the census-tract crude means because they borrow information from other census tracts in cases where the sample size per tract is very small. In addition, the CEB estimates adjust for important factors in survey response, including site, participant sex and age, and survey type (MESA or auxiliary sample).

The aesthetic quality scale was created by summing responses to three questions. Respondents were asked to report their level of agreement (1=strongly agree—5=strongly disagree) with the following statements: (1) there is a lot of trash and litter on the street in my neighborhood; (2) there is a lot of noise in my neighborhood; and (3) my neighborhood is attractive. Item (3) was reverse coded so that higher values on this scale indicate better aesthetic quality. Cronbach's alpha for the aesthetic quality scale was.67.

The safety scale was created by summing responses to two questions. Respondents were asked to report their level of agreement (1=strongly agree—5=strongly disagree) with the following statements: (1) I feel safe walking in my neighborhood day or night; and (2) violence is a problem in my neighborhood. Item (1) was reverse coded so that higher values on this scale indicate greater perceptions of safety. Cronbach's alpha for the safety scale was.64.

The social cohesion scale was created by summing the responses to four questions. Respondents were asked to report their level of agreement (1=strongly agree—5=strongly disagree) with the following statements: (1) people around here are willing to help their neighbors; (2) people in my neighborhood generally get along with each other; (3) people in my neighborhood can be trusted; and (4) people in my neighborhood share the same values. All items were reverse coded so that higher values on this scale indicate greater social cohesion. The Cronbach's alpha for the social cohesion scale was.72.

Higher values on the original neighborhood social environment scale, which combines information from the aesthetic quality, safety, and social cohesion scales, indicate a better overall social environment. For this analysis, we multiplied the original scale

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