Brain, Behavior, and Immunity 25 (2011) 1292–1298

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

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

Educational attainment but not measures of current socioeconomic circumstances are associated with leukocyte telomere length in healthy older men and women ☆

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ARTICLE INFO

Article history:
Received 21 February 2011
Received in revised form 1 April 2011
Accepted 15 April 2011
Available online 23 April 2011

Keywords:
Socioeconomic status
Telomeres
Education
Biological aging

ABSTRACT

Low socioeconomic status (SES) may be associated with accelerated biological aging, but findings relating SES with telomere length have been inconsistent. We tested the hypotheses that shorter telomere length and telomerase activity would be related more robustly to education, an early life indicator of socioeconomic position, than to current indicators of socioeconomic circumstances. Healthy men and women aged 53–76 years from the Whitehall II epidemiological cohort provided blood samples from which telomere length was assessed in 448 and telomerase activity in 416. Educational attainment was classified into four levels, while household income and grade of employment were measured as indicators of current socioeconomic circumstances. Age, gender, blood pressure, glycated hemoglobin, high density lipoprotein cholesterol, smoking, body mass index and physical activity were included as covariates. We found that lower educational attainment was associated with shorter telomere length after controlling statistically for biological and behavioral covariates. Neither household income nor employment grade was related to telomere length. The association between telomere length and education remained significant after adjusting for current socioeconomic circumstances. In men, highest levels of telomerase activity were found in the lowest education group. We conclude that low SES defined in terms of education but not current socioeconomic circumstances is associated with shortened telomeres. Low educational attainment may be an indicator of long-term SES trajectories, and be associated with accumulated allostatic load resulting in telomere shortening. Education may also promote problem-solving skills leading to reduced biological stress responsivity, with favorable consequences for biological aging.

1. Introduction

The pronounced social gradient in health and premature mortality is well established, and has become an issue of worldwide concern (CSDH, 2008). Individuals of lower socioeconomic status (SES) are prone to the early development of diseases of older age, including coronary heart disease (CHD), type 2 diabetes, chronic pulmonary disease and some cancers (Jemal et al., 2008; Mackenbach et al., 2008). The SES gradient has multiple determinants, including differential access to health care, health-related behaviors, physical exposures across the life course, and psychosocial factors (Adler and Rehkopf, 2008). Understanding how socioeconomic circumstances influence the pathophysiological processes underlying chronic physical illness may highlight novel approaches to prevention. Lower SES is associated with dysregulation of stress-related biological processes indicative of chronic allostatic load (McEwen, 1998; Seeman et al., 2010). Lower SES adults show impaired post-stress recovery in cardiovascular and hemostatic processes (Steptoe et al., 2002, 2003), autonomic dysregulation (Hemingway et al., 2005), heightened cytokine responses to acute stress (Brydon et al., 2004), and chronic mild inflammation (Loucks et al., 2006; Nazmi et al., 2010a).

One theory that might integrate these observations is that lower SES leads to acceleration of the aging process (Adams and White, 2004). This effect might be indexed by telomere length (Adler and Stewart, 2010). Telomeres are complex DNA–protein structures that cap and stabilize the physical ends of chromosomes (Blackburn et al., 2006). Mammalian telomeric DNA consists of tandem repeats of the sequence TTAGGG that extend over several thousand base-pairs. Synthesis and maintenance of telomeres is a

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doi:10.1016/j.bbi.2011.04.010

complex process requiring a specialized reverse transcriptase (telomerase) which adds TTAGGG repeats onto the DNA 3′ ends. In the absence of telomerase or when this enzyme is expressed at low levels, DNA synthesis during cell division results in the progressive shortening of telomeric DNA. In addition, due to its high G content, telomeric DNA is very susceptible to oxidative damage and the generation of single strand breaks. Hence, telomere shortening is also affected by the oxidative burden of the cell (von Zglinicki, 2002). Telomere erosion eventually compromises telomere integrity, triggering a DNA damage response which results in the onset of senescence (d'Adda di Fagagna et al., 2003). Telomerase may also have a direct role in chromosome end protection and in cell survival, independent of telomere length maintenance (Chan and Blackburn, 2004). Telomere shortening has been observed *in vivo* in association with normal aging (Aubert and Lansdorp, 2008) and with age-related disease, and short telomeres are associated with increased risk of premature myocardial infarction (Brouilette et al., 2003) and mortality (Cawthon et al., 2003; Epel et al., 2009).

The existing evidence relating telomere length with SES is inconsistent. Cherkas et al. (2006) showed in a large study of female twins that lower SES defined by occupational class was associated with shorter telomeres independently of chronological age, body mass, smoking and physical activity. But subsequent studies have failed to replicate this observation (Adams et al., 2007; Batty et al., 2009; Kananen et al., 2010; Risques et al., 2010) and in a study of older Chinese men, an association between higher SES and shorter telomeres was reported (Woo et al., 2009).

These findings have primarily emerged from opportunistic analyses of population studies carried out for other reasons, in which the sampling structure was not focused on SES. Studies have also varied in the measure of SES, and in the stage at life at which SES is ascertained. Occupational grade, income and educational attainment are the commonest measures. Occupation and income are indicators of current socioeconomic circumstances, whereas education is typically completed early in life and partly dictates life-course trajectories (Mirowsky and Ross, 2003). Inflammatory damage may have a particularly pronounced effect relatively early in life, when the rate of telomere attrition is high (Frenck et al., 1998), and SES in early adult life may predict later oxidative damage (Janicki-Deverts et al., 2009). Telomerase preferentially elongates shortened telomeres, and the cellular level of telomerase activity is under multiple additional controls. While these processes are poorly understood in normal human leukocytes, they could be related to telomere shortness. Therefore, we included telomerase enzyme activity levels in these analyses.

If long-term accelerated cellular aging is characteristic of lower SES, we conjectured that reduced telomere length might be associated more robustly with education than with income or occupational grade. This possibility was tested in a subsample from the Whitehall II study, a large population cohort recruited specifically to investigate the association between SES and cardiovascular disease risk (Marmot et al., 1991).

2. Methods

2.1. Participants

Participants in this study were recruited from the Whitehall II epidemiological cohort, a sample of 10,308 London-based civil servants initially assessed in 1985–1988 when aged 35–55 years (Marmot and Brunner, 2005). A subsample of 543 men and women of white European origin, with no history or objective signs of coronary heart disease, no previous diagnosis or treatment for hypertension, diabetes, inflammatory diseases, or allergies, was recruited for an investigation of the relationship between socioeconomic and psychosocial factors, physiological stress responsivity, and subclinical coronary artery disease (Hamer et al., 2010; Steptoe et al., 2010). Data collection was carried out from 2006 to 2008. Recruitment to the study was stratified by SES to insure an adequate distribution across the socioeconomic gradient. In this study, we conducted analyses on 506 individuals (277 men, 229 women) aged 62.77 years (SD 5.58, range 53–76 years) at the time of testing, who provided data on educational attainment. All participants gave full informed consent, and ethical approval was obtained from the UCLH Committee on the Ethics of Human Research.

2.2. Measurement of telomere length

Peripheral blood mononuclear cells (PBMC) were isolated from whole blood samples (20 ml) by density gradient centrifugation on Ficoll Paque Plus (Amersham Pharmacia Biotech) and then stored at −80 °C in RPMI-1640 with 10% DMSO and 20% fetal bovine serum, until the time of analysis. Genomic DNA was extracted from PBMC in a QIAcube workstation using the QIAamp DNA blood mini kit (Qiagen, Crawley, UK) according to manufacturer's instructions and stored in 10 mM Tris–HCl, 0.5 mM EDTA, pH 9.0 at −20 °C. Relative mean telomere length was measured in triplicate by a monochrome multiplex Quantitative Real-Time PCR (Q-PCR) assay using a Bio-Rad CFX96™ Real-Time PCR Detection System (Bio-Rad, Hemel Hempstead, UK), essentially as previously described (Cawthon, 2009). PCR reactions were carried out in a final volume of 25 µl containing approximately 20 ng of sample DNA diluted in 4 µl of pure water, 12.5 µl of QuantiFast SYBR Green master mix (Quiagen, Crawley, UK), the telomere primers telg and telc, each at a final concentration of 900 nM and the human beta-globin primers hbgu and hbgc, each at a concentration of 500 nM. Primer sequences were: telg, ACACTAAGGTTTGGGTTTGGGTTTGGGTTTGGGTTAGTGT; telc, TGTTAGGTATCCCTATCCCTATCCCTATCCCTATCCCTAACA; hbgu, CGGCGGCGGGCGGCGCGGGCTGGGCGGCTTCATCCACGTTCACCTTG and hbgd, GCCCGGCCCGCCGCGCCCGTCCCGCCGGAGGAGAAGTCTGCCGTT. The thermal cycling conditions were as follows: Stage 1: 15 min at 95 °C; Stage 2: 2 cycles of 15 s at 94 °C, 15 s at 49 °C; and Stage 3: 32 cycles of 15 s at 94 °C, 10 s at 62 °C, 15 s at 73 °C with signal acquisition (providing Ct values for the amplification of the telomere template), 10 s at 84 °C, 15 s at 87 °C with signal acquisition (providing Ct values for the amplification of the hbg template). Reactions containing serial dilutions of a reference DNA standard were included in each PCR plate to generate the telomere (T) and beta-globin gene (S) standard curves required for quantitation. Relative mean telomere length, expressed as a T/S ratio, was derived as previously described (Cawthon, 2009). The intra- and inter-assay coefficients of variation were 3.3% and 2.2%, respectively.

2.3. Measurement of telomerase activity

Leukocyte telomerase activity was measured by the Telomerase Repeat Amplification Protocol (TRAP) using a commercial assay (TRAPeze, Telomerase Detection Kit, Upstate/CHEMICON, Temecula, CA) as described previously (Lin et al., 2010a). PBMCs were thawed by incubating the sample tubes at 37 °C for 2 min, then washed twice with 10 ml of cold DPBS (PBS without Mg^{2+} and Ca^{2+}; Invitrogen, Carlsbad, CA, USA). Live cells were counted using a hemocytometer (Bright-Line hemocytometer, Reichert, Buffalo, NY, USA) using Trypan blue (Invitrogen). One million live cells were pelleted and lysed with 1 × CHAPS (3-(3-cholamidopropyl) dimethylammonio-1-propanesulfonate) buffer according to the TRAPeze kit manufacturer instructions. An extract corresponding to 5000 cells/µl was prepared for each PBMC sample and two concentrations corresponding to 5000 and 10,000 cells were assayed for each sample to insure that the assay was in the linear range.

The reaction was performed according to the TRAPeze kit manufacturer instructions and radioactive products fractionated by 10% polyacrylamide-8 M urea sequencing gel electrophoresis. The gel was exposed to a phosphoimager plate overnight and scanned on STORM 860 (GE Healthcare, Piscataway, NJ). 293 T human cancer cells were used as positive control standards, and telomerase activity was expressed as 1 unit = the product of one 293 T cells/10,000 PBMCs. Telomerase activity was then quantified using ImageQuant 5.2 software (GE Healthcare, Piscataway, NJ) as described previously (Lin et al., 2010a).

2.4. Measurement of socioeconomic status

Participants were allocated to one of four educational attainment groups: no qualifications; O levels (Ordinary level, the basic educational qualification in the UK in the era in which participants were students); A (advanced level, indicating graduation from high school); and college/university degree. Information about household income was collected in 11 income categories, subsequently compressed to three categories for analysis: lower income (<£20,000 per annum), intermediate (£20,000–40,000) and higher (>£40,000). Occupational status was defined by the current or most recent grade attained in the British civil service, divided into three categories (lower, intermediate and higher).

2.5. Other measures

Telomere length is related to a number of risk factors for aging-related disease, including blood pressure, disturbed glucose metabolism, high density lipoprotein (HDL) cholesterol, smoking, adiposity and physical activity (Cherkas et al., 2008; Gardner et al., 2005; Valdes et al., 2005; Willeit et al., 2010; Yang et al., 2009). Since these biological and behavioral factors are in turn related to SES, they were taken into account in the analyses described here. Body mass index (BMI) was computed from heights and weights measured using standard methods (Marmot et al., 1991). Systolic blood pressure (BP) was estimated from two readings obtained after resting quietly in a seated position for 30 min. Glycated hemoglobin A1c and HDL-cholesterol were measured from fasting samples. Physical activity was estimated from the number of times per week that the individual participated in vigorous or moderate activity, and was divided into three categories: none, up to twice a week, and three or more times per week. Smoking was assessed by self-report. The age of the sample meant that a substantial proportion were no longer in paid employment. Since retirement has a marked effect on health-related processes (Westerlund et al., 2009, 2010), current employment status was included as a covariate in the statistical modeling.

2.6. Statistical analysis

Of the 543 participants, measures of telomere length were obtained from 434 participants, telomerase activity from 416, and 333 participants had measures of both. Of the 506 individuals who provided data on educational attainment, 403 had telomere length measures, 389 telomerase activity, and 311 both telomere length and telomerase activity (25 were missing for both measures). Individuals included and excluded from analyses of different parameters did not differ in sociodemographic, biological or behavioral factors. Telomerase activity measures were skewed, so were log transformed before analysis. Associations between educational attainment and demographic, biological and behavioral factors were analyzed using analysis of variance, testing for linear contrasts (Rosenthal and Rosnow, 1985). The relationship between education and telomere length was analysed using analysis of covariance, fitting three *a priori* defined models. In model 1, effects were adjusted for age, gender, current paid employment, systolic BP, glycated hemoglobin, and HDL-cholesterol, so as to control for sociodemographic and biological risk factors. Behavioral factors (smoking, BMI and physical activity) were added in model 2. Model 3 tested whether associations between education and telomeres were independent of current socioeconomic circumstances by including household income as an additional covariate. Similar methods were used in the analysis of telomerase activity, and in analyzing associations between telomeres and income and grade of employment.

3. Results

Table 1 summarizes the characteristics of the different educational attainment groups. One hundred and eighty (35.6%) of participants had a college/university degree, 153 (30.2%) had obtained A levels, 132 (26.1%) O levels, and 41 (8.1%) had no educational qualifications. There was no difference in gender distribution between

Table 1
Characteristics of educational attainment groups.

	No qualifications (n = 41)	O levels (n = 132)	A/S level (n = 153)	Degree (n = 180)	P linear trend
Gender (men, %)	15 (36.6%)	77 (58.3%)	84 (54.9%)	101 (56.1%)	0.25
Age (years)	66.5 ± 5.5	63.2 ± 6.7	62.3 ± 5.4	62.0 ± 5.3	0.001
Paid employment (%)	8 (19.5%)	47 (35.6%)	54 (35.3%)	84 (46.7%)	0.001
Income category (%)					
<£20,000	19 (48.7%)	33 (25.6%)	28 (18.9%)	18 (10.1%)	0.001
£20–40,000	18 (46.2%)	64 (49.6%)	58 (39.2%)	61 (34.3%)	
>£40,000	2 (5.1%)	32 (24.8%)	62 (41.9%)	99 (55.6%)	
Grade of employment (%)					
Lower	28 (68.3%)	45 (34.1%)	25 (16.3%)	8 (4.4%)	0.001
Intermediate	13 (31.7%)	68 (51.5%)	74 (37.0%)	45 (25.0%)	
Higher	0 (0%)	19 (14.4%)	54 (35.3%)	127 (70.6%)	
Systolic BP (mmHg)	128.5 ± 17.1	123.9 ± 14.6	122.8 ± 17.8	123.2 ± 15.3	0.044
Glycated hemoglobin A1c (%)	5.65 ± 1.05	5.44 ± 0.38	5.51 ± 0.39	5.38 ± 0.37	0.004
HDL lipoprotein (mmol/l)	1.66 ± 0.37	1.74 ± 0.44	1.68 ± 0.45	1.75 ± 0.50	0.44
Body mass index (kg/m^2)	25.67 ± 3.19	25.89 ± 3.54	26.12 ± 4.26	25.51 ± 3.97	0.90
Current smoker (%)	5 (12.2%)	5 (3.8%)	11 (7.2%)	5 (2.8%)	0.086
Physical activity (%)					
None	5 (12.2%)	16 (12.1%)	20 (13.1%)	19 (10.6%)	0.27
Up to 2/week	27 (65.9%)	78 (59.1%)	91 (59.5%)	103 (57.2%)	
⩾3/week	9 (8.1%)	38 (28.8%)	42 (27.5%)	58 (32.2%)	

Table 2
Associations between educational attainment and telomere length.

	No qualifications	O levels	A/S level	Degree	*P* linear trend
Mean telomere length (S.E.M.)					
Model 1: adjusted for age, gender, paid employment, systolic BP, glycated hemoglobin and HDL-cholesterol	0.968 (0.015)	0.988 (0.007)	0.995 (0.007)	1.001 (0.007)	*0.040*
Model 2: as model 1 plus smoking, BMI and physical activity	0.969 (0.015)	0.988 (0.007)	0.995 (0.007)	1.000 (0.007)	*0.044*
Model 3: as model 2 plus household income	0.967 (0.015)	0.987 (0.007)	0.996 (0.007)	1.002 (0.007)	*0.030*

educational attainment groups. However, participants with lower education were slightly older, were less likely to be currently in paid employment, and had lower incomes and lower employment grades (all $p < 0.001$). There was also an educational gradient in systolic BP ($p = 0.044$) and glycated hemoglobin ($p = 0.004$) but not in HDL-cholesterol, BMI, or physical activity. Glycated hemoglobin showed a cubic effect ($p = 0.009$), with lower levels in the O level and degree groups. Smoking tended to be more common in the lowest educational category ($p = 0.086$).

Relative telomere length (T/S ratio) averaged 0.994 ± 0.074. Telomere length was negatively correlated with BMI after adjusting for age and gender ($r = -0.097$, $p = 0.045$), and tended to be greater among nonsmokers than smokers ($p = 0.052$ adjusting for age and gender). Telomerase activity was greater among women than men ($p < 0.001$), but was not related to biological or behavioral risk factors. Telomere length and telomerase activity were not correlated ($r = 0.018$).

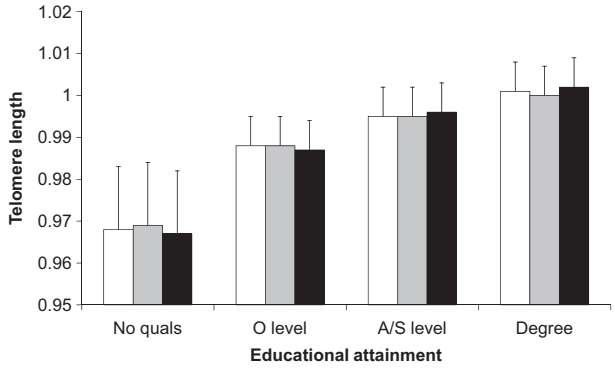

Fig. 1. Relative mean telomere length in participants with no educational qualifications (no quals), basic attainment (O levels), high school graduation (A levels), and college/university (degree). Model 1 (clear bars) is adjusted for age, gender, current paid employment, systolic BP, glycated hemoglobin and HDL-cholesterol, model 2 (shaded bars) additionally for smoking, BMI and physical activity, and model 3 (black bars) for household income. Error bars are standard error of the mean.

Table 2 summarizes associations between telomere length and educational attainment. Telomere length was positively associated with educational attainment after adjustment for age, gender, paid employment and biological risk factors (Model 1, $p = 0.040$). The difference was maintained after additional adjustment for BMI, smoking and physical activity (Model 2, $p = 0.044$). Adding smoking status in 1985–1988 as a covariate to control for smoking history did not appreciably modify the results. Interestingly, participants with greater education had longer telomeres even when current socioeconomic circumstances were taken into account by adjusting for income (Model 3, $p = 0.030$), and grade of employment ($p = 0.045$, data not shown). Replacing the categorical measure of income with the full range did not alter the results. The fully adjusted model is illustrated in Fig. 1, where it is evident that a graded association between education and telomere length is present.

By contrast, telomere length was not associated with grade of employment or income either in basic models or after adjustment for biological and behavioral factors ($p = 0.98$ and 0.93, respectively). These models are summarized in Table 3, which shows the small and nonsignificant differences in mean leukocyte telomere length across categories of employment or income.

There were no significant associations between education, income or grade of employment and telomerase activity in the analyses combining men and women. But separate analyses by gender indicated that telomerase activity differed across educational attainment groups in men, after adjustment for age, gender, paid employment, biological and behavioral risk factors ($p = 0.033$). The effect was non-linear (Fig. 2), with the highest values in the no qualification group, the lowest in the O level group, and intermediate levels in the A level and college/university degree groups. Thus in men, the short telomeres of the lowest education group were associated with the greatest telomerase activity.

4. Discussion

The results of this study suggest that in healthy men and women in the age range 53–76 years, greater education is associated

Table 3
Associations between grade of employment, income, and telomere length.

Mean telomere length (S.E.M.)				
Grade of employment	*Lower*	*Intermediate*	*Higher*	*P linear trend*
Model 1: adjusted for age, gender, paid employment, systolic BP, glycated hemoglobin and HDL-cholesterol	0.994 (0.008)	0.990 (0.006)	0.997 (0.006)	*0.51*
Model 2: as model 1 plus smoking, BMI and physical activity	0.993 (0.008)	0.990 (0.006)	0.998 (0.006)	*0.45*
Income	*<£20,000*	*£20,000–40,000*	*>£40,000*	*P linear trend*
Model 1: adjusted for age, gender, paid employment, systolic BP, glycated hemoglobin and HDL-cholesterol	0.992 (0.009)	0.990 (0.006)	0.997 (0.007)	*0.71*
Model 2: as model 1 plus smoking, BMI and physical activity	0.994 (0.009)	0.990 (0.006)	0.996 (0.007)	*0.86*

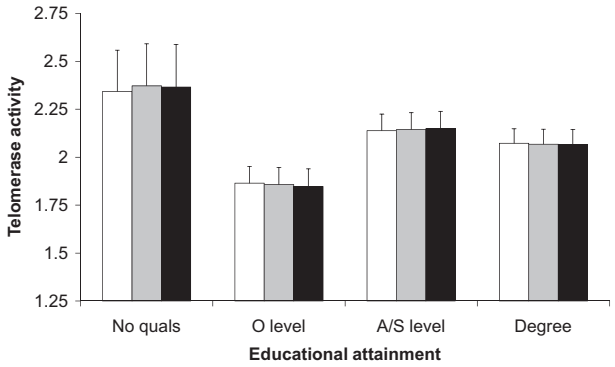

Fig. 2. Telomerase activity in men with no educational qualifications (no quals), basic attainment (O levels), high school graduation (A levels), and college/university (degree). Model 1 (clear bars) is adjusted for age, current paid employment, systolic BP, glycated hemoglobin and HDL-cholesterol, model 2 (shaded bars) additionally for smoking, BMI and physical activity, and model 3 (black bars) for household income. Error bars are standard error of the mean.

with longer leukocyte telomeres. This effect was independent of age and gender, and of biological and behavioral risk factors including blood pressure, glycated hemoglobin, HDL-cholesterol, BMI, smoking status and physical activity. By contrast, we found no significant associations between household income or occupational grade and telomere length. Interestingly, the relationship between lower education and shorter telomeres remained significant after adjustment for current socioeconomic circumstances, suggesting that the impact of education is independent of its association with SES based on social position at older ages. The relationship between education and telomerase activity was more complex, with relatively high levels in the least educated men, but lower levels in men with basic qualifications.

Previous investigations of SES and telomeres have generated mixed findings. In a study of 1552 female twins aged 18–75 years (Cherkas et al., 2006), telomere length was greater in higher status women as defined by occupation. The principal difference was between manual and nonmanual groups, while the trend by educational attainment was not significant. Adams et al. (2007) found no relationship between telomere length and household income or an occupational social class categorization in 318 men and women aged 50, and no effects were observed in 1542 men in Scotland, using education, employment status or area-based measures of SES (Batty et al., 2009). More recently, telomere length was not related to education in a study of adults aged 30–87 years in Finland (Kananen et al., 2010), or in an analysis of the National Long Term Care Survey (NTLCS) in the USA (Risques et al., 2010).

There are a number of reasons why associations between education and telomere length were detected in this study but not in earlier investigations. Previous investigators have carried out opportunistic analyses of surveys collected for other reasons, and the samples selected may have introduced sources of variance that obscured SES effects. For example, the Scottish study was a case-control investigation of coronary heart disease (Batty et al., 2009), the study from Finland included a large proportion of individuals with anxiety disorders (Kananen et al., 2010), while the majority of participants in the NTLCS had impairments in physical functioning and activities of daily living (Risques et al., 2010). Another relevant issue is that educational attainment does not carry the same socioeconomic significance in different periods, because of changes in educational opportunities; for instance the proportion of the population in the UK attending university or college has increased substantially over the past 50 years. Thus study samples with wide age ranges may not allocate people to consistent educational categories. The present analyses were carried out with an ethnically homogenous cohort of men and women in a relatively limited age range who had all been employed in the British civil service. Participants were only invited if they had no history or objective signs of cardiovascular and inflammatory disease, both of which are known to affect telomeres. The focus of the study on older adults without serious illness may have allowed educational differences in telomere length to emerge more clearly than in previous studies. The age range may also be relevant, with the accumulated effect of adult SES being more apparent in people aged 53–76 years than in younger participants (Adams et al., 2007).

It is striking that telomere length was related to education but not to measures of recent or current socioeconomic circumstances such as household income or occupational grade. One possible explanation is that education is an indicator of socioeconomic position at the onset of adult life that sets and individual's socioeconomic trajectory for the future. Effects of SES on telomeres may take many years to accumulate, so education may provide a more robust indicator of SES through early adult life and middle age than measures taken at the time of the study. A second possibility is that there are sensitive periods in the life course at which SES is likely to have more pronounced effects on cellular aging. If the stress associated with lower SES leads of inflammatory damage early in life, then such effects may be captured more precisely by education than by current socioeconomic circumstances in middle aged individuals. In this context, it is notable that Janicki-Deverts et al. (2009) observed an association between SES indicators in early adult life (education and occupation) and correlates of oxidative damage 10 and 15 years later.

A third possibility is that education provides skills for coping with life experience, over and above the social and economic resources represented by income or occupational status. It has been argued that education supplies 'learned effectiveness' in negotiating life, enhanced capacity to mobilize material and informational support, cognitive flexibility, and problem-solving skills that aid adaptive coping (Mirowsky and Ross, 2003). Such properties might enhance ability to adapt to daily stressors and chronic adversity. Experimental studies have shown that lower SES is associated with impaired post-stress recovery in cardiovascular responses (Steptoe et al., 2002, 2003), together with heightened inflammatory responses (Brydon et al., 2004). These effects may contribute to the cumulative allostatic load that has been recorded in lower SES individuals (Seeman et al., 2010). Telomere shortening may be a further manifestation of accelerated cellular aging among less educated individuals. This hypothesis is also consistent with the finding that associations between education and telomere length were independent of behavioral risk factors, suggesting that more direct psychobiological processes are involved.

Results for telomerase activity were less consistent than for telomere length, since differences between education groups were not progressively graded and effects were observed only for men. High telomerase activity is generally considered to be an indicator of healthy functioning, promoting telomere maintenance in non-malignant cells. However, high telomerase levels in the presence of short telomeres may provide a compensatory protective mechanism without measurable net telomere lengthening (Hemann et al., 2001; Zhu et al., 1999). We found that the greatest telomerase activity was recorded in the lowest education group which also had the shortest leukocyte telomeres on average. In contrast, the three more educated groups showed progressive elevations in telomerase activity coupled with longer telomeres. Such discontinuity in relationships with mean leukocyte telomere length are emerging in other clinical studies. For example, a recent case-control study found that breast cancer cases had 15-fold higher odds of being in the lowest telomere length quartile than controls; in contrast, in the upper three length quartiles, the correlation of cases vs.

controls with telomere length was weak (Pooley et al., 2010). If telomerase activity in PBMCs increases in response to damage signaling from short telomeres (Lin et al., 2010b), the men in the lowest education category may be at particularly high risk for cellular damage.

Low SES is associated with alterations in inflammatory and immune processes, including elevated levels of inflammatory markers (Gruenewald et al., 2009; Koster et al., 2006), heightened interleukin (IL) 6 following acute stress (Brydon et al., 2004), and greater susceptibility to experimentally-administered infections (Cohen et al., 2008). Life course studies indicate that lower SES early in life predicts inflammation and vulnerability to infection in later life, in many cases independently of current adult socioeconomic circumstances (Cohen et al., 2004; Nazmi et al., 2010b; Tabassum et al., 2008). It is possible that the reduced leukocyte telomere length we observed in less educated participants is a mechanism related to T cell replicative senescence and impaired immunity (Effros, 2011), contributing to immune-related health at older ages.

This study was carried out with a relatively healthy, ethnically homogenous sample of late middle-aged men and women, and results may not generalize to other groups. Causal conclusions may not be drawn, since unmeasured factors may be responsible for the associations between telomeres and educational attainment. Additionally, these analyses were carried out using PBMCs, and lymphocyte subpopulations were not differentiated. Telomerase activity varies lymphocyte subpopulations (Lin et al., 2010a), and it is conceivable that the distribution of subpopulations differed with educational attainment. This may therefore have contributed to the differences in leukocyte telomere length that were observed. Nevertheless, the findings indicate that a relationship between telomeres and SES can be observed when appropriate measures are used in individuals purposely sampled to represent distinct socioeconomic groups. Shorter telomeres in less educated participants may reflect more rapid cellular aging, which would be consistent with the heightened risk of age-related disease in lower SES groups.

Acknowledgments

This study was supported by the Medical Research Council UK (G0601647) and the British Heart Foundation (RG/05/006).

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