Short Sleep Duration Is Associated with Shorter Telomere Length in Healthy Men: Findings from the Whitehall II Cohort Study

Marta Jackowska1, Mark Hamer1, Livia A. Carvalho1, Jorge D. Erusalimsky2, Lee Butcher2, Andrew Steptoe1

1 Research Department of Epidemiology and Public Health, University College London, London, United Kingdom, 2 Cardiff School of Health Sciences, Cardiff Metropolitan University, Cardiff, United Kingdom

Abstract

Background: Shorter telomere length and poor sleep are more prevalent at older ages, but their relationship is uncertain. This study explored associations between sleep duration and telomere length in a sample of healthy middle and early old age people.

Methods: Participants were 434 men and women aged 63.3 years on average drawn from the Whitehall II cohort study. Sleep duration was measured by self-report.

Results: There was a linear association between sleep duration and leukocyte telomere length in men but not in women (P = 0.035). Men reporting shorter sleep duration had shorter telomeres, independently of age, body mass index, smoking, educational attainment, current employment, cynical hostility scores and depressive symptoms. Telomeres were on average 6% shorter in men sleeping 5 hours or fewer compared with those sleeping more than 7 hours per night.

Conclusion: This study adds to the growing literature relating sleep duration with biomarkers of aging, and suggests that shortening of telomeres might reflect mechanisms through which short sleep contributes to pathological conditions in older men.

Citation: Jackowska M, Hamer M, Carvalho LA, Erusalimsky JD, Butcher L, et al. (2012) Short Sleep Duration Is Associated with Shorter Telomere Length in Healthy Men: Findings from the Whitehall II Cohort Study. PLoS ONE 7(10): e47292. doi:10.1371/journal.pone.0047292

Editor: Stefan Kiechl, Innsbruck Medical University, Austria

Received July 6, 2012; Accepted September 14, 2012; Published October 29, 2012

Copyright: © 2012 Jackowska et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The study was supported by the Medical Research Council UK (G0601647) and by the British Heart Foundation (RG/05/006). Marta Jackowska is supported by the Biotechnology and Biological Sciences Research Council and by Unilever Discover. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The corresponding author (Marta Jackowska) declares that her PhD is partly funded by a commercial funder Unilever Discover. This does not alter the authors’ adherence to all of the PLOS ONE policies on sharing data and materials.

* E-mail: marta.jackowska.09@ucl.ac.uk

Introduction

Mean telomere length is an indicator of biological age, and is modified by genetic as well as environmental factors [1,2]. Shortening of telomeres has been linked with cardiovascular outcomes [3] as well as with inflammation [3,4], low socioeconomic status [5], chronic stress [6], depression [7], hostility [8], smoking [9,10] and obesity [10,11].

Short sleep duration is also associated with cardiovascular disease [12,13] and other health outcomes such as obesity [14], raised levels of inflammatory markers [15], and depressive symptoms [16]. To date the association between sleep duration and telomere length has only been studied in women [17–19], or in the context of sleep apnea [20,21]. Therefore we explored associations between telomere length and self-reported sleep duration in a sample of healthy middle and early old age healthy men and women. Although men have shorter telomere length [4,9] and experience poorer sleep than women [22,23], the relationship between sleep duration and telomere length remains uncertain in men. Therefore this study took an explorative approach to test whether associations between sleep duration and telomere length would differ between men and women.

Methods

Study population

Participants were drawn from the Whitehall II epidemiological study [24] and were eligible if they were free from coronary heart disease, stroke, hypertension, inflammatory diseases, diabetes, active cancer and allergies. Disease status was ascertained through a telephone screening interview as well as by inspecting clinical data obtained in the previous 7 phases of the Whitehall II study. Data were collected between 2006 and 2008. All participants gave written consent, and the study was approved by the University College London Hospital committee on the Ethics of Human Research.
Measures
Leukocyte relative mean telomere length was measured in triplicate by a monochrome multiplex Quantitative Real-Time PCR (Q-PCR) assay using a Bio-Rad CFX96TM Real-Time PCR Detection System (Bio-Rad, Hemel Hempstead, UK) (see [25] for more details).

Sleep duration was measured by asking participants to describe how many hours of sleep they have on an average weeknight, and responses were categorized into ‘5 hours or less’, ‘6 hours or less’, ‘7 hours or less’, ‘more than 7 hours’.

Depressive symptoms were measured with the Centre for Epidemiologic Studies Depression scale (CES-D) [26] and cynical hostility was assessed with the Cook Medley Hostility Scale [27]. Information about age, smoking, education, body mass index (BMI; kg/m²) and current employment status was also collected.

Statistical analysis
Associations between telomere length and sleep duration were assessed with analysis of variance testing for linear contrasts. Since we have previously shown that shorter telomere length is associated with lower education [25] and greater hostility [8], these were included as covariates in addition to age, BMI, smoking, current employment status and depressive symptoms. Analyses were stratified by gender. Data were analyzed using SPSS version 18 (Chicago, Ill, USA).

Results
There were 228 women and 206 men in the sample, and 31% of participants had a university degree (see Table 1). Around 6% of respondents smoked and BMI was 25.9 on average. 6.7% percent of the sample reported sleeping 5 or fewer hours on average, while 34.8% slept between 5 and 6 hours; 43.1% reported sleeping between 6 and 7 hours and the remainder slept longer than 7 hours (see Table 1).

Short sleep hours were more likely to be reported by men with the lowest level of education (P = 0.025), while women who were in paid employment were least likely to sleep shorter than 7 hours (P = 0.010) (see Table 2). In both men and women short sleep duration was associated with more depressive symptoms (P = 0.031 and P = 0.001, respectively), and with higher hostility scores in women (P = 0.034). Sleep duration was unrelated to gender in this sample (P = 0.302).

Average relative telomere length (T/S ratio) of the sample was 0.994 (SD = 0.075). Telomere length was unrelated to gender in this sample. Telomere length was shorter among men who smoked (P = 0.013) and those who had greater hostility scores (P = 0.001), but was unrelated to age, BMI, employment status, educational attainment and depression scores in either men or women.

There was a linear association between telomere length and sleep duration in men (P = 0.033) (see Table 2), so that men with greater sleep duration had longer telomeres, independently of age, educational attainment, employment status, BMI, smoking, hostility and depressive symptoms. There was no association between sleep duration and telomere length in women. When sensitivity analyses were performed to remove participants who might have been depressed (using a conventional cut off score of 16) the linear association between sleep duration and telomere length remained statistically significant in men (P = 0.008), and was still not significant among female participants (P = 0.409).

Table 1. Characteristics of study participants.

| Variable                  | Mean (SD)/frequency (%) |
|---------------------------|-------------------------|
| Gender                    |                         |
| Male                      | 206 (47.5%)             |
| Female                    | 228 (52.5%)             |
| Age                       | 63.3 (5.6)              |
| Education attainment      |                         |
| No qualification          | 34 (7.8%)               |
| 0-levels                  | 113 (26.0%)             |
| A/5 levels                | 121 (27.9%)             |
| Degree and above          | 135 (31.1%)             |
| Paid work                 |                         |
| Yes                       | 152 (35.0%)             |
| No                        | 282 (65.0%)             |
| Current smoker            |                         |
| Yes                       | 27 (6.2%)               |
| No                        | 407 (93.8%)             |
| BMI*(kg/m²)               | 25.9 (4.0)              |
| Cynical hostility (range 0–10) | 2.6 (2.4)               |
| Depressive symptoms (CES-D; range 0–36) | 6.7 (6.6)               |
| Sleep duration            |                         |
| ≤5 hours                  | 29 (6.7%)               |
| ≤6 hours                  | 151 (34.8%)             |
| ≤7 hours                  | 187 (43.1%)             |
| >7 hours                  | 67 (15.4%)              |

*SD = standard deviation.
*BMI = Body mass index.
*CES-D = Centre for Epidemiological Studies Depression scale.

Discussion
We found that in men sleep hours were related to telomere length in a linear fashion, so men sleeping 5 or fewer hours had the shortest telomere length while those reporting more than 7 hours the longest. These associations were independent of relevant covariates including depressive symptoms.

Evidence relating sleep with telomere length in population-based studies is limited. Apart from studies of sleep apnea [20,21] the relationship between sleep measures and telomere length has been explored only in women [17,18]. Fraser et al. [18] found no association between telomere length and sleep duration in a study of 245 middle-aged women, although sleep quality was inversely related with telomere length. This relationship was independent of age, race, income, BMI and perceived stress. A second study of over 4000 women from the Nurses’ Health Study revealed that short sleep duration (≤6 hours) was related to shorter telomere length only in participants younger than 50 years, and not in older women [17]. In our study women were aged 64 years on average, so this may be why we did not see an association in women. The linear association between sleep duration and telomere length in men has not been reported before, to the best of our knowledge.

The mechanisms through which sleep might be related to telomere attrition are yet to be established. Although sleep duration was unrelated to gender in our analyses, the literature suggests that men experience poorer sleep as they grow older [28] and tend to have shorter telomere length than women as well as.
more rapid telomere attrition [4,9]. Short sleep duration and telomere length are both associated with inflammation [4,11,29]. Oxidative stress may also be implicated, since prolonged sleep deprivation leads to increased oxidative stress [30] and is associated with exacerbated telomere shortening [31]. Short sleep duration and telomere length are also both associated with increased sympathetic tone, since shorter sleep duration increases sympathetic nervous system activity [32,33]. Sleep duration may impact telomere length through neuroendocrine pathways as well [34], since stress and a dysregulated diurnal rhythm of stress mediators, impact telomere length through neuroendocrine pathways as well [32,33]. Sleep duration and telomere length are both associated with exacerbated telomere shortening [31]. Short sleep deprivation leads to increased oxidative stress [30] and is associated with inflammation [4,11,29]. Oxidative stress may also be implicated, since prolonged sleep deprivation leads to increased oxidative stress [30] and is associated with exacerbated telomere shortening [31].

Dysfunctional telomeres are risk factors for adverse health conditions, and may accelerate the progression of age-related disorders as well [38]. In addition to a strong hereditary component, telomere length can be influenced by psychological and sociodemographic characteristics [8,11,25]. Modifiable risk factors such as smoking and obesity have also been associated with telomere shortening [9,10]. Such data are valuable in helping to identify populations who might be at an increased risk for telomere attrition, and consequently subject to more accelerated aging processes. Sleep is another factor that is subject to modification, so could provide an opportunity to ameliorate the health profile at older ages. Our study and Liang et al.’s [17] data, if confirmed by future studies, could offer a new avenue for intervention in aging.

The data are cross-sectional so causal conclusions cannot be drawn as to whether short sleep duration contributes towards telomere shortening, or whether telomere shortening is a marker of biological processes that impair sleep. Although we controlled for age, BMI, smoking education attainment, current employment status, cynical hostility and depressive symptoms, other unmeasured factors could be responsible. Pre-existing illness is unlikely to be the explanation, since respondents in this study were drawn from the Whitehall II study, a well characterized epidemiological cohort that has been studied for more than 20 years, so we are confident that physical and mental illness are not responsible. Sleep was measured by self-report, and this might be affected by current mood and memory biases [39]. An objective measure of sleep duration, such as accelerometry would have been more desirable, but is often prohibited in epidemiological cohorts by financial constraints and additional participant burden. Associations between self-reported and objectively measured sleep duration have been reported previously [40]. Participants were white civil servants and the findings cannot be extrapolated to other populations.

In conclusion, our study adds to the growing literature relating lifestyle factors with telomere length, and we report for the first time that short sleep duration in healthy older men is associated with shorter telomere length. Longitudinal studies are needed to establish whether shorter sleep leads to accelerated telomere shortening and advanced cellular aging.

### Author Contributions
Conceived and designed the experiments: MH AS. Performed the experiments: JDE LB. Analyzed the data: MJ AS. Wrote the paper: MJ AS LAC JDE.
References

1. Aviv A (2006) Telomeres and human somatic fitness. J Gerontol B Psychol Sci Soc Sci 61: 871–873.
2. Blackburn EH (2000) Telomeres states and cell fates. Nature 408: 53–56.
3. Fitzpatrick AL, Kromvil RA, Gardner JP, Pusty BM, Jenny NS, et al. (2007) Leukocyte telomere length and cardiovascular disease in the cardiovascular health study. Am J Epidemiol 165: 14–21.
4. Bekarot S, De Meyer T, Ritzschel ER, De Buyzere ML, De Bacquer D, et al. (2007) Telomere length and cardiovascular risk factors in a middle-aged population free of overt cardiovascular disease. Aging Cell 6: 639–647.
5. Cherkas LF, Aviv A, Valdes AM, Hunkin JL, Gardner JP, et al. (2006) The effects of social status on biological aging as measured by white-blood-cell telomere length. Aging Cell 5: 361–365.
6. Epel ES, Blackburn EH, Lin J, Dhabhhar FS, Adler NE, et al. (2004) Accelerated telomere shortening in response to life stress. Proc Natl Acad Sci U S A 101: 17312–17315.
7. Wiorkowicz OM, Mellon SH, Epel ES, Lin J, Dhabhhar FS, et al. (2011) Leukocyte telomere length in major depression: correlations with chronicity, inflammation and oxidative stress - preliminary findings. Plos One 6: e17837. Accessed 12 April 2012.
8. Brydon L, Lin J, Butcher L, Hamer M, Erulimaizky JD, et al. (2012) Hostility and cellular aging in men from the Whitehall II cohort. Biol Psychiatry 71: 767–773.
9. Nawrot TS, Staessen JA, Gardner JP, Aviv A (2004) Telomere shortening in sleep apnea syndrome. Respir Med 104: 1225–1229.

10. Valdes AM, Andrew T, Gardner JP, Kimura M, Oelsner E, et al. (2005) Telomere length trajectory and its determinants in persons with coronary artery disease: a cross-sectional population-based study. Am J Epidemiol 169: 1052–1063.
11. Farzaneh-Far R, Lin J, Epel E, Lapham K, Blackburn E, et al. (2010) Telomere length and cellular aging in midlife women with poor sleep quality. J Aging Res In Press.
12. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA (2011) Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis. Obesity, cigarette smoking, and telomere length in women. Lancet 366: 662–664.
13. Meerlo P, Sgoifo A, Suchecki D (2008) Restricted and disrupted sleep: effects on psychological and cellular aging in men from the Whitehall II cohort. Biol Psychiatry 71: 767–773.
14. Lusardi P, Mugellini A, Preti P, Zoppi A, Derosa G, et al. (1996) Effects of a psychoeducational intervention on leukocyte telomere length in healthy older men and women. J Sleep Res 18: 221–228.
15. Tomiyama AJ, O'Donovan A, Lin J, Puterman E, Lazaro A, et al. (2012) Does stressor: allostasis and allostatic load. Metabolism 55: S20–S23.
16. Radloff LS (1977) The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1: 385–401.
17. Cook WW, Medley DM (1954) Proposed postility and pharisaic - virtue scales of the MMPI. J Appl Psychol 30: 414–418.
18. Ide D, Papaliaga MN, Vgontzas AN, Lin HM, Pojsic S, et al. (2009) Women sleep objectively better than men and the sleep of young women is more resilient to external stressors: effects of age and menopause. J Sleep Res 18: 221–228.
19. Spath-Schwalbe E, Scholler T, Kern W, Deroza G, et al. (2007) Telomere length and cardiovascular risk factors in a middle-aged population free of overt cardiovascular disease. Aging Cell 6: 639–647.
20. Spath-Schwalbe E, Scholler T, Kern W, Fehm HL, Born J (1992) Nocturnal sleep dysfunction induces metabolic and mitochondrial compromise. Nature 470: 359–365.
21. Kim J, Lee S, Bhattacharjee R, Khalifa A, Kherandish-Gozal L, et al. (2010) Leukocyte telomere length and plasma catestatin and myeloid-related protein 8/14 concentrations in children with obstructive sleep apnea. Chest 130: 91–99.
22. Launderdale LS, Knutson KL, Yan LL, Rathouz PJ, Hulley SB, et al. (2006) Subjectively measured sleep characteristics among early-middle-aged adults: the CARDIA study. Am J Epidemiol 164: 5–16.
23. van den Berg JF, Miedema HME, Tuten JHM, Hofman A, Neeen AK, et al. (2009) Sex differences in subjective and actigraphic sleep measures: a population-based study of elderly persons. Sleep 32: 1367–1375.
24. Marmot M, Brunner E (2005) Cohort Profile: The Whitehall II study. Int J Epidemiol 34: 251–256.
25. Tomiyama AJ, O'Donovan A, Lin J, Brydon L, et al. (2011) Educational attainment but not measures of current socioeconomic circumstances are associated with leukocyte telomere length in healthy older men and women. Brain Behav Immun 25: 1292–1298.
26. McEwen BS (2006) Sleep deprivation as a neurobiologic and physiologic stressor: allostasis and allostatic load. Metabolism 55: S20–S23.
27. Richter T, Von Zglinicki T (2007) A continuous correlation between oxidative stress and telomere shortening in fibroblasts. Exp Gerontol 42: 1039–1042.
28. Meerp P, Sguito D, Suckeck D (2008) Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stem systems and stress responsivity. Sleep Med Rev 12: 197–210.
29. Lusardi P, Mugellini A, Preti P, Zoppi A, Derosa G, et al. (1996) Effects of a restricted sleep regimen on ambulatory blood pressure monitoring in normotensive subjects. Am J Hypertens 9: 503–505.
30. Kumari M, Badrick E, Ferrie J, Perski A, Marmot M, et al. (2009) Self-reported sleep duration and sleep disturbance are independently associated with cortisol secretion in the Whitehall II study. J Clin Endocrinol Metab 94: 4801–4809.
31. Spath-Schwalbe E, Scholler T, Kern W, Fehm HL, Born J (1992) Nocturnal sleep dysfunction induces metabolic and mitochondrial compromise. Nature 470: 359–365.
32. Tomiyama AJ, O'Donovan A, Lin J, Puterman E, Lazarro A, et al. (2012) Does cellular aging relate to patterns of allostasis? An examination of basal and stress reactive HPA axis activity and telomere length. Physiol Behav 106: 40–45.
33. Choi J, Fauce SR, Effros RB (2008) Reduced telomerase activity in human T lymphocytes exposed to cortisol. Brain Behav Immun 22: 600–605.
34. Sahin E, Cella S, Liska M, Modilja J, Muller FL, et al. (2011) Telomere dysfunction induces metabolic and mitochondrial compromise. Nature 470: 359–365.
35. Krystal AD, Edinger JD (2008) Measuring sleep quality. Sleep Med 9: S10–S17.
36. Lauderdale DS, Knutson KL, Yan LL, Lin K, Rathouz PJ (2008) Self-reported and measured sleep duration: how similar are they? Epidemiology 19: 835–845.