

Older adults with higher income or marriage have longer telomeres

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Abstract

Background: telomere length has been used to represent biological ageing and is found to be associated with various physiological, psychological and social factors.

Objective: to explore the effects of income and marriage on leucocyte telomere length in a representative sample of older adults.

Design and subjects: cross-sectional analysis among 298 adults, aged 65–74, randomly selected from the community by census.

Methods: telomere length was measured by quantitative PCR. Participants provided information on sociodemographics, physical illness and completed questionnaires rating mental state and perceived neighbourhood experience.

Results: telomere length was negatively associated with lower income [coefficient -0.141 (95% CI: -0.244 to -0.020), $P = 0.021$] and positively associated with the marital status [coefficient 0.111 (95% CI: -0.008 to 0.234), $P = 0.067$] when controlling for gender, age, educational level, physical diseases (including diabetes, hypertension, cardiovascular diseases, cerebrovascular disease and Parkinson's disease), depressive symptoms, minor mental symptoms, cognitive impairment and perceived neighbourhood experience (including social support, perceived security and public facilities).

Conclusions: these results indicate that older adults with higher income or being married have longer telomeres when other sociodemographics, physical diseases, mental status and neighbourhood experience are adjusted.

Keywords: *telomere, income, marital status, neighbourhood, stress, older people*

Introduction

The telomere is the specific structure located on the end of each chromosome. It protects the chromosome from recombination or degradation [1]. In vertebrates, the telomere is composed of repeated sequences of 'TTAGG'. The telomere is the substrate of telomerase, which is one of the DNA polymerases, and can prolong chromatin based on the characteristics of DNA. During the process of mitosis, the telomere will keep losing sequences of TTAGG, which gradually shortens it. As the telomere is shortened to a certain degree, its protection against the recombination and degradation of the chromosome is diminished. As a consequence, the chromosome will become unstable, thus damaging the vitality of the cell [2].

Telomere shortening is considered as the biological clock and a measure of the cellular ageing. Influences from physiological, psychological and social factors are related to this ageing process. From the physiological aspect, physical diseases such as diabetes, hypertension, atherosclerosis, heart failure, cerebrovascular disease and Parkinson's disease are associated with accelerated ageing [3]. Patients with those degenerative diseases have shorter telomere length than the general population. As for psychological stress or mental conditions, more stress is found to lead to shorter telomere length. Chronic stress is especially associated with faster telomere shortening [4]. Accelerated leucocyte telomere shortening has been shown to be associated with self-perceived stress and psychiatric disorders. Patients with affective disorders, such as depressive and bipolar disorders, have a shorter telomere

length that is 10 years older in cellular ageing than non-patients [5]. Lung *et al.* [6] also conclude that the average telomere length of major depressive disorder patients was significantly shorter than that of their community controls.

In terms of social factors and telomere length, social deprivation or environmental factors in early life has been associated with telomere length in adult life [7]. In the meanwhile, the socioeconomic status (SES) has also been noted to be associated with telomere shortening. However, their results are inconsistent. Cherkas *et al.* [8] find that females of lower SES have shorter telomere length. Woo *et al.* [9] conclude that males with higher self-rated SES have shorter telomeres. On the other hand, Batty *et al.* [10] find that there is little association between SES and telomere length. Reasons for the conflicting findings may include the various definitions and different ways of the measurement of the SES. Income as an alternative indicator of the SES is easier to measure and more objective than self-rated SES. Income inequality has been found to be related to health conditions. Yet its association with telomere length is not clarified. Roux *et al.* [11] fail to detect significant difference from various income levels. But Shiels *et al.* [12] find that telomere attrition is associated with lower income. The marital status is another potential predictor of telomere length. Only one study reveals that unmarried middle-aged individuals have shorter telomere [13]. Therefore, the aim of this study was to explore the possible roles of income and marital status in the shortening of leucocyte telomere length among older adults. For a better estimation of the relationships between income or marriage and leucocyte telomere length, we took physical diseases, mental state and sociodemographics into account.

Subjects and methods

A random household sample of 500 older adults aged 65–74 was selected from four townships of a prefecture in southern Taiwan. This sample was representative of the older population in Taiwan. Details of the sampling and characteristics of these subjects were published elsewhere [14]. This study was approved by the Institutional Review Board of the E-Da Hospital. All participants of this study signed the written informed consent, were invited to provide information including gender, age, marital status, educational level, monthly income and physical illness, had venous blood withdrawn for telomere length measurement and completed all questionnaires rating their mental state and neighbourhood experience.

Mental state assessment

Three mental states were assessed, respectively, in this study. Depressive symptoms were scored using the Taiwanese depression questionnaire (TDQ). The TDQ was constructed by revising the CES-D with cultural consideration with 0–3 points, 18 questions to screen depression [15]. The wording, sequences and its concurrent validity were tested in the clinical

and community population. The 18-item TDQ had a sensitivity of 0.89 and a specificity of 0.92 at a cut-off score of 19 for major depressive disorder. The TDQ score was treated as a continuous variable in this study. Minor mental symptoms were assessed by the Chinese health questionnaire (CHQ) [16]. The CHQ is derived from a Chinese translation of the general health questionnaire, with the addition of specially designed, culturally relevant items. The CHQ is a 12 question, 2 reverse question, 0–1 point questionnaire. Discriminant function analysis is used to select a subset of 12 items which discriminate well between possible cases of minor psychiatric morbidity and normals in the community. The CHQ score was treated as a continuous variable in this study. The short portable mental status questionnaire (SPMSQ) is used to detect cognitive impairment. The 10-item SPMSQ is easily administered by clinicians and trained interviewers [17]. Educational level had been taken into account in scoring individual performance. The presence of cognitive impairment was treated as a categorical variable.

Environmental factor assessment

Perceived neighbourhood experiences assessed by the NQI were further divided into three subscales measuring social support, perceived security and services and facilities, respectively. The NQI, a self-reported instrument to measure perceived neighbourhood quality, was developed in Taiwan [18]. Lower social support, lower perceived security and inadequate facilities have all been related to higher residential dissatisfaction. The NQI has good internal consistency and test–retest reliability, as well as convergent validity.

Telomere length measurement

Leucocyte telomere length was measured by the quantitative PCR technique. We compared telomere repeat sequence copy to single-copy gene (36B4) copy number in the sample [19]. Duplicate DNA samples were amplified in parallel 25 µl PCR reaction comprising 15 ng genomic DNA, 1X SensiMix NoRef SYBR Green master mix and 1X SYBR Green (Quantace, UK). The 300 nmol/l of telomere-specific primer sequences of the telomere [36B4(encodes acidic ribosomal phosphoprotein)] were forward, 5'-CGG TTT GTT TGG GTT TGG GTT TGG GTT TGG GTT TGG GTT-3', and reverse, 5'-GGC TTT GCC TTA CCC TTA CCC TTA CCC TTA CCC TTA CCC T-3' or 300 nmol/l of 36B4 forward, 5'-CAG CAA GTG GGA AGG TGT AAT CC-3' and 500 nmol/l of 36B4 reverse, 5'-CCC ATT CTA TCA TCA ACG GGT ACA A-3'. All PCRs were run on a Corbett Research Rotor-Gene 6000 Real-time Thermal Cycler (Corbett Research, Cambridge, UK). The thermal cycling profile begins with the 95°C incubation for 10 min to activate the Taq DNA polymerase followed by cycling of 15 s at 95°C and 1 min at 58°C for either 20 cycles for telomere or 30 cycles for 36B4. Before running samples, the linear range of the assay was determined by generating a standard curve using serially diluted DNA (200–1.56 ng in 2-fold dilutions)

in quadruplicate. Both PCR reactions exhibited good linearity across this input range ($r^2 > 0.99$). Test samples were then checked to confirm that they fall within the range, and any that did not were diluted as necessary and rerun. The specificity of all amplifications was determined by melting curve analysis. Forty-eight study samples, a calibrator sample and one no-template control sample (all in duplicate) were processed for each run. The PCR data were analysed with the comparative quantitation approach as previously described and implemented with the Corbett Research Rotor-Gene 6000 version 1.7 analysis software. During this analysis, the amplification efficiency was calculated for each sample along with the mean efficiency of the run, which is used in calculating the relative concentration of each sample relative to the calibrator sample. This calculation coupled with the use of the same calibrator samples on all runs allows for any inter-run variation. This process was done for both telomere (T) and single-copy (S) gene reactions, and telomere length was expressed as a ratio of the two, the T/S ratio, of the mean data from duplicate runs. The T/S ratio was checked for reproducibility by rerunning 76 samples on another day. The T/S ratio was analysed as a continuous variable.

Analytical method

Descriptive statistics and univariate linear regression were applied to show the participants' characteristics and their correlation with leucocyte telomere length. Multivariate linear regression was used to predict the length of the leucocyte telomere by incorporating gender, age, educational level, marital status, monthly income, physical diseases, depressive symptoms, minor mental symptoms, cognitive function, social support, perceived security and sufficient facilities. Five regression models would be generated sequentially with sociodemographic factors only, sociodemographics plus disease factors, sociodemographics plus mental state factors, sociodemographics plus neighbourhood experience factors and sociodemographics plus all factors, respectively. To adjust for the possible unequal influence from the living environment, we calculated robust standard errors by clusters according to neighbourhood units (township).

Results

Two hundred and ninety-eight participants were recruited from four neighbourhoods in Chia-Yi County, Taiwan. More of them were male (59.4%) and married (76.8%), received 6 years of education (47.0%) and had a monthly income of <1,000 USD (74.2%) (Table 1). Their mean age was 69.2 (SD: 2.7) years. Most (70.5%) of them had at least one chronic physical condition and needed long-term treatment. Hypertension (21.5%), cardiovascular diseases (18.8%) and diabetes (10.1%) are the three commonest physical diseases. The mean TDQ score was 11.9 (SD: 10.2); the mean CHQ score was 2.5 (SD: 2.6); the mean NQI score was 27.2 (SD: 8.3) with a mean social support subscale of 14.1 (SD: 4.8), mean perceived security subscale

Table 1. Characteristics of participants ($n = 298$)

	Count (%) or mean (SD)	Range
Male	177 (59.4)	
Age (year)	69.2 (2.7)	65–74
Marital status		
Married	229 (76.8)	
Single	3 (1.0)	
Separated/divorced	2 (0.7)	
Widowed	64 (21.5)	
Educational level		
Illiterate	136 (45.6)	
Primary school	140 (47.0)	
Middle school	12 (4.0)	
High school	8 (2.7)	
College	2 (0.7)	
Monthly income (NTD)		
≤30,000	221 (74.2)	
30,001 – 70,000	62 (20.8)	
70,001 – 100,000	12 (4.0)	
>100,000	3 (1.0)	
Diseases		
Diabetes	30 (10.1)	
Hypertension	64 (21.5)	
Cardiac diseases	56 (18.8)	
Cerebrovascular disease	11 (3.7)	
Parkinson's disease	1 (0.3)	
Depressive symptoms (TDQ ^a score)	11.9 (10.2)	0–48
Minor mental symptoms (CHQ ^b score)	2.5 (2.6)	0–12
Cognitive impairment ^c	18 (6.0)	
Neighbourhood experience (NQI ^d)		
Social support	14.1 (4.8)	8–32
Perceived security	6.3 (2.4)	2–12
Adequacy of facilities	5.2 (1.9)	3–10
Telomere length (T/S ratio)	1.71 (0.68)	0.40–3.68

^aTaiwanese depression questionnaire score.

^bChinese health questionnaire score.

^cRated by short portable mental status questionnaire score and criteria: three or more errors implying cognitive impairment, one more error allowed for participants with a grade school education or less, one less error allowed for participants beyond the high school education level.

^dNeighbourhood quality index subscales.

of 6.3 (SD: 2.4) and mean adequacy of facilities subscale of 5.2 (SD: 1.9). Eighteen (6%) participants were cognitively impaired. The mean leucocyte telomere length (T/S ratio) was 1.71 (SD: 0.68).

By using the univariate linear regression, we found that the state of being married was the only significant predictor of telomere length (coefficient 0.135; 95% CI: 0.022 to 0.261; $P = 0.020$) when all other factors were not adjusted. In a series of multivariate linear regression models (Table 2), Model 1 was generated by incorporating sociodemographic factors only. In Model 1, lower income (monthly income <1,000 USD) was significantly associated with leucocyte telomere length (coefficient -0.139 ; 95% CI: -0.236 to -0.023 ; $P = 0.018$). The effect of marriage was attenuated when all the other sociodemographic factors were included in the analysis. Model 2 was generated by incorporating sociodemographic and disease factors. In Model 2, lower income remained significantly associated with telomere length

Table 2. Linear regression models predicting leucocyte telomere length

	Univariate		Multivariate									
	Coefficient (95% CI)	P-value	Model 1		Model 2		Model 3		Model 4		Model 5	
			Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value
Sociodemographics												
Female	0.041 (-0.066 to 0.141)	0.479	-0.005 (-0.10 to 0.100)	0.938	-0.006 (-0.113 to 0.102)	0.920	-0.021 (-0.124 to 0.088)	0.735	0.000 (-0.105 to 0.105)	0.996	-0.019 (-0.128 to 0.094)	0.769
Age (year)	-0.047 (-0.026 to 0.011)	0.422	-0.058 (-0.027 to 0.009)	0.320	-0.062 (-0.028 to 0.008)	0.296	-0.065 (-0.028 to 0.008)	0.269	-0.060 (-0.027 to 0.008)	0.302	-0.067 (-0.029 to 0.008)	0.266
Illiterate	0.022 (-0.082 to 0.121)	0.707	-0.005 (-0.104 to 0.096)	0.939	-0.007 (-0.107 to 0.095)	0.908	-0.034 (-0.134 to 0.077)	0.596	-0.017 (-0.116 to 0.088)	0.617	-0.046 (-0.149 to 0.071)	0.485
Married	0.135 (0.022 to 0.261)	0.020	0.114 (-0.001 to 0.231)	0.052	0.108 (-0.009 to 0.227)	0.071	0.108 (-0.008 to 0.226)	0.068	0.123 (0.008 to 0.242)	0.036	0.111 (-0.008 to 0.234)	0.067
Lower income ^a	-0.086 (-0.202 to 0.028)	0.139	-0.139 (-0.236 to -0.023)	0.018	-0.129 (-0.230 to -0.012)	0.029	-0.145 (-0.238 to -0.024)	0.014	-0.141 (-0.239 to -0.024)	0.017	-0.141 (-0.244 to -0.020)	0.021
Diseases												
Diabetes	0.055 (-0.082 to 0.232)	0.348			0.049 (-0.093 to 0.228)	0.406					0.023 (-0.134 to 0.197)	0.711
Hypertension	-0.038 (-0.163 to 0.082)	0.517			-0.025 (-0.151 to 0.099)	0.680					-0.029 (-0.157 to 0.095)	0.632
Cardiovascular diseases	0.033 (-0.085 to 0.154)	0.571			0.024 (-0.098 to 0.149)	0.678					0.003 (-0.127 to 0.133)	0.964
Cerebrovascular disease	-0.010 (-0.252 to 0.211)	0.863			-0.013 (-0.258 to 0.207)	0.830					-0.020 (-0.288 to 0.207)	0.746
Parkinson's disease	-0.070 (-2.157 to 0.518)	0.229			-0.060 (-2.207 to 0.637)	0.305					-0.055 (-1.989 to 0.707)	0.350
Mental state												
Depressive symptoms ^b	0.086 (-0.001 to 0.009)	0.137					0.140 (-0.004 to 0.015)	0.235			0.127 (-0.004 to 0.015)	0.289
Minor mental symptoms ^c	0.062 (-0.009 to 0.030)	0.289					-0.057 (-0.045 to 0.026)	0.612			-0.035 (-0.043 to 0.031)	0.760
Cognitive impairment ^d	0.027 (-0.162 to 0.263)	0.643					-0.027 (-0.245 to 0.153)	0.648			-0.028 (-0.252 to 0.159)	0.655
Neighbourhood experience ^e												
Social support	0.025 (-0.008 to 0.013)	0.668							0.133 (-0.001 to 0.025)	0.080	0.115 (-0.004 to 0.024)	0.149
Perceived security	-0.063 (-0.033 to 0.010)	0.278							-0.117 (-0.049 to 0.006)	0.118	-0.117 (-0.051 to 0.007)	0.131
Adequacy of facilities	-0.049 (-0.039 to 0.015)	0.400							-0.050 (-0.044 to 0.022)	0.506	-0.043 (-0.044 to 0.024)	0.572

Multivariate regression models were generated sequentially with sociodemographic factors only (Model 1), sociodemographics plus disease factors (Model 2), sociodemographics plus mental state factors (Model 3), sociodemographics plus neighbourhood experience factors (Model 4) and sociodemographics plus all factors Model 5), respectively.

^aMonthly income <1,000 USD.

^bTaiwanese depression questionnaire score.

^cChinese health questionnaire score.

^dShort portable mental status questionnaire score and criteria.

^eNeighbourhood quality index subscales.

(coefficient -0.129 ; 95% CI: -0.230 to -0.012 ; $P = 0.029$). The effect of marriage was attenuated when disease factors were further included in the analysis though none of the physical diseases was significantly associated with telomere length. Model 3 was generated by incorporating sociodemographic and mental state factors. In Model 3, lower income was still significantly associated with telomere length (coefficient -0.145 ; 95% CI: -0.238 to -0.024 ; $P = 0.014$). The effect of marriage was attenuated when mental state factors were further included in the analysis though depressive symptoms, minor mental symptoms and cognitive impairment all failed to predict telomere length. Model 4 was generated by incorporating sociodemographic and neighbourhood experience factors. In Model 4, lower income remained significantly associated with telomere length (coefficient -0.141 ; 95% CI: -0.239 to -0.024 ; $P = 0.017$). Marriage was also a significant predictor of telomere length (coefficient 0.123 ; 95% CI: 0.008 to 0.242 ; $P = 0.036$) when neighbourhood factors were included in the analysis. None of the neighbourhood experience subscales was significantly associated with telomere length. Finally, Model 5 was generated by incorporating all related factors. In Model 5, lower income was significantly associated with telomere length (coefficient -0.141 ; 95% CI: -0.244 to -0.020 ; $P = 0.021$). The effect of marriage was attenuated when all the other factors were included in the analysis. In the meanwhile, none of the physical diseases, mental state and neighbourhood experience factors was significantly associated with telomere length.

Discussion

The results of this study suggest that lower income is significantly associated with cellular ageing in this population-based cohort of adults aged 65–74. Older adults with higher income was found to be significantly associated with longer telomere length (coefficient 0.141 ; 95% CI: 0.020 – 0.242 ; $P = 0.021$) compared with those with lower income. Older adults with lower income might have fewer social resources, worse health and, hence, shorter telomere length. This finding is consistent with those of previous studies [8, 12]. However, we cannot discard the possibility of a reciprocal relationship between income and telomere length. Being unmarried is found to be associated with shorter telomere length among middle-aged adults [13]. To a lesser extent, our study also found that unmarried, widowed, or single older adults had shorter telomeres. Since being unmarried is associated with worse health [20] and the presence of systematic inflammation [21], telomere length may potentially function as a cumulative oxidative stress and inflammation. This is consistent with our finding that the marital status was less significantly associated with telomere length in Models 2, 3 and 5. In those models, physical diseases and mental state were taken into account.

Previous studies have shown that several chronic diseases are associated with shorter telomeres [22], but our study did not come to the same conclusion. Though telomere shortening is one of the well-documented triggers for cellular senescence, there is some controversy regarding the causal

relationship between telomere shortening and cellular ageing [23]. Based on this tenet of telomere biology, individuals with a relatively shorter age-adjusted telomere length due to inherent and environmental factors will have accelerated cellular ageing, possibly resulting in higher disease susceptibility [24]. In our study, chronic diseases were not significantly associated with shorter telomeres. This implies that the aetiology of those chronic diseases is not mainly from cellular ageing.

In our study, depressive symptoms and minor mental symptoms were not associated with the telomere length. This is not consistent with the previous researches in which depression had been linked to a state of accelerated ageing, affecting the cardiovascular, cerebrovascular, neuroendocrine, metabolic and immune systems [9, 25]. One of the possible explanations for our finding was that we used depressive symptoms rather than psychiatric diagnosis. A one-time evaluation of psychiatric symptoms is different from a psychiatric disorder with its fluctuating severity at different times of the interview. Cognitive function has had a modest positive correlation with telomere length in previous studies [26, 27]. In our study, there was no significant correlation between cognitive impairment and telomere length. Complexity of causal factors of cognitive impairment among older adults may make the results of different studies diverse.

Neighbourhood experience represents the quality of the living environment and may be associated with psychological stress from the environment. Psychological stress has been linked to telomere length in theory [28] and then confirmed by several laboratories [29, 30] in specific populations. In our study, social support, perceived security or adequacy of facilities was not significantly associated with telomere length. The different age, and ethnic characteristics and different measurements of psychosocial stressors may account for the inconsistent findings.

Some limitations of this study are noted. The design of this study is cross-sectional; further longitudinal study is needed to confirm the possible causal relationships between psychosocial factors and the telomere length. Furthermore, the moderating effect of culture and ethnic characteristics on the associations between income, marriage and telomere length deserve attention among different study populations.

Key points

- Telomere length is a marker of cellular ageing, and older adults with higher income or marriage have longer telomere.
 - The relationship between income and telomere is not accounted for by physical diseases, mental state and neighbourhood experience.
 - The relationship between marriage and telomere is partly accounted for by physical diseases and mental state.
 - Unmarried older adults or those with lower income may be experiencing accelerated cellular ageing.
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Conflicts of interest

None declared.

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