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Spousal concordance in telomere length: New evidence from older adults in the US

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Abstract

Telomere length (TL) has been associated with a range of aging outcomes as well as mortality. Recent research has shown both high heritability (~70%) of TL as well as moderate spousal similarity (r~0.3) using European datasets. This paper explores the level of spousal concordance in telomere length in the Health and Retirement Study, a national sample of adults in the US. The results show that the spousal correlations are lower (r~0.11). Regression-based associations in TL in the US are low (beta~0.08) and also vary by the number of times respondents have been married, where spouses married a single time have higher associations in TL (beta~.12) than spouses married more once (beta~0.03). I also find variation in spousal TL association levels based on husband's education level. These findings suggest the possibility of both assortative mating patterns related to telomere length as well as likelihood of shared environmental factors that cause TL similarity in people who are socially connected.

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Data Availability Statement: The relevant data are third-party data and therefore cannot be made publicly available. However, data are available from the Health and Retirement Study at the University of Michigan. Data can be received by applying here: http://hrsonline.isr.umich.edu/index.php?p=shoavail&iyear=XO. The data will be made available to others in the same manner as it was accessed by the authors of this study.

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Introduction

Telomeres are repetitive DNA structures located at the ends of chromosomes that are thought to maintain genomic stability and shorten over time with each cell division [1]. They have been used as a measure of biological aging that has been shown in some (but not all) studies to be associated with mortality [2–5]. Some have proposed that they may be a marker of "healthy aging" rather than one of survival [6, 7], though either explanation may be related to the tendency for women to have greater TL than men [8–11]. There is growing interest in understanding the genetic factors, including the patterns of paternal vs. maternal inheritance, that predict telomere length (TL) as well as whether there are important environment and gene-environment interaction effects.

Some work has suggested the relatively large importance of biological factors as well as early environments that might shape TL over the life course. Broer et al. [12] meta-analyze data from several cohorts to estimate a heritability of TL around 70% and also show evidence of stronger mother-child correlations in TL than father-child correlations. Hjelmborg et al. [13] note that TL attrition is much slower in adults than in children and that having a long or a short TL is largely determined before adulthood. The authors find that heritability and early life environment are the main determinants of TL throughout the human life course.

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While the analysis in Broer et al. [12] focuses on genetic pathways, a secondary set of results focused on spousal similarity in TL and found moderate correlations (r~.3). This estimate is the first in the literature and has not been extended by other researchers. Broer et al. [12] suggest a few possible interpretations of this correlation. First, the resemblance could be induced by living together for a long time due to shared environmental exposures. A second possibility is an ascertainment effect—focusing on older adults who are married (and thus survived into old age) will produce a sample who is likely to have above average TL. A third possibility, not raised by Broer et al. [12], is of genetic assortative mating. Domingue et al. [14] suggest a moderate level of correlation across the genomes of spouses, compared with unrelated non-spouses.

Depending on the pathways that produce spousal similarity in TL, assessments of heritability of TL as well as intergenerational analysis become more difficult. Non-random mating patterns of parents can lead to heritability estimates that are understated. These assortative mating patterns may also make estimated associations between paternal-child and maternal-child TL difficult to interpret. In contrast, TL spousal similarity may reflect a largely environmental pathway, which could suggest a larger set of interventions during older adulthood that could benefit longevity than is suggested by Hjelmborg et al. [13] and other researchers as well as be used as a clinical signal to investigate the health of spouses (and possibly other family members and neighbors or co-workers) of individuals with low TL.

In order to explore these possibilities, this paper conducts the second investigation of spousal associations in TL in the literature and the first investigation with US data. Using the Health and Retirement Study, this paper analyses data for nearly 1,500 spousal pairs (Broer et al. [12] use over 1,900 spouses across 5 datasets) and finds spousal associations in TL that vary by spousal characteristics. In particular, spousal TL associations are higher for couples who have one marriage than those involved in their second (or higher) marriage. This suggests assortative mating may play a smaller role than shared environment in producing spousal TL associations.

Data

The Health and Retirement Study began in 1992 as a nationally representative longitudinal study of aging of individuals born from 1931–1941 and their spouses [15]. The focus of the first and subsequent surveys has been in collecting data on the aging process by focusing on health, work, family, and related domains. There are now >10,000 individuals with genetic data collected. Of these, nearly 6,000 have telomere data, where the subjects were selected based on membership in the one-half random sample of the HRS that were preselected to have enhanced face-to-face interviews in 2008. Faul et al. [16] note that this sample was selected at the household level to ensure that the same request was made to both members of a household. There were a small number of exclusion criteria: (1) needing to be interviewed by proxy, (2) residing in a nursing home, or (3) preferring to be interviewed by telephone. Respondents who provided a saliva sample did not differ by age, sex, education, or income from those who were asked but did not consent [16]. Consent for the DNA collection was obtained in person at the time of the interview. The HRS study protocol was approved by the University of Michigan Institutional Review Board.

Measurement of TL has been fully detailed in Faul et al. [16], which I summarize for the reader. A saliva sample was obtained directly using an Oragene Collection Kit for the 85% of HRS respondents who consented. Saliva samples were immediately sent to a central laboratory where the DNA was extracted and stored frozen at −80 C until being plated and shipped for genetic analyses. Average TL was assayed using quantitative PCR (qPCR) by comparing

telomere sequence copy number in each participant's sample (T) to a single-copy gene copy number (S), where the resulting T/S ratio is proportional to mean TL. A total of 5,916 participant samples from the HRS cohort were tested. Of these participant samples, 88.9 percent passed all quality control criteria further outlined in Faul et al. [16].

Descriptive statistics for the sample of spouses in the HRS who have telomere assessments with a T/S ratio 3 or lower are presented in Table 1, which is stratified by gender. Wives in the sample are on average 65.5 years old and completed 12.7 years of schooling. Husbands are 68.7 years old on average and have completed 12.9 years of schooling. Nearly two-thirds of the respondents report being married only once. S1 Table shows that the full sample of respondents are quite similar to the sample of spouses in TL, age, and educational attainment and also shows the descriptive statistics of the pooled spousal sample.

Results

The correlation between spouses in the data is 0.11 (not shown), which is smaller than the reports in Broer et al. [12] of ~0.3 using European samples. Table 2 presents the key empirical results that focus on spousal similarity in TL, which allows statistical adjustments to the similarity estimate above. The beta from the regression shows an association between husband TL (the dependent variable) and wife TL of 0.085. As expected, husband age is negatively related to husband TL; otherwise, few wife or husband characteristics predict TL (see S2 Table for additional analysis of individual level predictors of TL). In order to explore alternative hypotheses for the sources of the association in spousal TL, columns 2 and 3 stratify the sample based on whether the husbands have been married once or more than once. The results show much stronger adjusted association in spousal TL among those spouses married once (0.12) than those married more than once (0.026), this difference is statistically significant at the 9% level.

Table 1. Descriptive statistics of spouses characteristics and telomere length in the HRS.

Wives (N~1500)				
Variable	Mean	Std Dev	Min	Max
Telomere Length	1.35	0.32	0.23	2.96
Age (2008)	65.49	9.78	33.00	90.00
Educational Attainment	12.71	2.96	0.00	17.00
White	0.86	0.35	0.00	1.00
Black	0.08	0.28	0.00	1.00
Other Race	0.06	0.23	0.00	1.00
Number of Marriages	1.44	0.76	0.00	7.00
Single Marriage	0.67	0.47	0.00	1.00
Husbands (N~1500)				
Variable	Mean	Std Dev	Min	Max
Telomere Length	1.29	0.33	0.23	2.85
Age (2008)	68.69	9.43	26.00	93.00
Educational Attainment	12.88	3.36	0.00	17.00
White	0.86	0.35	0.00	1.00
Black	0.09	0.28	0.00	1.00
Other Race	0.05	0.22	0.00	1.00
Number of Marriages	1.46	0.75	0.00	7.00
Single Marriage	0.65	0.48	0.00	1.00

Notes: observations with Telomere Length above 3 are not included.

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Table 2. Adjusted associations between spousal telomere length in the HRS. Full Sample and stratified by husband's number of marriages.

Outcome	TL	TL	TL
Sample	**Spousal**	**Husband Single Marriage**	**Husband 2+ Marriages**
Spousal TL	0.085***	0.119***	0.026
	(0.027)	(0.034)	(0.043)
Husband Education	-0.001	0.002	-0.009*
	(0.003)	(0.004)	(0.005)
Husband Black Race	0.094	0.038	0.194
	(0.082)	(0.105)	(0.133)
Husband Other Race	0.042	0.025	0.081
	(0.045)	(0.064)	(0.066)
Husband Single Marriage	0.020		
	(0.025)		
Wife Education	0.005	0.003	0.009
	(0.004)	(0.004)	(0.006)
Wife Black Race	-0.006	0.076	-0.153
	(0.084)	(0.108)	(0.135)
Wife Other Race	0.006	0.025	-0.016
	(0.043)	(0.063)	(0.059)
Wife Single Marriage	-0.005	0.005	0.003
	(0.025)	(0.038)	(0.033)
Husband Age	-0.004**	-0.004	-0.003
	(0.002)	(0.003)	(0.002)
Wife Age	-0.000	-0.001	0.000
	(0.002)	(0.003)	(0.002)
Constant	1.414***	1.398***	1.463***
	(0.091)	(0.119)	(0.147)
Observations	1,492	975	517
R-squared	0.038	0.050	0.028
Chi2			3.042
P			0.081

Notes: each observation is a spousal pair. Standard errors in parentheses

*** $p<0.01$

** $p<0.05$

* $p<0.1$

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In unreported results, splitting the sample based on length of current marriage at 40 years (the median value), produces 0.097 for long marriages and 0.073 for short marriages. S3 Table shows robustness of results for alternative exclusion criterion based on the TL.

Table 3 further stratifies the results by educational attainment of the spouse. For husbands with low education (column 1), the spousal association is lower (0.05) than husbands with higher education (0.12 in column 2), though the p-value for this difference is $p<0.18$. In contrast, there is no evidence of differences in spousal similarity in TL that varies by wife's educational attainment (columns 3 and 4).

Conclusions

TL has been shown to be an important predictor of old age health and potentially linked to mortality. However, the key determinants of TL are largely unknown. On one hand,

Table 3. Adjusted associations between spousal telomere length in the HRS stratified by education level.

Outcome	TL	TL	TL	TL
Sample	**Husband HS grad or Less**	**Husband Greater than HS Grad**	**Wife HS grad or Less**	**Wife Greater than HS Grad**
Spousal TL	0.049	0.124***	0.074**	0.087**
	(0.038)	(0.038)	(0.033)	(0.039)
Husband Education	-0.009*	-0.007	0.002	0.001
	(0.005)	(0.009)	(0.004)	(0.005)
Husband Black Race	0.146	0.034	0.033	-0.033
	(0.121)	(0.112)	(0.113)	(0.114)
Husband Other Race	0.102	-0.032	-0.016	0.007
	(0.065)	(0.062)	(0.056)	(0.070)
Husband Single Marriage	0.002	0.034	0.084**	0.015
	(0.036)	(0.035)	(0.033)	(0.036)
Wife Education	0.006	0.004	-0.007	-0.006
	(0.005)	(0.005)	(0.005)	(0.009)
Wife Black Race	-0.053	0.051	0.057	0.158
	(0.121)	(0.121)	(0.116)	(0.115)
Wife Other Race	-0.050	0.051	0.024	0.045
	(0.060)	(0.063)	(0.055)	(0.065)
Wife Single Marriage	-0.015	0.011	-0.047	-0.008
	(0.036)	(0.035)	(0.032)	(0.037)
Husband Age	-0.006**	-0.001	0.001	0.003
	(0.002)	(0.002)	(0.002)	(0.003)
Wife Age	0.000	-0.002	-0.006***	-0.009***
	(0.002)	(0.002)	(0.002)	(0.003)
Constant	1.612***	1.366***	1.592***	1.656***
	(0.134)	(0.164)	(0.117)	(0.171)
Observations	751	741	820	672
R-squared	0.049	0.039	0.047	0.062
Chi2		1.876		0.060
P		0.171		0.806

Notes: each observation is a spousal pair. Standard errors in parentheses

*** $p<0.01$

** $p<0.05$

* $p<0.1$

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heritability estimates of TL are often in the range of 70%, suggesting the likelihood of important genetic factors. Related evidence has shown that early childhood conditions are strong predictors of late life TL. These findings could suggest that late life interventions to reduce TL shortening may be ineffective. On the other hand, spousal similarity in TL (of unrelated people) may instead suggest that environmental factors continue to shape TL in middle and older age individuals and point to the possibility of effective interventions during the middle and later stages of the life course. The findings in this study present new evidence of the possible importance of these later life factors. These findings do have several limitations worth considering. First, using a relatively old sample such as the HRS, may induce mortality selection into the sample and accompanying results. This process may create a sample of survivors who have longer TL than the individuals who attrite. Because the sample is of spouses, mortality bias

may be compounded further. Results in S1 Table and S2 Table suggest that these effects may be modest because the spousal sample TL is quite similar to the full sample and the associations between age and TL in the sample is also quite modest. A second major limitation is the lack of investigation of specific environmental measures of exposures that might shape TL, especially related to stressful events, shared diet, and shared toxicant exposures. The broad proxy in this paper is the number of marriages (1 vs. more than 1); additional work with richer data will be needed to explore specific exposure that might be responsible for similarity in spousal TL, especially those who have lived together for a long period of time.

Using a large set of spouses from a national sample of older individuals in the US, this study shows modest correlations in spousal TL as well as evidence that couples who have been together longer have higher levels of similarity in their TL. Findings also suggest that spousal similarity in TL is lower in couples with less-educated husbands. A possible explanation is a larger discordance in environmental conditions in these couples, especially if the average husband has low-wage employment with higher levels of toxicant, stress, or other negative exposures than might be typical for the average wife in this subsample. Additional research is needed that explores potential determinants of these environmentally induced TL patterns.

Supporting information

S1 Table. Descriptive statistics of full sample and pooled spousal sample. Notes: observations with Telomere Length above 3 are not included.
(DOCX)

S2 Table. Associations between individual characteristics and telomere length in the HRS. Notes: Standard errors in parentheses. *** $p<0.01$, ** $p<0.05$, * $p<0.1$.
(DOCX)

S3 Table. Adjusted associations between spousal telomere length in the HRS: Exploring robustness to removal of outlier TL measurements. Notes: 1 SD + M is one standard deviation more than the mean. Standard errors in parentheses. *** $p<0.01$, ** $p<0.05$, * $p<0.1$.
(DOCX)

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