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Negative results

Association between telomere length and cognitive ability in a community-based sample

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ABSTRACT

Prior research suggests that telomere length is a biomarker of cognitive aging; however, literature has demonstrated conflicting findings to date. The present study uses data from the Dallas Heart Study, $N = 2606$, to assess the association between telomere length and cognitive ability on the Montreal Cognitive Assessment. The data do not support a relationship between telomere length and general cognitive functioning, ($\beta = 0.016$, SE = 0.31, $p = 0.407$). The data further replicate the negative findings within current literature.

1. Introduction

Telomeres are repetitive G-rich nucleotide sequences that shorten due to repeated cell division, stabilize chromosomes, and protect cells from degradation (Blackburn, 1991). Research suggests a relationship between shortened telomere length and diminished cognitive ability, although findings have been disparate across populations, gender, age, and cognitive measurements (Harris et al., 2006; Mather et al., 2011; Zhan et al., 2018). This relationship remains mixed and inconclusive. The present study examined this relationship using a large and diverse community-based sample.

2. Methods

Data were obtained from the second phase of the Dallas Heart Study (DHS), an epidemiological study that examined factors relevant to cardiovascular risk within a multiethnic sample of adults. Initial data collection occurred between 2000 and 2002 (DHS-1); the study was later converted into a longitudinal study by collecting a second wave of data (DHS-2). Follow-up data were obtained from the participants in DHS-1 that choose to continue participation. Data from new participants were also collected to account for attrition between DHS-1 and DHS-2. For the current analysis, cross-sectional data from DHS-2 were only analyzed because during this particular phase, cognitive ability (Montreal Cognitive Assessment [MoCA]) was assessed once and genotype data (telomere length) obtained. The MoCA (Nasreddine et al., 2005) is a brief screening instrument to detect mild cognitive impairment and used during the DHS-2 to measure cognitive ability. MoCA test items and methods used to determine telomere length in the DHS have been reported elsewhere, respectively (King et al., 2014; Nasreddine et al., 2005). The study was approved by the University of Texas Southwestern Medical Center Institutional Review Board, and a written informed consent was obtained from all participants. After exclusions based on missing data, 2606 of 3408 participants were analyzed. In a cross-sectional analysis of data obtained from DHS-2, multiple linear regressions were conducted. Two whole-sample models were conducted—whole-sample model 1, fully adjusted for only age and gender, whereas whole-sample model 2, fully adjusted for the following covariates: age, gender, ethnicity, body mass index, diabetic status, and tobacco use (see Table 1). The same covariates were adjusted for in stratified models 3, 4, 5, and 6, examining differences in gender, ethnic/racial groups, age, and education level, respectively; SPSS Statistics for Windows, version 24.0 (Armonk, NY; IBM SPSS Inc., 2017) was used for all analysis.

3. Results

In Table 1, descriptive statistics are listed. Within the sample, the average score for the MoCA was $M = 23.27$ (SD = 4.02), with the

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Table 1
Descriptive statistics

Variable	Sample, N = 2606	
	n (%)	Mean (SD)
Gender		
Female	1580 (61)	
Male	1026 (39)	
Age		
<50 y	1290 (49.5)	
≥50 y	1316 (50.5)	
Ethnicity		
African American	1371 (52.6)	
White	848 (32.5)	
Hispanic	387 (14.9)	
Education		
≤12 y	1058 (40.6)	
>12 y	1548 (59.4)	
Diabetic status		
Diabetic	426 (16.3)	
Nondiabetic	2180 (83.7)	
Tobacco use		
History of use	1150 (44.1%)	
No history of use	1456 (55.9%)	
Telomere length[a]		1.79 (0.25)
MoCA score[b]		23.27 (4.02)
Body mass index (kg/m^2)		31.35 (7.51)
Age, mean in years		49.82 (11.7)
Education, mean in years		12.61 (2.17)

Key: MoCA, Montreal Cognitive Assessment.
[a] Telomere length expressed as a T/S ratio—the copy number of the telomere DNA (T) to a single-copy gene (S).
[b] The maximum score is 30.

Table 2
Models 1–6: Association between telomere length and MoCA score

Sample	B	*p* value	*SE*	95% confidence interval	
				Lower	Upper
Whole-sample Model 1[a]	0.257	0.407	0.31	−0.35	0.86
Whole-sample Model 2[b]	0.167	0.579	0.30	−0.42	0.76
Gender					
Female[c]	0.371	0.347	0.02	−0.40	1.14
Male[c]	−0.136	0.771	−0.01	−1.05	0.78
Ethnicity					
African American[d]	0.393	0.325	0.03	−0.39	1.18
White[d]	0.518	0.216	0.04	−0.30	1.34
Hispanic[d]	−0.292	0.706	−0.02	−1.81	1.23
Age					
<50 y[e]	0.285	0.493	0.42	−0.53	1.10
≥50 y[e]	0.603	0.163	0.43	−0.24	1.45
Education					
≤12 y[f]	−0.056	0.906	0.47	−0.96	0.86
>12 y[f]	−0.214	0.493	0.31	−0.83	0.40

Key: MoCA, Montreal Cognitive Assessment.
[a] Whole-sample model (adjusted for covariates gender and age).
[b] Whole-sample model (adjusted for covariates: gender, age, body mass index, ethnicity, tobacco use, and diabetic status).
[c] Gender-stratified model.
[d] Ethnicity-stratified model.
[e] Age-stratified model.
[f] Education level–stratified model.

minimum to maximum score range of 7 to 30, respectively. In the whole-sample model 1, no significant relationship was observed between telomere length and MoCA scores ($\beta = 0.016$, $p = 0.407$). In the whole-sample model 2, no significant relationship was observed between telomere length and MoCA scores ($\beta = 0.167$, $p = 0.58$). In model 3, no relationship was found in females ($\beta = 0.371$, $p = 0.347$) or males ($\beta = -0.136$, $p = 0.77$). In model 4, no relationships were found in African Americans ($\beta = 0.393$, $p = 0.33$), whites ($\beta = 0.518$, $p = 0.22$), or Hispanics ($\beta = -0.292$, $p = 0.71$). In model 5, no relationships were found for participants ≥50 years ($\beta = 0.603$, $p = 0.16$) or <50 years ($\beta = 0.285$, $p = 0.49$). For model 6, no relationship was found for participants with ≤12 years of education ($\beta = -0.056$, $p = 0.91$) or >12 years ($\beta = -0.214$, $p = 0.49$; Table 2).

4. Discussion

The present study examined the relationship within an ethnically diverse community-based sample of over 2000 people with a wide age range. No relationship between telomere length and cognitive ability was observed. These findings are consistent with recent meta-analytic findings reported by Zhan et al. (2018). Furthermore, 2 separate whole-sample basic models were conducted. The first model only corrected for age and gender because there is a strong association between cognitive ability and education level (Hagenaars et al., 2016). The second whole-sample model adjusted for education and covariates of interest. For both whole-sample models adjusting and not adjusting for education level, the relationship between telomere length and cognitive ability remains undetermined. Prior research reflects these conflicting findings on the relationship between age, cognitive ability, and telomere length. Martin-Ruiz et al. (2005) examined the oldest population studied to date (≥85 years) and determined that telomere length is not associated with cognitive ability, mortality, or age-related illnesses. In contrast, other studies were able to detect an effect for age groups of 60–79 years (Canela et al., 2007; Yaffe et al., 2011). One potential limitation is that only a measure of cognitive ability was used rather than multiple specific measures. Type of cognitive measurement may contribute to disparate findings. Harris et al. (2006) detected an effect on only one of four tests used. Mather et al. review (2011) asserts that a single biomarker is insufficient to determine aging across various underlying biological systems. They also suggest that different biomarkers may be appropriate only during certain age ranges. This would explain the sparse and conflicting findings. Furthermore, the MoCA is a screening tool for mild cognitive impairment and may have reduced the ability to detect an effect because it was used in the general population and not a cognitively impaired population. In summary, the present study found no significant relationship between telomere length and global cognitive function in a large, diverse, community-based sample.

Disclosure

Dr Brown has research grants from NIH, the Stanley Medical Research Institute, and Otsuka and serves on an advisory board for Allergan. Dr Rossetti, Ms. Kaja, and Ms. Reyes have nothing to declare. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neurobiolaging.2018.11.006.

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