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Physical activity and telomere length in U.S. men and women: An NHANES investigation

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ABSTRACT

The principal objective was to determine the extent to which physical activity (PA) accounts for differences in leukocyte telomere length (LTL) in a large random sample of U.S. adults. Another purpose was to assess the extent to which multiple demographic and lifestyle covariates affect the relationship between PA and LTL. A total of 5823 adults from the National Health and Nutrition Examination Survey (NHANES 1999–2002) were studied cross-sectionally. Employing the quantitative polymerase chain reaction method, LTL was compared to standard reference DNA. PA was indexed using MET-minutes using self-reported frequency, intensity, and duration of participation in 62 physical activities. Covariates were controlled statistically. Telomeres were 15.6 base pairs shorter for each year of chronological age ($F = 723.2$, $P < 0.0001$). PA was inversely related to LTL after adjusting for all the covariates ($F = 8.3$, $P = 0.0004$). Telomere base pair differences between adults with High activity and those in the Sedentary, Low, and Moderate groups were 140, 137, and 111, respectively. Adults with High activity were estimated to have a biologic aging advantage of 9 years (140 base pairs ÷ 15.6) over Sedentary adults. The difference in cell aging between those with High and Low activity was also significant, 8.8 years, as was the difference between those with High and Moderate PA (7.1 years). Overall, PA was significantly and meaningfully associated with telomere length in U.S. men and women. Evidently, adults who participate in high levels of PA tend to have longer telomeres, accounting for years of reduced cellular aging compared to their more sedentary counterparts.

1. Introduction

Dozens of investigations indicate that all-cause mortality decreases as physical activity (PA) increases (Samitz et al., 2011), even among those at high risk (Booth et al., 2016). Research also shows that coronary heart disease mortality is much lower in the physically active compared to the inactive (Sattelmair et al., 2011). Risk of other chronic diseases, such as breast cancer (Wu et al., 2013), type 2 diabetes (Aune et al., 2015), hypertension (Whelton et al., 2002), and general cancer (Li et al., 2016; Liu et al., 2016) tend to be significantly lower in active adults compared to their sedentary counterparts. Moreover, in a recent meta-analysis including 80 studies and over 1.3 million participants, physical activity, particularly vigorous activity, was shown to be especially valuable for reducing mortality (Samitz et al., 2011).

There are many mechanisms through which regular PA could reduce disease and mortality. One of these pathways could be telomere length (Mundstock et al., 2015a). Telomeres are nucleoprotein structures positioned at the end of chromosomes. These end-caps protect genetic information and reduce degradation over time. As a consequence of mitosis, telomeres naturally shorten. As telomeres shorten, cell senescence increases and eventually cell apoptosis results.

In general, telomere shortening contributes to biologic aging and telomere shortening can be hastened by a number of factors that promote inflammation and oxidative stress (Houben et al., 2008; Wolkowitz et al., 2011). For example, obesity (Mundstock et al., 2015b), smoking (Huzen et al., 2014), poor diet (Lian et al., 2015; Marcon et al., 2012; Lee et al., 2015), type 2 diabetes (Zhao et al., 2013), and low socioeconomic levels (Shiels et al., 2011) are all predictive of shorter telomeres in adults.

Because telomere length is a biomarker of cell aging, the relationship between chronological age and telomere length is substantial (Needham et al., 2013; Brown et al., 2016). Evidence is growing in support of the concept that telomere length accounts for differences in the function and fate of cells (Aubert & Lansdorp, 2008). Using nearly 20,000 adults, researchers showed that adults with telomeres in the shortest category had 25% greater risk of death compared to those in the longest telomere category (Weischer et al., 2012). Similarly, Njajou et al. found that telomere length accounted for years of healthy life (Njajou et al., 2009), and other researchers revealed that shorter telomeres predict higher mortality in women (Carty et al., 2015).

As summarized in a recent meta-analysis (Mundstock et al., 2015a), several investigations have studied the relationship between physical

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activity and telomere length using a variety of methods and >41,000 subjects. To date, roughly 54% of studies have failed to detect a significant relationship, 41% have found a positive association, and 5% have uncovered a curvilinear relationship. The authors (Mundstock et al., 2015a) conclude that "a possible significant association between physical activity and telomere length remains an open question" (p. 70).

One of the weaknesses of studies that have investigated the link between PA and telomere length is the methods employed to measure PA. According to Mundstock et al., a wide-variety of methods have been used, many which have not been validated (Mundstock et al., 2015a). Another issue has been the failure of some investigations to control for potential mediating variables.

The present study was designed to overcome some of the limitations of past studies by using a comprehensive and valid measure of PA, by controlling for a number of potential mediating variables, by using a large sample of randomly selected U.S. adults, and by presenting results based on U.S. PA guidelines. The primary purpose was to determine the extent to which PA, indexed using MET-minutes, accounts for differences in telomere length in 5823 U.S. men and women. Ancillary objectives were to ascertain the extent demographic and lifestyle factors affect the PA and telomere relationship, and to determine if current U.S. activity guidelines optimize the association between physical activity and telomere length.

2. Methods

2.1. Sample

The National Health and Nutrition Examination Survey (NHANES) is an ongoing study conducted by the Centers for Disease Control and Prevention (CDC) that provides estimates of the lifestyle, health, and nutrition status of U.S. civilians. In order for NHANES findings to be generalized broadly across the U.S., a multistage, probability sampling design is employed (Curtin et al., 2012).

NHANES data containing telomere length values are available for only a 4-year period, 1999–2002. The telomere data became accessible to the public in November 2014. All of the data used in the present study are cross-sectional. Moreover, the NHANES data sets are all posted online and are available to the public (NHANES, 1999–2006).

During the 1999–2000 and 2001–2002 NHANES cycles, all participants ages 20 years and older were invited to give a DNA sample. Of the 10,291 eligible adults, 7827 adults provided a valid DNA sample (76%). Participants ≥85 years old were excluded because NHANES recorded the age of all participants ≥85 years old as 85 to maximize confidentiality.

Participants were required to have complete data. A total of 5823 participants, 2766 men and 3057 women, were included in the analyses. The National Center for Health Statistics Ethics Review Board approved collection of the NHANES data and posting of the files for public use (NHANES, 1999–2014). Written informed consent was acquired from each NHANES participant.

2.2. Measurement methods

The exposure variable was physical activity, indexed using MET-minutes, and the outcome measure was leukocyte telomere length. The demographic covariates were: age, gender, race, and education, and the lifestyle covariates included body mass index (BMI), smoking (pack-years), and alcohol use.

2.2.1. Telomere length

According to NHANES (2001–2002), "Each sample was assayed 3 times on 3 different days. The samples were assayed on duplicate wells, resulting in 6 data points. Sample plates were assayed in groups of 3 plates, and no 2 plates were grouped together more than once. Each assay plate contained 96 control wells with 8 control DNA samples. Assay runs with 8 or more invalid control wells were excluded from further analysis (<1% of runs). Control DNA values were used to normalize between-run variability. Runs with more than 4 control DNA values falling outside 2.5 standard deviations from the mean for all assay runs were excluded from further analysis (<6% of runs). For each sample, any potential outliers were identified and excluded from the calculations (<2% of samples). The mean and standard deviation of the T/S ratio were then calculated normally. The interassay coefficient of variation was 6.5%" (NHANES, 2001–2002). Mean T/S ratio values were converted to base pairs using the formula: $3274 + 2413 \times (T/S)$.

2.2.2. Physical activity

To quantify the amount of physical activity reported by each participant, MET-minutes were calculated. A MET is a metabolic equivalent. It represents the ratio between one's metabolic rate while physically active and at rest (Bushman et al., 2014).

Participants reported their activity by recording which, if any, of 62 physical activities they participated in during the past 30 days. For each activity, participants reported if their involvement was moderate or vigorous, based on NHANES definitions. Each mode of activity was assigned one of two specific predetermined MET values, depending on if the activity was reported as moderate or vigorous intensity. Participants also reported the number of times in the past 30 days they engaged in each activity and the average duration of each activity.

A MET score for each activity was calculated using the compendium of physical activity (Ainsworth et al., 2000). The MET values assigned by NHANES for each of the 62 activities are reported on the NHANES website (NHANES, 2004). Total MET-minutes was estimated by summing the MET-minutes for each activity and a weekly MET-minute score was calculated for each participant. Several investigations support the validity of self-reported MET-minutes, as MET-minutes have been shown to predict years of potential life gained (Janssen et al., 2013), cardiometabolic risk (Soriano-Maldonado et al., 2016), and risk of cancer, ischemic heart disease, stroke, and diabetes (Kyu et al., 2016).

Total physical activity was categorized using two methods, relative and absolute. First, because participants were part of a large, national sample, groups were formed based on relative activity levels (total MET-minutes). Quartiles could not be used because >25% of the sample was sedentary. Therefore, participants reporting no regular physical activity were classified as Sedentary, and the remaining adults, each reporting some regular physical activity in the past 30 days, were divided into sex-specific tertiles. The four resulting categories representing *relative* physical activity were labeled: Sedentary, Low, Moderate, and High.

Another set of activity categories was based on the 2008 Physical Activity Guidelines for Americans (CDC, 2008). The categories were formed using cut-points provided by the guidelines, which recommend that adults engage in 500 to 1000 MET-minutes per week, or more (CDC, 2008). Four categories were developed based on the cut-points from the guidelines (G): Sedentary-G (those reporting no regular physical activity), Insufficient-G (those performing some regular activity, but not reaching the minimum standards of the guidelines), Moderate-G (those performing 500–1000 MET-minutes of activity per week), and High-G (those performing >1000 MET-minutes of activity per week).

2.2.3. Demographic covariates

To delineate races and ethnicities, NHANES used: Non-Hispanic White, Non-Hispanic Black, Mexican American, Other race or Multi-racial (Other), and Other Hispanic. Education level was defined as: Less than high school, high school diploma (including GED), and more than high school.

2.2.4. Lifestyle covariates

Several lifestyle variables were employed as potential mediating factors. Smoking was treated as a continuous variable and was indexed using pack-years, defined as the number of cigarettes smoked per day

multiplied by the number of years smoked, divided by 20. BMI was calculated using the standard formula: weight in kilograms divided by height in meters squared, kg/m^2 (Pescatello & American College of Sports Medicine, 2014). Categories based on standard cut-points were used: underweight (<18.5), normal weight (≥18.5 and <25.0), overweight (≥25.0 and <30.0), obese (≥30.0), or missing (Pescatello & American College of Sports Medicine, 2014).

Three categories were used to index alcohol use by NHANES: abstainers, moderate drinkers, and heavy drinkers, each reflecting intake over the past 12 months. Abstainers reported no alcohol intake. Moderate drinkers were men reporting >0 and <3 alcoholic beverages per day or women reporting >0 and <2 drinks per day. Heavy drinkers were men reporting 3 or more drinks per day, or women reporting 2 or more alcoholic beverages per day.

2.3. Statistical analyses

A sample weight is assigned to each person participating in NHANES (Johnson et al., 2013). Each weight reflects the number of individuals in the U.S. represented by that NHANES participant. According to NHANES, the sample weights reflect the unequal probability of selection, nonresponse adjustment, and adjustment to independent population controls (Johnson et al., 2013). When unequal selection probability is applied, unbiased national estimates result from using the sample weights in statistical analyses (Johnson et al., 2013). For the present study, sample weights were based on 4 years of MEC (mobile examination center) records. To produce weighted frequencies, SAS SurveyFreq was used, and SAS SurveyMeans was employed to estimate weighted means, each generalizable to the U.S. adult population.

Because the outcome variable, telomere length, deviated from a normal distribution, it was transformed by natural logarithm before inclusion in the statistical analyses. The extent to which mean telomere lengths differed across the physical activity categories was evaluated using regression analysis and the SAS SurveyReg procedure. Partial correlation was employed using the SAS SurveyReg and LSmeans procedures to determine the extent to which the adjusted telomere length means differed across the physical activity categories, after adjusting for differences in the covariates.

Because individuals with short telomeres are at greater risk of several diseases (Chen et al., 2014; Scheller Madrid et al., 2016; Allende et al., 2016), the extent to which adults in the various activity categories had different odds of possessing short telomeres was calculated using SAS SurveyLogistic. Short telomeres were operationalized as those in the lowest sex-specific quartile of the sample.

All *P*-values were two-sided and statistical significance was accepted when alpha was <0.05. The analyses were performed using SAS Version 9.4 (SAS Institute, Inc., Cary, NC).

3. Results

Findings of the present investigation are based on complete data for 5823 participants. Table 1 shows the frequencies and weighted percentages for the exposure variable and each of the covariates. Mean (±SE) age of the sample was 46.3 ± 0.4 years. Age and telomere length were strongly, linearly, and inversely associated. For each year of chronological age, telomeres were 15.6 base pairs shorter ($F = 723.2$, $R^2 = 0.17$, $P < 0.0001$). Age-squared was not predictive of telomere length.

According to Table 2, *relative* physical activity was inversely related to telomere length, after adjusting for all the demographic variables ($F = 9.2$, $P < 0.0002$). Similarly, after adjusting for differences in all the demographic and lifestyle covariates, participants in the High PA category had significantly longer telomeres than adults in the Sedentary, Low, or Moderate groups ($F = 8.3$, $P = 0.0004$). Adults in the Sedentary, Low, and Moderate PA categories did not differ significantly in telomere length (Table 2).

Table 1
Descriptive characteristics of the sample ($n = 5823$).

Variable	*N*	Weighted %	SE
Age (years)			
20–29	1053	17.5	1.0
30–39	1027	21.1	0.8
40–49	1023	22.0	0.8
50–59	789	16.9	0.8
60–69	936	11.1	0.6
70–84	995	11.4	0.5
Gender			
Men	2766	47.9	0.5
Women	3057	52.1	0.5
Race			
Non-Hispanic White	2826	71.7	2.0
Non-Hispanic Black	1090	10.5	1.3
Mexican American	1458	7.6	0.9
Other race	150	3.5	0.6
Other Hispanic	299	6.7	1.6
Education			
<High school	2108	23.4	1.1
High school diploma	1352	26.4	0.8
>High school	2363	50.2	1.4
Smoking (pack-years)			
Non-smoker	4710	77.9	0.9
1–14	733	14.1	0.5
15 or more	380	8.0	0.7
Body mass index			
Underweight	84	1.8	0.2
Normal weight	1637	31.1	0.7
Overweight	2047	33.7	1.0
Obese	1865	30.5	1.0
Missing	190	2.9	0.3
Alcohol use			
Abstainer	2371	36.0	2.4
Moderate drinker	1730	31.4	1.7
Heavy drinker	1722	32.6	1.0
Physical activity-relative			
Sedentary	3407	50.8	1.6
Low	843	16.3	0.8
Moderate	807	16.4	1.0
High	766	16.4	1.2
Physical activity-guidelines			
Sedentary-G	3407	50.8	1.6
Insufficient-G	798	15.4	0.8
Moderate-G	489	9.6	0.6
High-G	1129	24.2	1.4

Note: Values in the column, weighted %, reflect the distribution of participants after the NHANES sample weights were applied. The Physical Activity-Relative categories were based on the distribution of MET-minute levels for the present NHANES sample. Participants reporting no regular physical activity were classified as Sedentary, and the remaining adults, each reporting some physical activity in the past 30 days, were divided into sex-specific tertiles. The Physical Activity-Guidelines categories were based on the 2008 U.S. Physical Activity Guidelines. Specifically, Sedentary-G included those reporting no regular physical activity, Insufficient-G included those performing some regular activity, but not reaching the minimum standards of the guidelines, Moderate-G included those performing 500–1000 MET-minutes of activity per week, and High-G included those performing >1000 MET-minutes of activity per week. Age and smoking (pack-years) were treated as continuous variables in the analyses.

As shown in Table 3, mean telomere lengths also differed significantly across physical activity levels based on the U.S. guidelines (G). Specifically, adults in the High-G category had significantly longer telomeres than participants in the Sedentary-G, Insufficient-G, or Moderate-G physical activity groups, after controlling for the demographic variables ($F = 5.2$, $P = 0.0052$), and after adjusting for all the covariates simultaneously ($F = 4.3$, $P = 0.0133$).

Results also showed a significant relationship between the prevalence of short telomeres and *relative* physical activity (Rao-Scott Chi-Square: 51.7, $P < 0.0001$). Specifically, prevalence of short telomeres

Table 2
Differences in mean telomere length (base pairs) by level of weekly MET-minutes of physical activity (relative) in U.S. women and men, after adjusting for the covariates.

	Weekly physical activity (relative)					
Covariate	Sedentary Mean ± SE	Low Mean ± SE	Moderate Mean ± SE	High Mean ± SE	F	P
Age	5765[a] ± 40	5775[a] ± 51	5815[a] ± 48	5923[b] ± 52	8.2	0.0004
Demographics	5786[a] ± 39	5793[a] ± 45	5828[a] ± 45	5938[b] ± 46	9.2	0.0002
Demographics and lifestyle	5811[a] ± 41	5814[a] ± 44	5841[a] ± 47	5952[b] ± 49	8.3	0.0004

[a,b]Means on the same row with the same superscript letter were not statistically different ($P > 0.05$). The physical activity categories were based on relative MET-minute levels. Participants reporting no regular physical activity were classified as Sedentary, and the remaining adults, each reporting some physical activity in the past 30 days, were divided into sex-specific tertiles. Across the four categories of relative physical activity, weighted percentages were: 50.8% ($n = 3407$) reported no regular physical activity (Sedentary), 16.3% ($n = 843$) reported Low levels, 16.4% ($n = 807$) reported Moderate levels, and 16.4% ($n = 766$) reported High levels of physical activity (MET-minutes). Because sample weights were applied to each participant, differences in the size of each category should be interpreted relative to percentages, not *N*. Means on the same row were adjusted for the covariates in the left column. The demographic covariates were: age, sex, race, and education. The lifestyle covariates were: body mass index, cigarette smoking, and alcohol use.

(sex-specific lowest quartile) decreased as level of *relative* activity increased: Sedentary (29.7%), Low (22.5%), Moderate (23.5%), and High PA (14.2%).

Table 4 shows the relationship between *relative* PA level and the odds of possessing short telomeres (i.e., lowest sex-specific quartile). Results indicated that those in the Sedentary category had 1.95 times the odds of having short telomeres compared to those in the High physical activity category (reference group), with all the demographic and lifestyle covariates controlled statistically. Odds of possessing short telomeres did not differ between the Sedentary, Low, and Moderate levels of activity.

4. Discussion

The focus of the present investigation was to determine the extent of the relationship between physical activity, indexed using MET-minutes per week, and telomere length, a bio-marker of cellular aging, in a large, nationally representative sample of U.S. women and men, ages 20–84. Findings showed that adults with High levels of physical activity had significantly longer telomeres than their counterparts, whether categorized using a relative measure of PA (Table 2) or cut-points established by U.S. guidelines (Table 3). Moreover, adults with High levels of PA were about half as likely to possess short telomeres compared to the other activity categories (Table 4).

Regression results indicated that telomere shortening occurred at the rate of 15.6 base pairs per year of age. Using the four categories based on *relative* PA, after controlling for all the covariates simultaneously, adults in the High activity group had telomeres that were 140 base pairs longer than Sedentary participants, on average. Given this difference, interpretation of the results suggests that highly active U.S. adults have a biologic aging advantage of approximately 9 years over sedentary adults (140 base pairs ÷ 15.6), given the same age, gender, race, education, BMI, smoking status, and alcohol use. The difference in cell aging between those with High and Low activity also appears meaningful at 8.8 years (137 base pairs ÷ 15.6), as well as the difference between those in the High and Moderate PA categories (7.1 years; 111 base pairs ÷ 15.6).

In both the relative and guideline-based activity categories, adults in the highest PA category had the longest telomeres and those in the sedentary category had the shortest telomeres. However, activity based on the *relative* cut-points and categories was a better predictor of telomere length than activity based on the U.S. guidelines. This was probably because the *relative* PA categories were sex-specific and included adults in the High activity category who reported MET-minute levels that were significantly greater than the upper cut-point (i.e., >1000 MET-minutes) established by the U.S. guidelines. Specifically, to be assigned to the High activity category using the within-sample or relative cut-points, adults had to be in the upper sex-specific tertile of those reporting a measureable number of MET-minutes. Women had to accumulate at least 1375 MET-minutes per week, and men had to report a minimum of 1887 MET-minutes per week to fit into the highest tertile. On the other hand, to be part of the High-G category based on the U.S. activity guidelines required only that adults accumulate >1000 MET-minutes per week (CDC, 2008).

In 2016, research by Kyu et al. showed that very high levels of physical activity, beyond current U.S. recommendations, account for added protection against breast cancer, colon cancer, heart disease, and stroke (Kyu et al., 2016). Although U.S. guidelines encourage adults to accumulate 500–1000 MET-minutes of activity per week or more, "more" seems to result in greater disease prevention (Kyu et al., 2016). The present study showed similar findings.

If a causal relationship between PA and telomere length is assumed, this study suggests that current national guidelines are too conservative at the upper end. Many health benefits are missed when only 1000 MET-minutes per week are achieved (Kyu et al., 2016). In the present study, men had to attain ≥1887 MET-minutes per week and women ≥1375 to be included in the category with the longest telomeres.

Controlling statistically for differences in the demographic and lifestyle variables had almost no impact on the association between *relative* PA and telomere length. In each case, significant differences remained significant. Consequently, the covariate analyses indicate that little of

Table 3
Differences in mean telomere length (base pairs) by level of weekly guideline-based MET-minutes of physical activity in U.S. men and women, after adjusting for the covariates.

	Weekly guideline-based physical activity					
Covariate	Sedentary-G Mean ± SE	Insufficient-G Mean ± SE	Moderate-G Mean ± SE	High-G Mean ± SE	F	P
Age	5765[a] ± 40	5800[a] ± 52	5784[a*] ± 68	5883[b] ± 44	4.9	0.0071
Demographics	5786[a] ± 39	5812[a] ± 45	5797[a] ± 64	5901[b] ± 39	5.2	0.0052
Demographics and lifestyle	5809[a] ± 41	5832[a] ± 43	5808[a] ± 65	5913[b] ± 43	4.3	0.0133

[a,b]Means on the same row with the same superscript letter were not statistically different ($P > 0.05$). Across the four guideline-based categories of physical activity, weighted percentages were: 50.8% ($N = 3407$) reported no physical activity (Sedentary-G), 15.4% ($N = 798$) reported Insufficient-G levels (>0 and <500 MET-minutes per week), 9.6% ($N = 489$) reported Moderate-G levels (≥500 and ≤1000 MET-minutes per week), and 24.2% ($N = 1129$) reported High-G levels of physical activity (>1000 MET-minutes per week). Because sample weights were applied to each participant, differences in the number of subjects in each category should be interpreted using percentages, not *N*. Means on the same row were adjusted for the covariates in the left column. The demographic covariates were: age, sex, race, and education. The lifestyle covariates were: body mass index, cigarette smoking, and alcohol use. The superscript notation a* indicates that the difference was borderline significant ($P > 0.05$ and $P < 0.06$).

Table 4
Odds of possessing short telomeres comparing adults with high activity levels to others ($n = 5823$).

Covariate	Physical activity level (relative)						
	Sedentary		Low		Moderate		High
	OR	95% CI	OR	95% CI	OR	95% CI	OR
Age	2.08	1.54–2.80	1.76	1.20–2.57	1.69	1.19–2.40	1.00
Demographics	1.99	1.45–2.74	1.74	1.23–2.46	1.70	1.19–2.43	1.00
All covariates	1.95	1.38–2.75	1.66	1.21–2.30	1.73	1.24–2.40	1.00

The outcome of interest was short telomeres, defined as telomeres in the lowest sex-specific quartile. The four physical activity categories were formed based on relative physical activity levels (MET-minutes). Participants reporting no regular physical activity were classified as Sedentary, and the remaining adults, each reporting some regular physical activity in the past 30 days, were divided into sex-specific tertiles. Specifically, Sedentary ($n = 3407$; 50.8%), Low ($n = 843$; 16.3%), Moderate ($n = 807$; 16.4%), and High ($n = 766$; 16.4%).

the association between relative PA and telomere length can be attributed to differences in age, gender, race, education, BMI, smoking, and alcohol use.

Comparing the associations between lifestyle factors other than PA and telomere length adds perspective to the current findings. For example, adults with a history of 15 or more pack-years of smoking had telomeres that were 112 base pairs shorter than non-smokers ($F = 6.1$, $P = 0.0063$), suggesting 7.2 years of increased cellular aging. Adults with obesity had telomeres that were 94 base pairs shorter than normal weight individuals, after adjusting for the covariates ($F = 3.5$, $P = 0.0201$), suggesting about 6 years of additional biological aging. On the other hand, alcohol use and telomere length were not associated ($F = 0.2$, $P = 0.8031$). Hence, it appears that physical activity may account for differences in telomere length as well or better than common lifestyle factors such as cigarette smoking, obesity, and alcohol use.

Why was physical activity predictive of longer telomeres? Although the precise mechanism is unknown, it is important to note that telomere length and cell senescence are closely related to inflammation and oxidative stress (Kordinas et al., 2016; Zhou et al., 2016; Zhang et al., 2016; Jurk et al., 2014; Babizhayev et al., 2011). Research shows that chronic physical activity suppresses inflammation and oxidative stress (Campos et al., 2014; Gomes et al., 2012; Nimmo et al., 2013), although an acute bout increases the inflammatory process short-term (Liburt et al., 2010). Physical activity may reduce inflammation and oxidative stress through multiple mechanisms, including reduced production of reactive oxygen species (Bjork et al., 2012), accelerated production of DNA-repairing enzymes (Radak et al., 2003), greater genetic expression of antioxidant proteins (Gomez-Cabrera et al., 2008), and exercise-induced release of cfDNA into the circulation (Pokrywka et al., 2015). Additionally, regular activity could moderate oxidative stress by decreasing tumor necrosis factor α (TNFα), C-reactive protein, and interleukin-6 (Teixeira-Lemos et al., 2011). Lastly, irisin, a hormone released by muscle, is directly related to telomere length (Rana et al., 2014). Several studies indicate that irisin levels increase progressively as levels of physical work and exercise increase (Daskalopoulou et al., 2014; Huh et al., 2014).

There were several limitations associated with the present investigation. First, the cross-sectional design of NHANES precludes causal inferences. Second, participants reporting high levels of PA could represent unique adults who engage in a lifestyle that is different from others. Because of this potential threat, a number of variables were controlled statistically. They had little effect on the outcome. However, there are always other unidentified variables that could account for the association between PA and telomere length.

Unmeasured variables that could explain some of the relationship between PA and telomere length include depression, psychosocial stress, and sleep disturbances. These factors are associated with decreased levels of PA and could affect telomere length. In two meta-analytic studies, Lin et al. (2016) and Ridout et al. (2016) showed that adults with depression have shorter telomeres than others. Similarly, Mathur et al. (2016) and Schutte et al. (Schutte & Malouff, 2016) each revealed weak but significant relationships between stress and telomere length in meta-analysis investigations. Additionally, research by Cribbet et al. (2014) showed that poor sleep quality and quantity are also associated with increased cellular aging.

Differences in vitamin and mineral consumption have also been shown to account for longer telomeres according to Mazidi et al. in two studies (Mazidi et al., 2017a; Mazidi et al., 2017b). These differences could partly explain why adults with high levels of PA tend to have longer telomeres.

Finally, the present study did not include assessment of telomerase activity. Research indicates that telomerase activity may increase as a result of a single treadmill running session (Zietzer et al., 2016), although self-reported PA does not seem related to telomerase activity (Ludlow et al., 2008).

There were also several strengths associated with the present study. First, telomere length was measured by a reputable lab using well-established methods, independent of this study. Moreover, telomere length was strongly related to chronological age, as it should be, and telomere length was significantly related to other risk factors, such as smoking and obesity, suggesting concurrent validity. Second, the sample was randomly selected by NHANES using a multistage, probability sampling design. The sample was large, multi-racial, and representative of the U.S. population 20–84 years of age, allowing broad generalization of the results. Lastly, statistical adjustments were made for differences in a number of covariates, including age, gender, race, education, smoking, BMI, and alcohol use. Findings indicated that the relation between physical activity and telomere length was independent of these factors.

5. Conclusions

Level of participation in physical activity was significantly and meaningfully associated with telomere length in a sample of 5823 men and women representing U.S. adults. According to the findings, telomere length does not differ among the sedentary and those engaged in low or moderate levels of physical activity. However, adults who participate in high levels of physical activity tend to have significantly longer telomeres than their counterparts, accounting for up to 9 years of reduced cellular aging. Results of the present investigation highlight the risk of accelerated aging among men and women who do not engage in high levels of physical activity.

Conflict of interest

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