Movement-Based Behaviors and Leukocyte Telomere Length among US Adults

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ABSTRACT

LOPRINZI, P. D., J. P. LOENNEKE, and E. H. BLACKBURN. Movement-Based Behaviors and Leukocyte Telomere Length among US Adults. Med. Sci. Sports Exerc., Vol. 47, No. 11, pp. 2347–2352, 2015. Introduction: Short leukocyte telomere length (LTL) has become a hallmark characteristic of aging. Some, but not all, evidence suggests that physical activity (PA) may play an important role in attenuating age-related diseases and may provide a protective effect for telomeres. The purpose of this study was to examine the association between PA and LTL in a national sample of US adults from the National Health and Nutrition Examination Survey. Methods: National Health and Nutrition Examination Survey data from 1999 to 2002 (n = 6503; 20–84 yr) were used. Four self-report questions related to movement-based behaviors (MBB) were assessed. The four MBB included whether individuals participated in moderate-intensity PA, vigorous-intensity PA, walking/cycling for transportation, and muscle-strengthening activities. An MBB index variable was created by summing the number of MBB an individual engaged in (range, 0–4). Results: A clear dose–response relation was observed between MBB and LTL; across the LTL tertiles, respectively, the mean numbers of MBB were 1.18, 1.44, and 1.54 (P trend < 0.001). After adjustments (including age) and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 MBB, respectively, had a 3% (P = 0.84), 24% (P = 0.02), 29% (P = 0.04), and 52% (P = 0.004) reduced odds of being in the lowest (vs highest) tertile of LTL; MBB was not associated with being in the middle (vs highest) tertile of LTL. Conclusions: Greater engagement in MBB was associated with reduced odds of being in the lowest LTL tertile. Key Words: AGING, EPIDEMIOLOGY, PHYSICAL ACTIVITY, NHANES

Shortened leukocyte telomere length (LTL) characterizes human aging (5,26,27). Potentially reflecting systemic oxidative stress and inflammation (10,51), short LTL is linked with various cardiometabolic diseases (2,4,13,18,19,21,46,47). Physical activity (PA) may help attenuate age-related diseases, as previous research (8,14,20,23–25,34,37,39,44,49) demonstrates that physically active adults have longer mean LTL. However, some studies show no relation (22,32,33,40,45,52), with others reporting an inverted U relation (9,31,43) (review articles, see Ludlow (29,30)).

Given these mixed findings, coupled with the fact that most of these studies were convenience-based samples or used targeted populations (e.g., postmenopausal women) (29,30), here, we examine the association between PA and LTL in a national sample of US adults. To improve our understanding of associations between PA and LTL, specific attention was focused on data from four movement-based behaviors (MBB). These include moderate-intensity PA (MPA), vigorous-intensity PA (VPA), walking and cycling for transportation, and muscle-strengthening activities (MSA).

METHODS

Design and participants. Data were extracted from the 1999–2002 NHANES (only cycles with LTL data at the time of this writing). Procedures were approved by the National Center for Health Statistics review board. Consent was obtained from all participants. Analyses are based on data from 6503 adults (20–84 yr) who provided complete data for the study variables. In the 1999–2002 NHANES cycles, 9882 participants were between 20 and 84 yr of age. After
excluding those with missing MBB data, 9369 remained. After excluding those with missing covariate data, 7283 remained. Lastly, after excluding those with missing telomere data, 6503 remained (resultant sample) (Fig. 1). When comparing the final analytic sample \((n = 6503)\) with the 780 participants with missing telomere data \((7283 - 6503 = 780)\), there were no differences in age, number of MBB, body mass index (BMI), C-reactive protein (CRP), or smoking (all \(P > 0.05\)); however, those that were excluded were more likely to be female (60% vs 51.1%; \(P < 0.001\)), less likely to be non-Hispanic White (38.1% vs 50.4%, \(P < 0.001\)), and had a lower poverty-to-income ratio (PIR) (2.56 vs 2.71, \(P = 0.01\)). These are unweighted estimates.

**LTL.** Detailed methodology of the NHANES procedures for assessing LTL has been previously reported (35). Briefly, DNA was extracted from whole blood and the LTL assay was performed using quantitative polymerase chain reaction to measure LTL relative to standard reference DNA (T/S ratio) (35). Each sample was assayed at least twice, and among samples with a T/S ratio within 7% variability, the average value was used; for samples with variability greater than 7%, a third assay was run and in this case, the average of the two closest T/S values was used. Notably, in NHANES, telomere length in leukocytes was assessed. We acknowledge that LTL is not specific to skeletal muscle tissue; however, it may not be feasible to take muscle biopsies in large epidemiological studies. Previous work suggests that LTL is modestly \((r = 0.39)\) associated with muscle telomere length (1), which is in accordance with other studies (12), providing some justification for continued use of LTL measures, particularly in epidemiological studies.

**MBB.** In the 1999–2002 NHANES, four self-report items related to MBB were assessed, including PA participation during transportation and leisure time; notably, objective measures of PA (e.g., accelerometry) were not released until the 2003–2004 NHANES cycle. The four MBB included the degree of participation in MPA, VPA, walking/cycling for transportation, and MSA (yes/no responses).

For MPA: “Over the past 30 d, did you do moderate activities for at least 10 min that cause only light sweating or a slight-to-moderate increase in breathing or HR?”

For VPA: “Over the past 30 d, did you do vigorous activities for at least 10 min that caused heavy sweating or large increases in breathing or HR?”

For walking/cycling for transportation: “Over the past 30 d, did you walk or bicycle as part of getting to and from work or school or to do errands?”

For MSA: “Over the past 30 d, did you do any physical activities specifically designed to strengthen your muscles such as lifting weights, push-ups, or sit-ups?”

**MBB index.** An MBB index variable was created by summing the number of MBB an individual engaged in (range, 0–4).

**Covariates.** Covariates included age (continuous), age squared (due to nonlinearity between age and LTL), gender, race/ethnicity, PIR, smoking status (smokes every day, smokes on some days, no longer smokes, and never smoked), measured BMI (kg m\(^{-2}\)), and CRP (mg dL\(^{-1}\)).

**Analysis.** Statistical analyses were performed using procedures from survey data using Stata (version 12). Polytomous regression was used to examine the odds of being in the two lower tertiles (6,53) (vs upper tertile) of LTL based on the degree of engagement in MBB; those with an MBB index score of “0” served as the referent group.

### RESULTS

Table 1 displays the characteristics of the sample. The weighted mean numbers of MBB across the LTL tertiles, respectively, were 1.18, 1.44, and 1.54 (Table 1; Fig. 2). The weighted proportions of participants with 2+ MBB across the LTL tertiles, respectively, were 34.7%, 43.6%, and 49.2% (Fig. 2). Table 2 displays the polytomous regression results. After adjustments (including age) and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 MBB, respectively, had a 3% \((P = 0.84)\), 24% \((P = 0.02)\), 29% \((P = 0.04)\), and 52% \((P = 0.004)\) reduced odds of being in the lowest (vs highest) tertile of LTL; MBB was not associated with being in the middle (vs highest) tertile of LTL. When changing the referent group to the middle tertile (not shown in the table) and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 MBB, respectively, had a 5%
P = 0.60), 12% (P = 0.40), 28% (P = 0.02), and 56% (P = 0.009) reduced odds of being in the lowest (vs middle) tertile of LTL. Taken together, these findings suggest a dose–response relation between MBB and LTL; greater engagement in MBB was associated with lower odds of being in lowest versus highest LTL tertile and lowest versus middle tertile.

Given that some studies suggest a nonlinear relation between telomere length and morbidity (11,15), in addition to considering tertiles of LTL, further analyses examined the relation between MBB and five quintiles of LTL; across these five quintiles, respectively, the mean LTL values were 0.73, 0.88, 1.01, 1.14, and 1.44; notably, the 90th and 95th percentiles for LTL in this sample were 1.37 and 1.50, respectively. The mean numbers of MBB across the five quintiles of LTL, respectively, were 1.15, 1.27, 1.46, 1.52, and 1.55. This observed monotonic relation suggests that,
in this sample, LTL had a linear, rather than an inverted U-shaped, association with mean MBB number.

Additional analyses (not shown in tabular format) were computed to see if age moderated the association between MBB and LTL. Three additional multivariable polytomous regression models were computed for those 20–39, 40–64, and 65–84 yr. Results were not significant for the age groups 20–39 and 65–84 yr (data not shown); among those who were 40–64 yr and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 behaviors, respectively, had a 15% \( (P = 0.44) \), 32% \( (P = 0.08) \), 42% \( (P = 0.01) \), and 61% \( (P = 0.03) \) reduced odds of being in the lowest (vs highest) tertile of LTL.

Furthermore, all four MBB were entered separately into a multivariable polytomous regression model to examine their potential independent associations. After adjustments, those engaging in VPA and walking/cycling for transportation, respectively, had a 25% \( (P = 0.01) \) and 30% \( (P = 0.004) \) lower odds of being in the lowest (vs highest) LTL tertile; MPA [odds ratio (OR), 1.13; \( P = 0.15 \)] and MSA (OR, 0.92; \( P = 0.50 \)) were not independently associated with being in the lowest (vs highest) LTL tertile.

In addition to examining independent associations of the different MBB on LTL, it is of interest to examine whether MBB exclusivity (e.g., only engaging in MPA and not any of the three other MBB) is associated with LTL. Among the 6503 participants, 386 engaged in only VPA (i.e., reporting engaging in VPA but not in MPA, MSA, or walking for transportation), 1057 engaged in only MPA, 176 engaged in only MSA, and 417 engaged in only walking/cycling for transportation. Results for only VPA, MSA, and walking/cycling for transportation were not statistically significant (data not shown). Interestingly, however, those who engaged in only MPA had a 36% (OR, 1.36; \( P = 0.01 \)) and 25% (OR, 1.25; \( P = 0.06 \)) increased odds, respectively, in being in the lowest and middle tertiles (vs highest tertile) after adjustments. This is an unexpected finding, but this association, coupled with our observed finding of a dose–response association between MBB engagement and LTL, suggests that engaging in some MBB in isolation may not be favorable but may be a combined effect of attenuating the shortening of LTL when multiple MBB are engaged in regularly.

Lastly, given that some studies have demonstrated an inverted U relation between PA and LTL (29,30), we attempted to examine whether such a relation was observed for frequency of MSA; duration and frequency of MPA and VPA were not asked in the 1999–2002 NHANES cycles, and the majority (76%) of participants did not walk/cycle for transportation, so evaluating a dose–response relation between walking/cycling for transportation and LTL was not possible. No dose–response relation was observable for MSA; compared with those in the lowest MSA tertile (mean number of MSA in past 30 d, 5.6) and after adjustments in a linear regression, no association was observed between those in the middle (mean MSA, 12.9; \( \beta = -0.02; P = 0.13 \)) and upper (mean MSA, 27.4; \( \beta = -0.002; P = 0.88 \)) MSA tertiles with LTL.

**DISCUSSION**

Using a national sample of US adults, we observed a dose–response relation between MBB engagement (i.e., number of MBB they engaged in) and lower LTL. The potential mechanisms to explain a PA–LTL relation are not fully established. Among rodent models, several exercise-specific signaling mechanisms (e.g., TERT, IGF-1, eNOS, and AKT) have been associated with altered telomere biology (29,30) and thus may play an important role in preserving telomere phenotype (30,49,50). Future work is needed.
to improve our understanding of the mechanisms underlying this potential relation.

Importantly, the relation between MBB and LTL was observed only among those 40–64 yr old, which suggests that, if confirmed by prospective and experimental work, this may be an important age group in which targeted PA interventions should be developed, implemented, and evaluated. The unexpected finding that those who engaged in only MPA had increased odds of being in the lowest and middle tertiles (vs highest tertile) needs further investigation. Engaging in only MPA may result in an inadequate exercise stimulus to achieve exercise-induced LTL adaptations. The observed findings should be interpreted in the context of the study’s limitation, which include, for example, the cross-sectional design and an inability to fully tease out potential intensity/duration effects. In addition, given that the excluded sample due to missing LTL data differed by gender, race/ethnicity, and PIR when compared with the analytic sample, applicability to these subpopulations may be limited.

Owing to the limitations of the MBB items, we were not able to determine the duration and frequency of most of the MBB items but rather whether they engaged in the behavior or not. Previous research, however, suggests that there is likely a range in the amount of PA that provides health benefits without negatively affecting LTL (22,38,40,43). Data in very active adults suggest that if this range is exceeded, PA may result in a detrimental effect on LTL (22,43). For example, high levels of PA may increase demand on the body to repair and regenerate, resulting in shortening of LTL. This may explain why some studies do not always find a dose–response relationship between the amount of PA and LTL (22,32,33,40,45,48,52). Our findings suggest that engaging in more MBB is associated with reduced odds of being in the lowest LTL tertile, suggesting that engaging in multiple MBB may have a combined effect in minimizing LTL shortening.

Future epidemiological studies examining the extent to which MBB duration and frequency influence LTL are needed. Furthermore, future work examining tissue- and cell-specific telomere adaptations from exercise is warranted (30). Given the protective effects of telomerase activity (42), future epidemiological studies examining the effects of MBB on telomerase activity is warranted. Because of the combined effects of multiple health-enhancing behaviors on health (28,41), as well as LTL (16,17,36), future epidemiological work examining the additive and additive interaction effects of multiple health behaviors on LTL is warranted. Lastly, given that it is not entirely certain whether LTL is a cause or consequence of morbidity (e.g., cardiovascular disease), future longitudinal mediational models examining whether LTL mediates the relation between MBB and morbidity/mortality is warranted. However, prospective studies showing that shorter LTL is predictive of premature mortality from an increased risk of various chronic diseases (e.g., cardiovascular disease) are starting to emerge (7), but several issues (e.g., methodology used to assess LTL and potential regression to the mean) need to be carefully considered when examining and interpreting the prospective interrelations among PA, LTL, and morbidity/mortality (3).

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REFERENCES


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