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Effect of an 18-Month Meditation Training on Telomeres in Older Adults: A Secondary Analysis of the Age-Well Randomized Controlled Trial

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ABSTRACT

BACKGROUND: Shorter telomeres are associated with increased risk of cognitive decline and age-related diseases. Developing interventions to promote healthy aging by preserving telomere integrity is of paramount importance. Here, we investigated the effect of an 18-month meditation intervention on telomere length (TL) measures in older people without cognitive impairment.

METHODS: A total of 137 adults age ≥65 years were randomized to one of the 3 groups (meditation training, non-native language training, or passive control). We evaluated the 50th and 20th percentile TL and the percentage of critically short telomeres (<3 kbp) in peripheral blood mononuclear cells.

RESULTS: Mixed model analysis showed a time effect indicating a general decrease on the 50th percentile TL (F = 80.72, $p_{adjusted} < .001$), without a significant group effect or time × group interaction. No significant effect was detected in the 20th percentile TL or the percentage of critically short telomeres. Secondary analysis showed that only in the meditation training group 1) the 50th percentile TL positively correlated with class attendance time (r = 0.45, $p_{adjusted} < .011$), 2) the 50th and 20th percentile TL positively correlated with responsiveness to the intervention, evaluated through a composite score (r = 0.46, $p_{adjusted} < .010$ and r = 0.41, $p_{adjusted}$ = .029, respectively), and 3) lower scores on a measure of the personality trait "openness to experience" correlated with a lower percentage of critically short telomeres after the intervention (r = 0.44, $p_{adjusted}$ = .015).

CONCLUSIONS: In older adults, we found no evidence for a main effect of an 18-month meditation training program on TL compared with the control groups. Our findings highlight the importance of considering the impact of moderating factors when measuring the effectiveness of meditation-based trainings.

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Cellular aging, a complex and multifaceted process, lies at the core of age-related diseases, including cardiometabolic disorders, cancer, and neurodegenerative diseases (1,2). Epidemiological evidence shows that psychosocial factors play a key role in modulating the cellular aging process and therefore represent risk factors for most age-related diseases (3,4). The intricate relationship between cellular aging and telomere dynamics has emerged as a pivotal area of research, providing critical insights into the mechanisms that underlie aging and age-related diseases. Telomeres are composed of protective repetitive DNA sequences at the end of eukaryotic chromosomes (5). However, with each cell division, telomeres undergo attrition, which ultimately limits the replicative capacity of cells, leading to cellular senescence or programmed cell death (6–10). Senescent cells accumulate with age and contribute to tissue dysfunction and inflammation, which is characteristic of aging phenotypes (11). Shorter telomeres in older adults have been associated with increased risk of mortality and age-related diseases, such as cardiovascular disease, cancer, and Alzheimer's disease and other neurodegenerative diseases (12–16). Human longitudinal studies suggest that chronic psychological stress is an important pathway involved in telomere damage (15,17). Therefore, cognitive trainings and other lifestyle-based strategies to improve coping with psychosocial stress may have the potential to promote well-being and health in older people at risk of neurodegenerative diseases. Although there are currently no systematic reviews or meta-analyses specifically focused on meditation-based interventions for the prevention or treatment of age-related diseases, including cognitive impairment and dementia, a growing body of scientific research suggests that meditation-based interventions can have beneficial effects on psychological, neuroendocrine, and immune variables (18,19). Mindfulness meditation training appears to positively impact aging by

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improving attentional processes, emotional regulation, psychological well-being, and sleep quality, while mitigating risk factors such as stress, inflammation, and mood disorders (20). Interventions based on loving-kindness and compassion meditation training promote prosocial behaviors by cultivating perspective taking, empathy, and cognitive reappraisal (21,22). Additionally, fostering strong social connections and support networks can buffer against the negative impacts of stress (3). In the last 15 years, several studies have examined the relationship between meditation practice and telomere biology in young and middle-age adults, and there is empirical evidence suggesting that meditation practice, by improving the stress response, may help stabilize or lengthen telomeres and modulate the expression of telomere-related genes (23–26).

In this study, we examined the hypothesis that a long-term training program in meditation practices focused on improving stress management and well-being through attentional and emotional regulation can preserve telomere integrity in older adults without cognitive impairment. To test this hypothesis, as a secondary outcome of the Age-Well clinical trial (27,28), we evaluated the potential effect of an 18-month meditation-based intervention, a matched non-native language training, and a no-intervention group on telomere length measures in 137 adults without cognitive impairment (≥65 years). In addition, in meditation-based interventions, there is often variability in individual commitment to practice and adherence to the teacher's instructions (29). Therefore, as a secondary outcome of this study, we aimed to investigate whether telomere length was modulated by the total time attending classes and by the individual responsiveness to the interventions. Finally, we also explored potential underlying mechanisms relating baseline differences in participant's personality traits and changes in telomere length measures throughout the intervention, considering the associations between personality traits, health behavior, and health biomarkers (30), and previous evidence showing that baseline personality traits influenced the engagement of older adults in Mindfulness-Based Stress Reduction practices (31) and moderated meditation-related changes in telomere maintenance after a meditation retreat (25).

METHODS AND MATERIALS

Clinical Trial Setting and Design

Full details on the Age-Well trial design, eligibility, sample size, demographic data, randomization, masking, and interventions have been provided previously (27,28). Briefly, the Age-Well clinical trial is a monocentric, randomized, controlled superiority clinical trial including 137 older adults without cognitive impairment (≥65 years) with blinded end-point assessment. Participants were enrolled between November 24, 2016, and March 5, 2018; samples were collected in Caen, France. The sample size calculation of the Age-Well randomized controlled trial (RCT) was made for the main outcome of the Age-Well RCT, which was to explore the mean change in the volume and perfusion of both the anterior cingulate cortex and the insula after an 18-month meditation-based intervention in older adults without cognitive impairment (meditation group [MG]) compared to 1) a passive control group (CG) and 2) an 18-month foreign language training program (language group [LG]). The comparison of the meditation versus passive control arm was focused on the mean change in the volume and perfusion of the anterior cingulate cortex from the baseline preintervention visit to the end of the 18-month intervention, with an expected relevant effect size of 0.75, as suggested by a meta-analysis of meditation effects on neuroimaging markers. To demonstrate an effect size of 0.75 for each of the comparisons, with 80% power and a 2-sided type I error of 1.25% (Bonferroni correction for test multiplicity), 42 participants per arm (126 in total) needed to be included. The total number of participants included in the Age-Well RCT (N = 137) was higher than the required minimum of 126. All participants were native French speakers, had 7 years or more of education, and performed within the normal range for age and educational level on standardized cognitive tests.

Baseline characteristics of the participants included in the study are detailed in Table 1. There were no major differences between groups on any demographic or clinical characteristics. Participants were randomly assigned (1:1:1) to the 18-month meditation training intervention (n = 45), 18-month non-native language (English) training intervention (active control) (n = 46), or no-intervention (passive control) arm

Table 1. Baseline Characteristics of the Participants

	Total Population, N = 128	CG, n = 43	LG, n = 43	MG, n = 42	p Value
Age, Years	69.20 (3.70)	67.99 (2.48)	70.24 (3.09)	69.39 (3.48)	.046[a]
Women	77 (60.16%)	25 (58.14%)	23 (53.49%)	29 (69.05%)	.324
Years of Education	13.17 (3.14)	14.28 (2.87)	12.16 (3.09)	13.07 (3.16)	.009[a]
Years in Retirement	8.51 (5.28)	7.12 (4.59)	9.26 (5.12)	9.17 (5.89)	.107
Handedness Laterality	78.82 (39.86)	87.83 (15.37)	77.90 (39.70)	70.55 (53.94)	.669
Blood Pressure Level, mm Hg	55.28 (15.50)	52.05 (14.21)	56.57 (14.43)	57.55 (17.51)	.316
Systolic	134.91 (20.24)	129.74 (20.31)	137.15 (16.97)	137.90 (22.57)	.098
Diastolic	79.62 (10.03)	77.69 (15.37)	80.57 (8.82)	80.63 (10.51)	.278
Body Mass Index	26.18 (4.31)	25.80 (4.11)	26.52 (4.34)	26.21 (4.56)	.627
Mini-Mental State Examination Score	29.03 (1.05)	29.21 (0.91)	28.95 (1.02)	28.93 (1.20)	.477
Montgomery–Åsberg Depression Rating Scale Score	1.06 (1.28)	0.72 (1.01)	1.28 (1.53)	1.19 (1.19)	.110

Values are presented as n (%) or mean (SD). Values for the total population and in the 3 groups separately at baseline are indicated. Between-group comparisons were effectuated using Kruskal-Wallis test for continuous variables and with Pearson's χ^2 test for categorial variables.

CG, no-intervention control group; LG, non-native language training group; MG, meditation group.

[a]Differences between CG and LG.

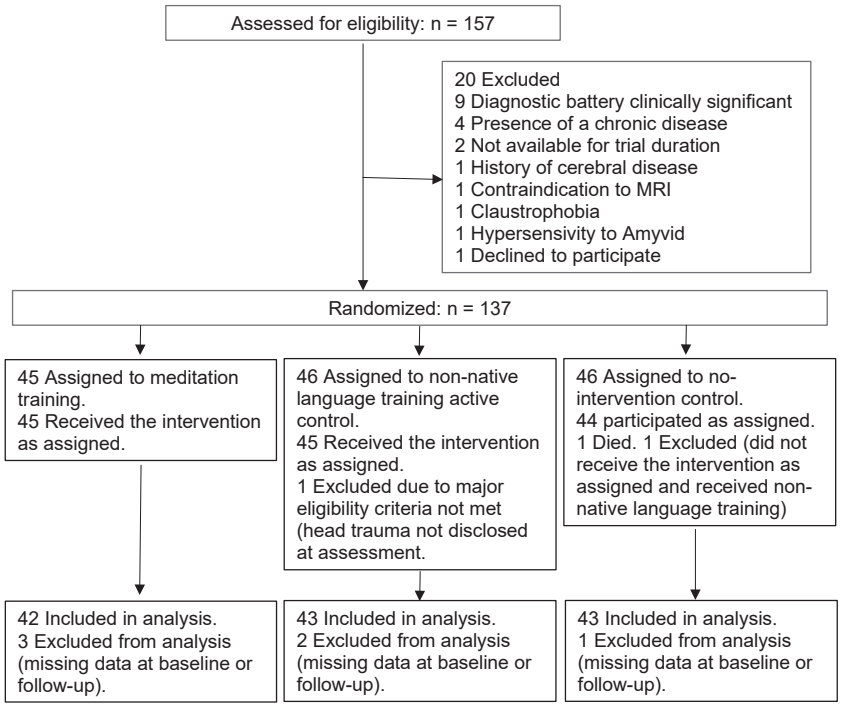

Figure 1. CONSORT flowchart. Of 137 randomized participants, 134 completed the trial. One participant was excluded from all analyses due to major eligibility criteria not being met (non-native language training), 1 died during follow-up (no-intervention control group), and 1 revealed not to have followed his allocated arm (randomized to no intervention but attended non-native language training). Six participants were excluded from analysis (missing data at baseline or follow-up due to low quality sample). CONSORT, Consolidated Standards of Reporting Trials; MRI, magnetic resonance imaging.

(n = 46) according to a randomization list with permuted blocks of varying size (6 and 9), which was generated centrally by a biostatistician at the EUCLID clinical trials platform. A flow diagram of the inclusion process is depicted in Figure 1. Of the 137 randomized participants, 134 completed the trial. One participant was excluded from all analyses due to a major eligibility criterion not being met (non-native language training), 1 died during follow-up (no-intervention CG), and 1 revealed that he had not followed his allocated arm (randomized to no intervention but attended non-native language training). Six participants were excluded from analysis (missing data at baseline or follow-up due to low quality sample). All participants gave their written informed consent to participate in the study. Blood samples were collected at the baseline pre-intervention visit (V1) and after 18 months at the post-intervention visit (V3). The Age-Well RCT of the Medit-Aging European project, sponsored by Institut National de la Santé et de la Recherche Médicale, was approved by the ethics committee (CPP Nord-Ouest III, Caen, France) and registered on ClinicalTrials.gov (NCT02977819).

Interventions

A full, detailed description of the interventions has been given previously (27,28).

The meditation intervention consisted of an original secular program of meditation training labeled "The Silver Santé Study Meditation Programme," which was specially designed for the study based on preexisting interventions, with the objective of personal development and healthy aging, and was provided by expert meditator instructors at the Pôle de Formations et de Recherche en Santé in Caen, France. A summary of the intervention's content and structure is presented in the Supplement.

Designed for French native speakers, the English language training was a cognitively stimulating intervention designed to reinforce each participant's abilities in understanding, writing, and speaking and included exercises aimed at enhancing vocabulary, grammar proficiency, and their practical application in reading, writing, and speaking. While the meditation training was anticipated to influence both cognitive control and emotion regulation, the English training was hypothesized to impact cognitive control.

The meditation and the non-native language training interventions were structurally equivalent in overall course length, class time, and home activities and were matched in administration, dosage, and duration. All intervention groups consisted of 14 participants. For each intervention, participants were provided with supports (manual and audio) for their practice. Participants were given a questionnaire of daily questions about the well-being of the person, the formal practice time for the day, the duration of their informal practice, and the motivation to practice during the day.

In the passive CG (no intervention), participants were requested not to change their habits and continue living as they used to before engaging in the study and until the end of the study. They were specifically asked not to engage in any meditation or non-native language training.

Peripheral Blood Mononuclear Cell Isolation

Blood samples were obtained from the antecubital vein into sodium heparin tubes. They were processed within 24 hours of extraction to isolate peripheral blood mononuclear cells

(PBMCs) using the Ficoll-Paque Plus method according to the manufacturer's instructions (Sigma). The PBMCs were resuspended at 10 million cells/mL in a freezing medium and placed in liquid nitrogen for storage.

TL Determination

The 50th and 20th percentile TL and the percentage of critically short telomere (%CST) values were measured in individual chromosomes from each participant at each timepoint using Life Length's proprietary Telomere Analysis Technology which uses a high-throughput quantitative fluorescent in situ hybridization technique (32) (Supplement).

Training-Responsiveness Composite Score

In both intervention groups (meditation and non-native language groups), we assessed whether and to what degree participants responded to the interventions by a continuous measure of responsiveness that evaluated the acquired skills at the end of the interventions, using different scales for each training to compute these scores (33) (Supplement).

Big Five Inventory

The Big Five Inventory is a self-report inventory designed to measure the Big Five personality dimensions, which are extroversion, agreeableness, conscientiousness, neuroticism, and openness to experience (34), translated and validated in French by Plaisant *et al.* (35). It is a multidimensional personality inventory (44 items) and consists of short phrases with relatively accessible vocabulary.

Statistical Analysis

Changes in telomere length in the Age-Well trial groups were the primary outcome of this study. Categorical variables were compared using Pearson's χ^2 tests, and continuous variables were compared using Kruskal-Wallis tests to assess differences among the 3 groups (i.e., meditation, non-native language training, and no intervention). A set of linear mixed models were fitted to analyze the variables of interest, i.e., the 50th and the 20th percentile TL, %CST, and the fixed effects of group and time, as well as their interaction (group $\times$ time). We included a random intercept for each participant to account for the correlation between repeated measures taken from the same individual. As secondary outcomes of this study, partial correlations for each TL variable and class attendance, training responsiveness, and baseline personality traits adjusted by the baseline value (V1) were performed; Pearson or Spearman correlations were used depending on the normality of the residues. A 2-sided p value $< .05$ was considered statistically significant.

We applied Bonferroni correction to adjust for multiple comparisons across all statistical analyses conducted in this study. Specifically, Bonferroni correction was applied to control the familywise error rate for the following primary analyses (mixed effects model analysis and all partial correlation analyses). By applying Bonferroni correction, we aimed to minimize the likelihood of type I errors due to conducting multiple statistical tests. All analyses were carried out using the statistical software R version 4.0.4 (36).

RESULTS

TL Measures

TL measures in PBMCs for the MG, LG, and no-intervention CG at baseline (V1) and postintervention (V3), as well as a mixed effects model analysis that includes group, time, and group $\times$ time interactions are shown in Table 2 and Figure 2. These analyses revealed significant effects of time for the 50th percentile TL ($F = 80.72$, $p_{adjusted} < .001$), i.e., a decrease in TL after the 18-month period, with no significant effect of group or group $\times$ time interactions. No significant effect of time, group, or group $\times$ time interaction was detected for 20th percentile TL and the %CST (<3 kbp).

There was no significant interaction of participant's age with any telomere measure (50th percentile $F = 0.71$, $p = .45$; 20th percentile $F = 1.22$, $p = .27$; %CTS $F = 1.12$, $p = .29$). TL measures distribution in the total population and separately by group is presented in Figures S1-S3, respectively.

Interaction Between Class Attendance and Changes in TL

No significant difference in class attendance was observed between the MG and the LG (Kruskal-Wallis $\chi^2_1 = 1.85$, $p = .17$). A mixed model analysis, which indicates group (MG and LG), time, class attendance, and group $\times$ time and group $\times$ class attendance interactions, showed a significant effect of class attendance on 50th percentile TLs ($F = 7.40$, $p = .007$, $p_{adjusted} = .04$). However, we found no significant group effect and no group $\times$ time or group $\times$ class attendance interaction (Table S1).

Considering the possibility that individual differences in the level of commitment to the interventions might have influenced the trajectory of TL measures over the 18-month training period, we assessed the correlation between the total hours of class attendance and the changes in TL measures in the LG and the MG (Table 3 and Figure 3). No significant correlation with class attendance was found when participants from both active interventions were combined (LG+MG). In the MG but not in the LG, the total hours of class attendance positively correlated with 50th and 20th percentile TL at V3 corrected by V1 ($r = 0.45$, $p < .004$ and $r = 0.33$, $p = .035$, respectively). However, only the correlation with 50th percentile TL survived the Bonferroni correction for multiple comparisons ($p_{adjusted} = .011$) (Table 2). Class attendance was not significantly correlated with changes in the %CST in any group.

Partial Correlations Between Training-Responsiveness Composite Scores and Changes in TL

Due to the different nature of the 2 interventions (LG and MG), the resulting scores of the instruments used to evaluate the acquired skills postintervention for each group represent different constructs and have different components. Because they are not directly comparable measures, the composite scores used to evaluate the MG and the LG were only used for partial correlation analysis within their corresponding group (for details, see Methods and Materials).

Table 2. Mean Total Scores for TL Measures

	CG, n = 43		MG, n = 42		LG, n = 43		Mixed Model							
							Group			Time		Group × Time		
	V1	V3	V1	V3	V1	V3	F	p Value	Adjusted p Value	F	p Value	Adjusted p Value	F	p Value	Adjusted p Value
50th Percentile TL	10,679.23 (952.38)	10,128.75 (876)	10,717.14 (1091.31)	10,025.91 (764.15)	10,666.81 (840.03)	10,135.93 (819.44)	0.04	.964	1.000	80.72	<.001	<.001	0.48	.621	1.000
20th Percentile TL	5638.00 (916.35)	5466.82 (820.81)	5601.14 (1071.7)	5397.84 (890.77)	5517.95 (817.32)	5448.42 (760.49)	0.09	.911	1.000	4.78	.030	.092	0.26	.771	1.000
% CST	9.6 (2.82)	9.75 (2.75)	9.76 (3.65)	9.86 (3.45)	10.22 (2.68)	9.77 (2.56)	0.14	.869	1.000	0.09	.761	1.000	0.51	.603	1.000

Values for each group at baseline (V1) and postintervention (V3) are presented as mean (SD). Median TL (50th percentile) and 20th percentile mean TL (both in base pairs) as well as the percentage of CSTs are presented in the table. The latter is defined as the percentage of the telomeres with a length <3 kbp. All measurements were performed in quintuplicate. Mixed effects model analysis indicates group (CG, LG, and MG), time, and group × time interactions. Bonferroni correction was used to adjust p values.

CG, no-intervention control group; CST, critically short telomere; LG, non-native language training group; MG, meditation group; TL, telomere length.

Correlation analysis between class attendance and responsiveness scores showed that only in the MG, participants who attended more classes responded the most to the intervention (MG: r = 0.51, p < .001; LG: r = 0.22, p = .146).

In the MG, the responsiveness composite score (i.e., acquired skills in response to the training) positively correlated with 50th and 20th percentile TL at V3 corrected by V1 (r = 0.46, p < .003 and r = 0.41, p = .010, respectively). Both correlations survived the Bonferroni correction for multiple comparisons ($p_{adjusted}$ = .010 and .029, respectively) (Table 3). Although in the MG, responsiveness to the intervention correlated with a lower %CST (r = −0.32, p = .046), this association did not survive Bonferroni correction. No significant correlation between the responsiveness composite score and TL measures was observed in the LG (Table 4 and Figure 4).

Interaction Between Baseline Personality Traits and Changes in TL

We conducted a mixed model analysis to assess TL with personality traits as covariates across the 3 groups (MG, CG, and LG). Moderator analyses show a significant effect of openness to experience on the 50th percentile TL that did not survive Bonferroni correction (F = 4.30, p = .04, $p_{adjusted}$ = .20), suggesting that with a larger sample size, this effect might become significant. No significant moderator effect of personality traits was observed for the 20th percentile or %CTS.

Correlation analysis revealed no significant moderation effect of baseline personality traits on TL measures when all participants were combined (CG+LG+MG). Similarly, we found no significant association with other personality dimensions or telomere measures in any group (50th percentile TL, Table 5; 20th percentile TL, Table 6; %CST, Table 7), except only in the MG, lower scores in baseline openness to experience significantly correlated with higher 20th percentile TL and lower %CST at V3 corrected by V1 (r = −0.37, p = .016, $p_{adjusted}$ = .08; r = 0.44, p = .004, $p_{adjusted}$ = .015, respectively) (Figure 5; Tables 6 and 7).

DISCUSSION

Aging is affected by a complex exposome that includes environmental, social, and behavioral factors (37). With the increasing number of elderly individuals in society, prioritizing the extension of healthy life expectancy has become essential. Key factors that contribute to diminished mental health and well-being in older demographic groups encompass stress, anxiety, depression, dementia, and insomnia (38,39). A potential strategy for addressing psychoaffective risk factors in older adults involves mental training aimed at stress reduction, attention regulation, and the enhancement of positive emotions through meditation practices (20,40–42). The Age-Well RCT is the first study to address the emotional and cognitive dimension of aging with a long-term nonpharmacological approach that includes both an active and a passive control group. The results of this trial validated the practicality of implementing 18-month meditation and foreign language interventions in older adults with minimal dropout and beneficial behavioral outcomes from meditation, although there were no significant changes in brain volume or perfusion of the anterior

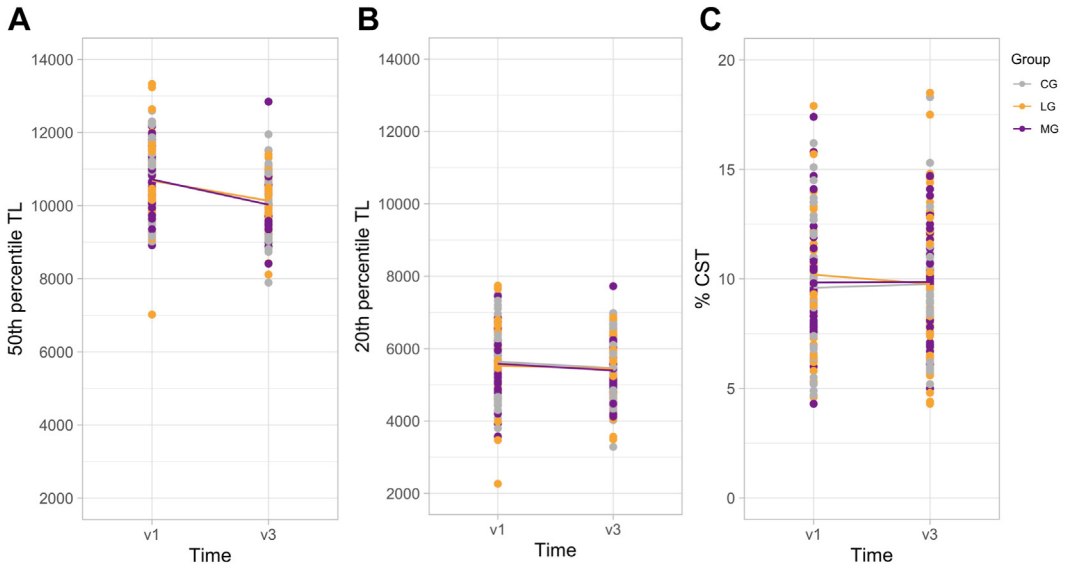

Figure 2. The 50th percentile TL, 20th percentile TL, and %CST trajectories in the 3 groups between V1 and V3 according to the mixed effects model analysis indicating group, time, and group × time interactions presented in Table 2. CG, no-intervention control group; CST, critically short telomere; LG, non-native language training group; MG, meditation training group; TL, telomere length; V1, baseline measures; V3, postintervention measures.

cingulate cortex and insula (27,28). The results reported here are a secondary analysis of the Age-Well RCT.

Our results show no evidence for a main effect of an 18-month meditation-based intervention on TL compared with an active (non-native language training) and a passive (no intervention) control group in older adults. No group or group × time effect on TL measures was detected after the 18-month intervention. Our findings are consistent with previous results showing no effects of a long-term randomized controlled meditation intervention on telomere length after 9 months of training (43). Taken together, currently there is no evidence for a benefit of long-term meditation trainings on TL in meditation-naïve older adults in rigorous randomized controlled longitudinal trials.

We found a time effect on the median TL (50th percentile, Bonferroni-adjusted p value $< .001$) driven by a TL decrease after the 18-month intervention. Notably, there was no significant change in the 20th percentile or the %CST (<3 kbp) throughout the intervention, reflecting the relative stability of the TL distribution in healthy older adults over an 18-month period and suggesting that there was no accumulation of shorter telomeres, which are the ones that represent potential health and mortality risks (12–16). Impaired cell viability and chromosome stability (44) as well as higher mortality risk (32,44–46) have been associated with the accumulation of short telomeres. Moreover, the presence of short telomeres seems to decrease regenerative capacity and increase susceptibility to degenerative diseases in slow-turnover tissues (e.g., lung and bone) and high-turnover tissues (e.g., bone marrow, skin, immune cells) (47). Because the distribution of TL in the cells is asymmetrical, the TL measures analyzed here are more representative values of telomere maintenance than average TL measures, because they provide a more accurate representation of the TL dispersion within a sample (32). Our results highlight the importance for clinical studies to explore not only the mean or median TLs but also the accumulation of short telomeres to avoid drawing biased conclusions about the potential health impact of TL changes.

It has been recognized that in meditation-based interventions, the individual commitment to practice is often variable (29). There was no significant difference in class attendance between the MG and the LG, and the mixed effects model analysis showed no significant group × class attendance interaction. However, secondary correlation analyses indicated that participants who attended more classes in the MG exhibited greater increases in TL across the intervention, whereas this was not observed in the LG. These findings suggest that individual differences that lead to a greater commitment to the practice may result in a protective effect of long-term meditation training on TL in older adults without cognitive impairment. These results highlight the need for future longitudinal RCTs with larger samples to further investigate potential modifiable factors that may influence responsiveness to meditation-based interventions. Additional correlation analyses between TL and clinical parameters are necessary to validate these promising observations.

We also examined changes in TL measures in relation to baseline major personality traits based on previous reporting that baseline personality traits influenced the utilization of Mindfulness-Based Stress Reduction practices during and postintervention in a community sample of older adults (31) and might have moderated meditation-related changes in telomere maintenance after a meditation retreat (25). We found no significant effect of baseline personality traits as moderators of TL in the mixed model analysis. However, correlation analysis per group showed that in the MG, but not in the LG or

Table 3. Partial Correlation Between TL Measures and Total Class Attendance

	LG + MG, $n = 85$			LG, $n = 43$			MG, $n = 42$		
	Estimate	Adjusted p Value	t Statistic	Estimate	Adjusted p Value	t Statistic	Estimate	Adjusted p Value	t Statistic
50th Percentile TL	0.252	.062	2.36	0.045	1.000	0.29	0.445	.011	3.10
20th Percentile TL	0.184	.280	1.70	0.044	1.000	0.28	0.330	.106	2.18
% CST	−0.011	.955	−1.00	−0.034	1.000	−0.22	−0.203	.611	−1.29

Values were adjusted by baseline level and corrected for multiple comparisons using Bonferroni correction to adjust p values.
CST, critically short telomere; LG, non-native language training group; MG, meditation group; TL, telomere length.

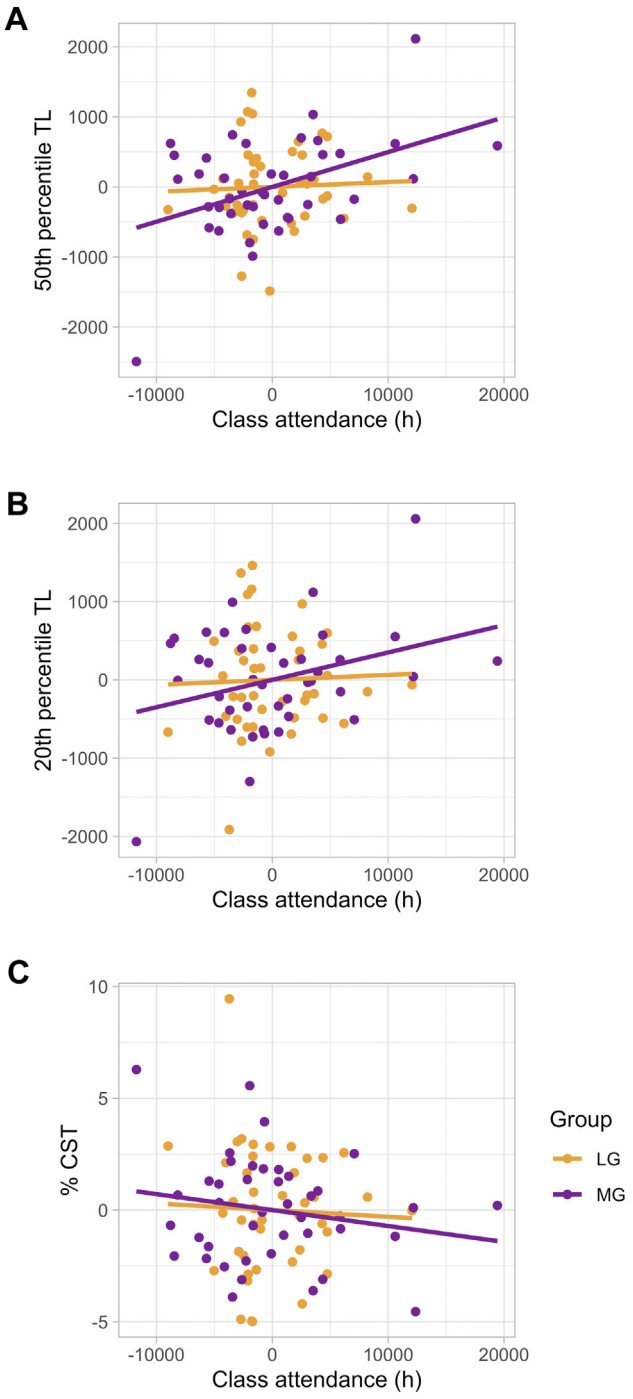

Figure 3. Class attendance (h) predicts higher 50th and 20th percentile TL in the MG. CST, critically short telomeres; LG, non-native language training group; MG, meditation training group; TL, telomere length.

CG, participants who had lower scores on the baseline openness to experience dimension showed improved telomere maintenance, with a higher 20th percentile TL and lower %CST

Table 4. Partial Correlation Between TL Measures and Responsiveness to the Training Composite Score in the LG and the MG

	LG, $n = 43$			MG, $n = 41$		
	Estimate	Adjusted p Value	t Statistic	Estimate	Adjusted p Value	t Statistic
50th Percentile TL	0.175	.807	1.12	0.455	.010	3.15
20th Percentile TL	0.047	1.000	0.30	0.405	.029	2.73
% CST	−0.028	1.000	−0.18	−0.317	.138	−2.06

Values were adjusted by baseline level and corrected for multiple comparisons using Bonferroni correction to adjust p values.
CST, critically short telomere; LG, non-native language training group; MG, meditation group; TL, telomere length.

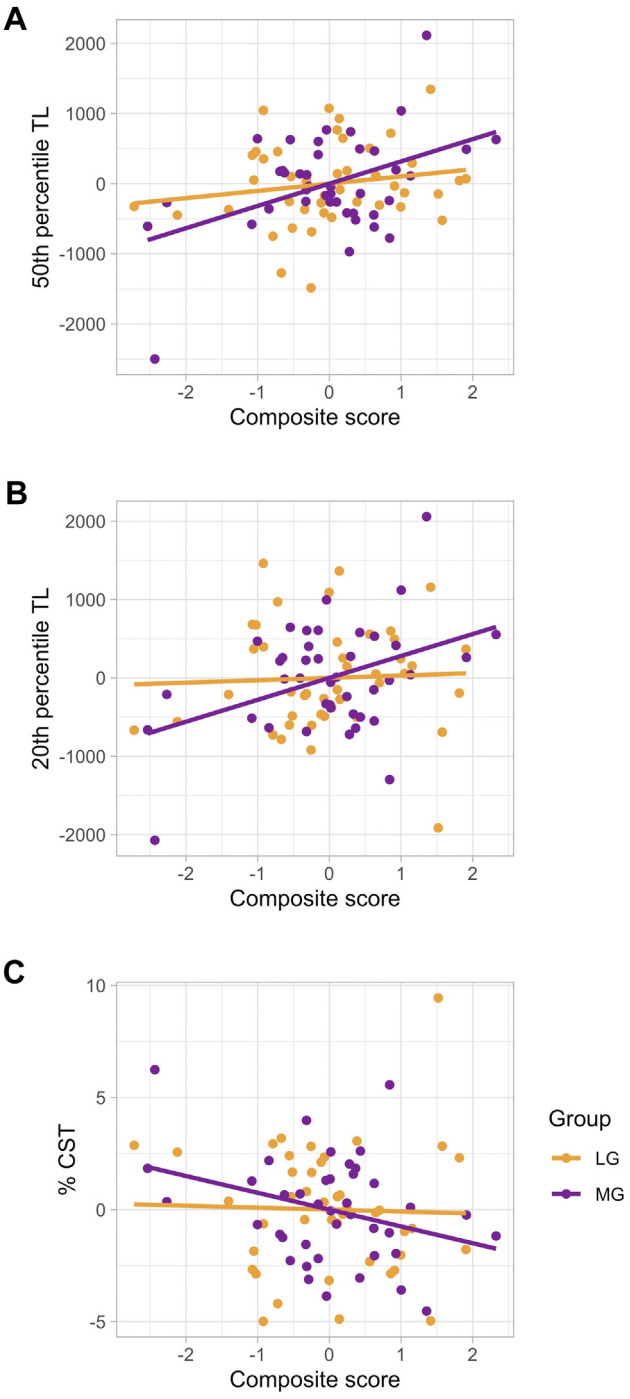

Figure 4. Responsiveness to the training (composite score) predicts higher 50th and 20th percentile TL and lower percentage of CSTs in the MG. CST, critically short telomere; LG, non-native language training group; MG, meditation training group; TL, telomere length.

at the end of the intervention. Low openness to experience scores have been associated with reduced longevity (48) and predicted poorer self-rated health in healthy control individuals

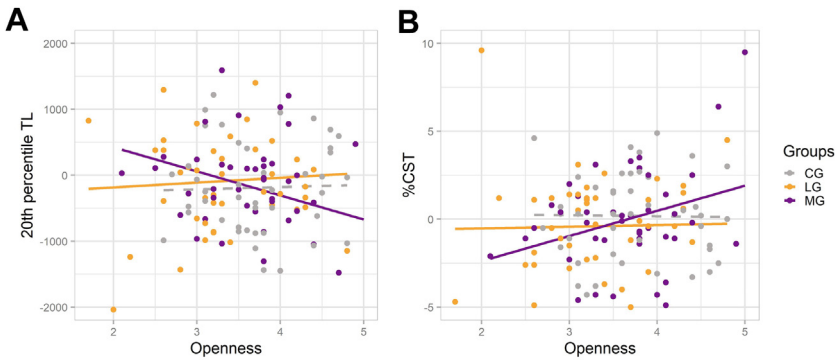

Figure 5. Lower baseline openness predicts **(A)** higher 20th percentile TL and **(B)** lower percentage of CSTs in the MG. CG, no-intervention control group; CST, critically short telomere; LG, non-native language training group; MG, meditation training group; TL, telomere length.

(49), which suggests that participants with lower baseline scores in openness to experience might have been more sensitive to improvements in biomarkers of cell aging than people with high baseline openness scores. Moreover, the fact that people with low openness to experience scores generally enjoy having a routine (50) might have been an advantage when it came to complying with the premises of the intervention, which, in addition to the 2 hours of class per week, involved 20 minutes of daily self-practice at home for 18 months (27).

Among the strengths of our study are the length of the intervention, the inclusion of a matched active control condition and a no-intervention group, the absence of attrition throughout the intervention, and the fact that sample manipulation was blinded to group allocation. As limitations of our study, it should be noted that our sample was not representative of a general aging population because all participants had at least 7 years of education, and they had no evidence of major neurological, psychiatric, or other chronic disease [described in (28)]. This may have represented a limitation in terms of the sensitivity of the sample to evidence a significant group or group × time effect on TL measures after the intervention in linear mixed models. Another limitation of our study is that other factors not examined here might have influenced the effect of the intervention on TL. For example, it was recently shown that baseline serum levels of BDNF (brain-derived neurotrophic factor), which is a mediator of cognitive performance and synaptic plasticity (51), predicted changes in TL after a 3-week meditation retreat (52). Moreover, here we did not explore the underlying mechanisms that support the correlations that we found regarding TL maintenance through secondary analysis in the different groups. In particular, the lack of a significant group × class attendance interaction does not rule out the possibility that the TL–class attendance correlation detected in the MG may be related to confounding factors. Understanding the precise pathways through which individual differences may prevent the accumulation of short telomeres would provide valuable insights into the biology of aging and may pave the way for future strategies to promote healthy aging. Another limitation of our study is that we analyzed TL only in PBMCs as a good proxy to study the impact of meditation in immune cells, which are particularly sensitive to stress and other psychosocial factors. Finally, it is important to note that the relationship between cellular senescence, TL, and age-related diseases is complex and multifactorial. Although telomere attrition is commonly associated with cellular senescence, recent research shows that postmitotic tissues can show age-dependent DNA damage at telomeric regions independent of telomere shortening and with the accumulation of senescence-related markers (53).

Conclusions

We found no improvement in TL in the meditation group compared with the control groups. Our results suggest that individual differences in commitment to the practice and baseline personality traits might have underpowered our

Table 5. Partial Correlation Between Changes in 50th Percentile Telomere Length (V3 − V1) and Baseline Big Five Personality Trait Scores in All Participants and Separately by Group

	All Participants, *N* = 128			CG, *n* = 43			LG, *n* = 43			MG, *n* = 42		
	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD
Extraversion	−0.017	1.000	−0.188	0.049	1.000	0.307	0.012	1.000	0.078	−0.086	1.000	−0.539
Agreeableness	0.113	1.000	1.270	0.057	1.000	0.360	0.098	1.000	0.622	0.084	1.000	0.525
Conscientiousness	−0.078	1.000	−0.871	0.077	1.000	0.487	−0.154	1.000	−0.985	−0.107	1.000	−0.670
Neuroticism	−0.020	1.000	−0.228	−0.182	1.000	−1.167	−0.044	1.000	−0.281	0.038	1.000	0.238
Openness	−0.115	.985	−1.297	−0.066	1.000	−0.418	0.006	1.000	0.038	−0.253	.550	−1.632

Values were adjusted by baseline level and corrected for multiple comparisons using Bonferroni correction to adjust *p* values.
CG, no-intervention control group; LG, non-native language training group; MG, meditation group; V1, baseline measures; V3, postintervention measures.

Table 6. Partial Correlation Between Changes in 20th Percentile Telomere Length (V3 − V1) and Baseline Big Five Personality Trait Scores in All Participants and Separately by Group

	All Participants, *N* = 128			CG, *n* = 43			LG, *n* = 43			MG, *n* = 42		
	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD
Extraversion	>0.001	1.000	>0.001	0.131	1.000	0.837	−0.058	1.000	−0.364	0.025	1.000	0.158
Agreeableness	0.143	.550	1.610	0.054	1.000	0.342	0.152	1.000	0.973	0.207	.975	1.320
Conscientiousness	−0.085	1.000	−0.950	−0.009	1.000	−0.055	−0.159	1.000	−1.016	−0.053	1.000	−0.333
Neuroticism	0.006	1.000	0.068	−0.278	.375	−1.828	−0.028	1.000	−0.178	0.271	.430	1.761
Openness	−0.156	.405	−1.761	−0.084	1.000	−0.530	0.002	1.000	0.017	−0.375	.080	−2.523

Values were adjusted by baseline level and corrected for multiple comparisons using Bonferroni correction to adjust *p* values.
CG, no-intervention control group; LG, non-native language training group; MG, meditation group; V1, baseline measures; V3, postintervention measures.

Table 7. Partial Correlation Between Changes in Percentage of CSTs (V3 − V1) and Baseline Big Five Personality Trait Scores in All Participants and Separately by Group

	All Participants, *N* = 128			CG, *n* = 43			LG, *n* = 43			MG, *n* = 42		
	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD	Estimate	Adjusted *p* Value	SD
Extraversion	−0.037	1.000	−0.416	−0.187	1.000	−1.204	0.099	1.000	0.628	−0.162	1.000	−1.025
Agreeableness	−0.160	.365	−1.808	−0.028	1.000	−0.180	−0.183	1.000	−1.178	−0.249	.580	−1.605
Conscientiousness	0.090	1.000	1.011	0.018	1.000	0.113	0.186	1.000	1.194	8.680	1.000	0.001
Neuroticism	−0.040	1.000	−0.445	0.272	.405	1.791	0.095	1.000	0.606	−0.300	.280	−1.967
Openness	0.183	.200	2.079	0.068	1.000	0.430	0.159	1.000	1.022	0.444	.015	3.095

Values were adjusted by baseline level and corrected for multiple comparisons using Bonferroni correction to adjust *p* values.
CG, no-intervention control group; CST, critically short telomere; LG, non-native language training group; MG, meditation group; V1, baseline measures; V3, postintervention measures.

analysis, indicating the need for longitudinal randomized and controlled trials with larger samples. Our findings also highlight the importance of integrating methodologies that capture and analyze potential moderating individual factors to better inform the design and implementation of meditation interventions and maximize their benefits for practitioners.

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