Psychoneuroendocrinology 108 (2019) 20–27

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Loving-kindness meditation slows biological aging in novices: Evidence from a 12-week randomized controlled trial

Khoa D. Le Nguyen[a], Jue Lin[b], Sara B. Algoe[a], Mary M. Brantley[c], Sumi L. Kim[d], Jeffrey Brantley[c,e], Sharon Salzberg[f], Barbara L. Fredrickson[a,*]

[a] Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, CB #3270, Chapel Hill, NC, 27599, USA
[b] Department of Biochemistry & Biophysics, University of California, 600 16th St, San Francisco, CA, 94158, USA
[c] Duke Integrative Medicine, Duke University, Durham, NC, USA
[d] Office of Religious Life, Duke University, Durham, NC, USA
[e] Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, USA
[f] Insight Meditation Society, Barre, MA, USA

ARTICLE INFO

Keywords:
Contemplative science
Metta
Compassion meditation
Cell aging
Positive psychology

ABSTRACT

Combinations of multiple meditation practices have been shown to reduce the attrition of telomeres, the protective caps of chromosomes (Carlson et al., 2015). Here, we probed the distinct effects on telomere length (TL) of mindfulness meditation (MM) and loving-kindness meditation (LKM). Midlife adults ($N = 142$) were randomized to be in a waitlist control condition or to learn either MM or LKM in a 6-week workshop. Telomere length was assessed 2 weeks before the start of the workshops and 3 weeks after their termination. After controlling for appropriate demographic covariates and baseline TL, we found TL decreased significantly in the MM group and the control group, but not in the LKM group. There was also significantly less TL attrition in the LKM group than the control group. The MM group showed changes in TL that were intermediate between the LKM and control groups yet not significantly different from either. Self-reported emotions and practice intensity (duration and frequency) did not mediate these observed group differences. This study is the first to disentangle the effects of LKM and MM on TL and suggests that LKM may buffer telomere attrition.

1. Introduction

Chronological age and biological age are not identical. The former is measured in years, whereas the latter is often indexed by telomere length. Telomeres are DNA-protein complexes at the ends of eukaryotic chromosomes that protect DNA against instability and degradation (Blackburn, 2005). Telomeres progressively shorten with cell division (i.e., aging) in general, but may also be replenished, or lengthened, by the enzyme telomerase (Blackburn, 2005). Shorter telomere length (TL) has predicted higher mortality risk and diseases of aging, including cardiovascular disease and diabetes (Blackburn et al., 2015). Although the evidence is not conclusive, TL has also been associated with psychosocial factors (Puterman and Epel, 2012; Shalev et al., 2013), with shorter TL linked to stress, measured objectively, as life adversities (Tyrka et al., 2010, but see Jodczyk et al., 2014, for a contrary, null result), subjectively, as perceived stress (Mathur et al., 2016), and physiologically, as HPA-axis activity (Tomiyama et al., 2012). Shorter TL has also been associated with trait neuroticism (van Ockenburg et al., 2014), anxiety (Hoen et al., 2013), and depression (Schutte and Malouff, 2015). Longer TL has been correlated with positive qualities such as conscientiousness (Edmonds et al., 2015), optimism and emotional intelligence (Schutte et al., 2016).

Meditation, known to enhance psychological well-being (Dimidjian and Segal, 2015), has been examined for its impact on health via telomere biology (Conklin et al., 2018 [$N = 62$]; Thimmapuram et al., 2017 [$N = 47$]). Meditation encompasses numerous mental training techniques aimed at cultivating beneficial qualities, including sustained attention, acceptance of thoughts and feelings, or the up-regulation of warm-hearted altruistic feelings (Dahl et al., 2015). Evidence shows that, compared to novice individuals, TL was larger in long-term meditators (Alda et al., 2016 [$n = 20$]; Hoge et al., 2013 [$n = 9$], significant effect emerged for female participants only). We located only two randomized controlled trials (RCTs) that manipulated meditation and measured TL, and each study recruited from a clinical population (i.e., breast cancer survivors). Results across these two RCTs were mixed, with one reporting that meditation buffered TL shortening

* Corresponding author.
E-mail address: blf@unc.edu (B.L. Fredrickson).

https://doi.org/10.1016/j.psyneuen.2019.05.020
Received 18 January 2019; Received in revised form 10 May 2019; Accepted 14 May 2019

(Carlson et al., 2015 [$N = 88$], marginally significant effect) and the other reporting a null effect (Lengacher et al., 2014 [$N = 134$]). Complementing these RCTs that measured TL, a greater number of RCTs (using both clinical and nonclinical populations) have manipulated meditation and measured telomerase activity (TA) and have reliably found meditation to increase TA (for a meta-analysis, see Schutte and Mahoff, 2014). In a matched-control study (non-randomized) that assessed both TL and TA, Conklin et al. (2018 [$N = 62$]) reported that, among experienced meditators, a 1-month intensive insight meditation retreat led to *increases* in TL and nonsignificant changes in TA, relative to a matched sample of non-retreat meditators. Epel et al. (2009) proposed that certain forms of meditation may benefit TL by decreasing negative cognition (e.g., rumination) and stress arousal (e.g., blood pressure), while promoting positive cognition (e.g., reappraisal) and biomarkers of health (e.g., heart rate variability). Supporting this view, in Conklin et al. (2018), neurotic and less agreeable retreatants reaped greater telomere-related benefits. Similarly, distress reduction and affect regulation appear to mediate the link between meditation and healthy telomere biology (Alda et al., 2016; Jacobs et al., 2011; Lavretsky et al., 2013).

One limitation of many meditation studies, including those that have examined telomere biology, is the use of multiple meditation practices within a treatment group (e.g., Conklin et al., 2018; Schutte and Mahoff, 2014). Among many kinds of contemplative practices, mindfulness meditation (MM; Kabat-Zinn, 1990) and variations of loving-kindness meditation (LKM; Salzberg, 1995) are often taught together in meditation interventions (e.g., Carlson et al., 2015). Both practices confer salutary effects. Mindfulness-based therapies have shown large and clinically significant effects on decreasing emotional distress and enhancing well-being (Gotink et al., 2015; Khoury et al., 2013). Although less studied (Zeng et al., 2015), LKM has been shown to increase compassion (Klimecki et al., 2014), enhance health and well-being more generally (Galante et al., 2014) and positive emotions specifically (Fredrickson et al., 2008; Zeng et al., 2015). These two practices, however, may activate distinct psychological processes (Feldman et al., 2010), which may translate into differently impacting telomere-related functioning. Therefore, it is important to differentiate the effects of these distinct contemplative practices.

To compare and contrast MM and LKM, we use the Shapiro et al. (2006) framework, which conceives mindfulness as having three components: intention, attention, and attitude. We observe that both MM and LKM involve training sustained attention, whether directed toward the contents of consciousness or social targets, and an open, accepting attitude. They differ, however, in intention. MM aims to observe present-moment conscious experience, which can involve directing attention to one category of experience (e.g., the breath) or open monitoring of experience without any explicit focus (Lutz et al., 2008). As a result, MM may engage high degrees of attentional processes, activating brain regions involved in conflict monitoring, selective attention, sustaining attention (required for focused attention) and regions involved in interoception, vigilance, and disengaging attention (required for open awareness; Lutz et al., 2008). On the other hand, LKM aims to cultivate warm-hearted positive emotions toward oneself and others. Although the practice requires directing attention toward social targets, it may engage attentional processes to a lesser degree compared to MM (Lutz et al., 2008). Instead, LKM preferentially engages socio-emotional processes, activating brain areas related to emotional processing, especially of positive affect (Desbordes et al., 2012; Klimecki et al., 2014) and social cognition (e.g. mentalizing, empathy; Mascaro et al., 2012).

Among the few studies that have experimentally compared the effects of MM and LKM, most have assessed outcomes on subjective states (e.g. Feldman et al., 2010; Fredrickson et al., 2017). For instance, Feldman et al. (2010 [$N = 190$]) found that MM, relative to LKM, increased decentering from thoughts, whereas Fredrickson et al. (2017 [$N = 339$]) examined but found no differences in daily negative and positive emotions between the two meditation practices. The only well-powered study to distinguish MM and LKM using a biological factor (Isgett et al., 2016) found that genetic variation in oxytocin signaling (i.e., *OXTR rs1042778* GG genotype) predicted more gains in positive emotions for LKM but not MM. To date, no research has compared LKM and MM regarding their effects on biological aging. Early studies on meditation and TL contain other methodological limitations: (a) a lack of RCTs that use novice, nonclinical samples to draw firm, generalizable causal inferences; and (b) small sample sizes (average nonclinical sample size in quasi-experiments: *N*s = 47–62).

The current research overcomes these limitations and asks the question: Do MM and LKM differ in their effects relative to the waitlist control group on TL change? The hypothesized mechanism of LKM is to cultivate daily positive emotions, which have been shown, over time, to build biomarkers of health (Kok et al., 2013). By contrast, the hypothesized mechanism of MM is to sharpen attention to the present moment. Therefore, we originally thought that LKM, through its effects on daily positive emotions, would benefit telomere length more than MM and relative to the control group. However, in light of our team's recent evidence that both LKM and MM increase practitioners' daily positive emotions with no between-participant differences in dose-response relations (i.e., Fredrickson et al., 2017), we now leave the research question open as to which practice may have a larger effect on TL change. In addition, previous literature hypothesizes that positive and negative affect may impact telomere biology (e.g. Epel et al., 2009), and intensive meditation practices robustly benefit telomere biology (Conklin et al., 2018). Therefore, we also explored whether changes in emotions and the duration and frequency of meditation practice mediated condition effects on TL changes.

In a longitudinal RCT conducted in 2012–2013 to test the biological effects of positive emotions (Fredrickson et al., 2017, Study 1; Isgett et al., 2016), we had assigned novice mid-life adults ($N = 176$) to one of three conditions: LKM (experimental group) MM (active control group), or a monitoring waitlist control. Meditation participants attended a 6-week, group-based workshop. They also reported nightly on their positive and negative emotions and their meditation practice that day. In 2016, we sought and received approval from the funding agency to redirect remaining grant funds to assess TL as a secondary outcome. We did so using extra stored blood samples that had been collected two weeks before the meditation workshops started and three weeks after they ended. We used general linear models to examine the effects of intervention conditions on changes in TL. In exploratory analyses, we tested whether emotions or meditation practice time mediated any observed effects.

2. Methods

2.1. Participants

Midlife participants ($N = 176$) were recruited from Durham and Orange County of North Carolina via paper and online advertisement. Eligible participants were between 35–64 years old (inadvertently, three participants enrolled in the study reported age outside this range: 65, 65, and 67). Each had home internet access, little to no meditation experience, and no current chronic illnesses or disabilities. Study information and consent documents were provided online. After participants indicated their consent—and before any contact with study personnel—they were assigned numeric identification codes and, blocked by gender, allocated (via a random number generator, similar to a coin toss) to one of the three experimental conditions: loving-kindness meditation (LKM; $n = 63$), mindfulness meditation (MM; $n = 62$), or a monitoring waitlist control group ($n = 51$). The study manager grouped randomized participants into scheduled evening workshops, each with a cap of 16 students. To maintain participant blindness, coupled participants (e.g., spouses) were randomized as a unit. Three participants (2 MM, 1 LKM) were assigned to a meditation workshop but did not attend any sessions and were therefore removed from the sample. Additionally, only participants who had complete data for TL pre- and post-intervention were retained for the final analyses. This resulted in a final sample of 142 participants. The Online Supplemental Material (OSM) provides the recruitment procedures and the CONSORT flow diagram. Data from this study (NIH-supported R01NR012899) have been reported on elsewhere (Fredrickson et al., 2015, Confirmation Study; Isgett et al., 2016; Fredrickson et al., 2017, Study 1) and will continue to support other and related investigations.

Of relevance for power analysis, previous RCTs on meditation and TL have tested clinical samples as well as meditation programs centered largely on mindfulness practice (e.g., Carlson et al., 2015; Lengacher et al., 2014), whereas prior studies of nonclinical samples have not been RCTs and often included experienced meditators on intensive retreats (e.g., Conklin et al., 2018). Absent a relevant effect size from past research, we conducted a power analysis post data collection assuming a medium effect size using G*powers (Faul et al., 2007). The analysis, which considers a three-group design as well as the number of covariates, revealed that to achieve a power of 0.80, we needed a minimum of 158 participants, which is smaller than our recruited sample (N = 176) but larger than our final sample with complete TL data (N = 142).

2.2. Procedure and meditation interventions

The Institutional Review Board of the University of North Carolina at Chapel Hill approved all procedures for the current study. Data collection took place in two waves between August 2012 and May 2013. The study lasted for 12 weeks, and the 6-week meditation workshops (for those in MM and LKM groups) took place from week 3 to week 9. Covariates and blood samples used for TL were collected in two lab visits at the beginning of the study and again at week 12. All study personnel involved in those lab visits were blind to participants' randomized condition. The timing of lab visits allowed for baseline assessment of daily emotions before workshops began as well as for a decoupling of the post-workshop biological assessments from any transient emotional uplift experienced as workshops concluded. Daily emotion reports were collected throughout the study, but only data during the 9-week period (week 3 – week 11) from the start of the workshops to before lab 2 were analyzed here. A few participants in the MM and LKM groups started their meditation workshop a bit earlier or later due to scheduling issues. Therefore, the daily data were realigned so that day zero and week zero are the day and week that participants attended their first workshop. Those randomized to the monitoring waitlist control group participated in all aspects of the study protocol and received training in MM or LKM after the last laboratory session.

2.2.1. Meditation interventions

The MM and LKM workshops were designed with the help of meditation experts, who were blind to study hypotheses (authors MMB, SLK, JB and SS; see Fredrickson et al., 2017 for more details on workshop development and procedures). As a framework for delineating and describing the similarities and differences between MM and LKM, they adopted Shapiro and colleague's three axioms of mindfulness (Shapiro et al., 2006). These three axioms are intention, attention, and attitude, which in combination produce a particular hallmark "meta mechanism" or fundamental shift in perspective characteristic of each workshop. Whereas the attitude of both MM and LKM were identical, namely, open and nonjudgmental, their respective intention, attention, and hallmark meta mechanism differed, as described below. Each meditation workshop was also designed to follow a similar secular, health-based format that used six progressive, 1-h small group sessions with comparable resources and encouragement for individual home practice (See Table S7 in the OSM for a summary of each workshop's instructional goals). Besides the workshop, participants received homework assignments and five 20-minute audio-recorded guided meditations and were encouraged to cultivate a daily meditation practice.

2.2.1.1. Mindfulness meditation.. In the context of an open and nonjudgmental attitude, the workshop instructor (SLK) presented the intention of MM as to be in the present moment. The attention of the practitioner is directed toward the contents of consciousness within the present moment. Progressively, over the six weeks, the targets of consciousness expanded, with practice directed toward breathing and hearing (Week 1), the body (Week 2), emotions (Week 3), thoughts (Week 4), and choiceless awareness (Week 5), with Week 6 being review and integration. The hallmark meta mechanism of MM was taught as a fundamental shift in perspective toward "reperceiving," or de-identifying with, the contents of consciousness (i.e. one's sensations, thoughts, and emotions), which in turn facilitates viewing one's experience with more clarity and objectivity (Shapiro et al., 2006, p. 377).

2.2.1.2. Loving-kindness meditation.. Similarly, in the context of an open and nonjudgmental attitude, the workshop instructor (MMB) presented the intention of LKM as to self-cultivate warm and friendly feelings. The attention of the practitioner is directed to various social targets as well as to physical sensations in the heart region. Progressively, over six weeks, the social targets of loving-kindness expanded, with practice directed toward a loved one (Week 1), oneself (Week 2), an acquaintance (Week 3), a difficult person (Week 4) and all beings (Week 5), with Week 6 being review and integration. The hallmark meta mechanism of LKM was taught as a fundamental shift toward warmth, kindness, and social connection.

2.3. Blood sample preparation and TL measurement

Blood samples from each participant were obtained via venipuncture during the lab sessions, immediately stored at −80 °C, and subsequently delivered on dry ice to the University of California, San Francisco for TL measurement in the laboratory of Elizabeth Blackburn.

DNA was extracted from frozen blood with the QIAamp DNA blood mini kit (QIAGEN, cat # 51,106). DNA quality criteria were OD260/OD280 between 1.7–2.0 and concentration > 10 ng/ul. Eleven samples did not yield enough DNA, and therefore telomere length data for these samples could not be determined. The TL assay methodology was identical to that of Lin et al. (2010; adapted from Cawthon, 2002, 2009). TL is expressed as the ratio (T/S) of telomeric (T) to single copy (S) gene product for a particular sample. All samples were run in triplicate wells on a 384-well plate. The average of the triplicate wells was calculated for T and S separately and a T/S ratio values was derived. This was repeated again to obtain a second T/S ratio for the same sample. If the first and second T/S value varied by more than 7%, the sample was run a third time and the two closest values were reported. The average inter-assay coefficient of variation (CV) of this data set was 2.1% (±1.4%). Lab personnel who performed the telomere length measurement were blind to the randomized group status of each sample and other demographic data.

2.4. Other measures

2.4.1. Emotions

Weekly averaged emotions were computed from daily assessments with the modified Differential Emotions Scale (Fredrickson, 2013). This scale measured the extent to which participants experienced 10 positive emotions (amusement, awe, gratitude, hope, inspiration, interest, joy, love, pride, and serenity) and 10 negative emotions (anger, contempt, disgust, embarrassment, fear, guilt, hate, sadness, shame, and stress). Participants reported their emotions for the past 24 h on a 5-point Likert scale (0 = Not at all, 4 = Extremely). For each participant, positive emotion (PE) and negative emotion (NE) scores were computed by averaging individual emotions in the respective categories. We assessed the reliability of the PE and NE scores for daily reports during the 9 weeks period (week 3 – week 11) by calculating McDonald's omega using the multilevel confirmatory factor analysis procedure described in Bolger and Laurenceau (2013, p. 138–140, calculated in Mplus version 7.2; Muthén and Muthén, 2015; see procedures and results in section 3C in the Online Supplemental Materials). The omega estimates indicated good reliability of within-person and between-person changes in emotions over time (within-person: omega_{PE} = .879; omega_{NE} = .761; between-person: omega_{PE} = .965; omega_{NE} = .890). We averaged daily reports to acquire weekly average emotions for further analyses.

2.4.2. Meditation practice

Two items in the daily reports were used to assess meditation practice. Participants were first asked: “Did you engage in any meditation since the last time you filled out this questionnaire?” If the response was yes, participants were then asked: “How much time (in minutes) did you spend on meditation since the last time you answered this question? If there were multiple episodes, make sure to add them all together.” If participants responded “no” to the first question, the duration variable was coded 0. Total practice frequency (days) and duration (converted to hours) across 9 weeks (week 3 – week 11) were calculated for each participant for further analyses.

2.4.3. Standard demographic variables

In line with prior research (Chae et al., 2014; Gardner et al., 2014; Müezzinler et al., 2013, 2014), we considered several demographic variables in our analyses of TL, including BMI, age, gender, and race. BMI measures at two lab visits were calculated as instrument-measured weight (in kg) over the square of instrument-measured height (in m). Data on races of participants (see Table 1 for race categories) were reduced to white vs. nonwhite for analysis, and Hispanic ethnicity was collected for reporting purpose.

2.5. Analytic approach

2.5.1. Primary model

To operationalize changes in TLs, we first subtracted TL measured at time 1 from TL measured at time 2 ($\Delta TL = TL_2 - TL_1$; see Dalecki and Willits, 1991). Experimental conditions (control, MM, and LKM) were recoded into two dummies variables, MM and LKM, which made the control group the reference group for comparison. To compare the effect of the LKM and MM against the control conditions on telomere length changes, we fitted a linear model of experimental conditions predicting ΔTL controlling for mean-centered baseline TL (Dalecki and Willits, 1991), which allows us to predict changes in cellular aging while accounting for participants’ initial biological age (i.e., TL_1; although comparable results emerge when modeling TL_2 controlling for TL_1 [see OSM Table S2] such an analysis does not support meaningful conclusions about change over time.). Also consistent with prior research (Blackburn et al., 2015; Chae et al., 2014; Gardner et al., 2014; Müezzinler et al., 2013, 2014), we controlled for demographic covariates including mean-centered age, gender (0 = female, 1 = male), nonwhite (Caucasian = 0, Non-Caucasian = 1), and BMI. For BMI, baseline BMI and changes in BMI (BMI_2 - BMI_1) were each included due to a significant increase in BMI across the entire sample, which is consistent with tendencies to gain weight in midlife (e.g. Kristal et al., 2005).

Contrasts were conducted for the full model to determine whether significant decreases in TL were evident in individual experimental conditions and to compare the effect on ΔTL of MM against LKM. Because these contrasts were computed from the same model, typically no multiple comparison correction is needed. However, adopting a more conservative approach, we also adjusted *p* value using the Benjamini-Hochberg procedure (Benjamini and Hochberg, 1995) to control for possible false discovery rate at the α level of .05.

2.5.2. Exploratory analyses of statistical mediation

We examined changes in weekly PE and NE during the workshop period (week 3 to week 9) as potential mediators for the effects of experimental condition. Because structural equation modeling is not well-suited to model intensive longitudinal data, we use weekly instead of daily emotion reports to fit a mediational, latent-curve model. The model including PE and NE was estimated using maximum likelihood estimation with robust standard errors, which can produce robust estimates given a skewed distribution of negative emotion data.

Additionally, we examined whether frequency or duration of meditation mediated the effect of LKM and MM on TL changes. As frequency and duration were highly correlated, they were tested separately to avoid issues related to multicollinearity. We ran models that included an overall effect of duration (or frequency) on TL changes to assess their mediation effect.

2.5.3. Sensitivity analyses

We removed demographic covariates from the full model and refitted the main ΔTL model to determine if the effects of experimental conditions remained. In addition, ΔTL models were fitted controlling for baseline PE during the 7 days prior to the meditation workshop,

Table 1
Demographic Characteristics, Telomere Lengths (TLs), and Covariates by Condition.

	LKM (*n* = 51)		MM (*n* = 54)	Waitlist (*n* = 37)		*Statistics*		*p*
	M	*SD*	*M*	*SD*	*M*	*SD*		
Age (years)	48.45 (36-65)	8.39	49.15 (34-67)	9.41	48.70 (35-64)	8.56	$F(2,139)$ = .08	.920
Time 1 TLs	1.04	.19	1.07	.19	1.05	.19	$F(2,139)$ = .54	.585
Time 2 TLs	1.01	.16	1.01	.18	.97	.16	$F(2,139)$ = .65	.522
Time 1 BMI	28.17	6.51	26.34	5.36	28.14	6.48	$F(2,139)$ = 1.49	.229
BMI changes	.14	.64	.08	.53	.07	.69	$F(2,139)$ = .19	.831
7-day baseline PE	1.75	.63	1.49	.84	1.37	.70	$F(2,138)$ = 3.18	.045
7-day baseline NE	.44	.35	.44	.29	.52	.49	$F(2,138)$ = .61	.543
Meditation hours[a]	13.66	6.35	10.34	5.72	0.13	.44	$F(2,139)$ = 76.10	<.001
Meditation days[a]	40.76	12.74	32.98	14.50	0.68	2.68	$F(2,139)$ = 132.60	<.001
	n	%	*n*	%	*n*	%		
Sex (female)	32	62.75	40	74.07	27	72.97	$\chi^2(2)$ = 1.85	.397
Race							$\chi^2(6)$ = 5.86	.439
Am. Indian/ Alaskan Native	0	.00	1	1.85	0	.00		
Asian	3	5.88	5	9.26	2	5.41		
Native Hawaii/ Pacific Islander	0	.00	0	.00	0	.00		
Black	9	17.65	3	5.56	4	10.81		
White	39	76.47	45	83.33	31	83.78		
Hispanic ethnicity	1	1.96	3	5.56	1	2.70	$\chi^2(2)$ = 1.10	.578

[a] Practice variables (i.e., meditation hours and meditation days) represent totals over 9 weeks.

which unexpectedly differed by condition (see below).

3. Results

3.1. Preliminary analyses

No participants reported adverse effects from MM or LKM. Table 1 presents the descriptive statistics of study variables and demographic characteristics by condition. Analyses of variances indicated no significant differences among experimental conditions in age, telomere length measured at time 1 and time 2, initial BMI, and negative emotions. For all participants, BMI significantly increased ($t[141] = 2.03$, $p = .045$), but there was no difference in BMI changes across conditions. Chi-square tests also showed no differences in gender, race, and Hispanic ethnicity across three conditions. Unexpectedly, baseline positive emotions differed across conditions ($F[2138] = 3.18$, $p = .045$), specifically the LKM group ($M = 1.75$, $SD = 0.69$) was higher in positive emotions than the waitlist control group ($M = 1.37$, $SD = 0.63$; Tukey's HSD $p = 0.046$). Positive emotions were therefore used as a control variable in sensitivity analyses. We also compared duration (hours) and frequency (days) of meditation among the three conditions as a manipulation check for the meditation intervention. As expected, participants in the LKM and MM group meditated on more days and for longer hours than those in the control group (days meditated: $F[2139] = 132.6$, $p < .001$; hours meditated: $F[2,139] = 76.1$, $p < .001$). Surprisingly, however, *all* pairwise comparisons across conditions differed (Tukey's HSD, all *ps* $< .001$), with the number of meditation days and hours increasing by group in the following order: control, MM, LKM. In light of the unexpected practice differences between meditation groups (mean days/week: MM = 3.7, LKM = 4.5; mean hours/week: MM = 1.15, LKM = 1.52) these two practice variables were also tested as possible mediators of TL changes.

Additional exclusion analyses show no differences in the above variables between the analyzed and excluded samples except for gender, meditation duration, and frequency (see Table S1 in the OSM). There were a higher percentage of females in the excluded sample (88.24%) compared to the analyzed sample (69.72%). Unsurprisingly, participants who dropped out during the study or did not provide complete data were also less likely to practice meditation regularly.

Table 2 shows correlations among all variables included in the analyses (collapsed across experimental conditions). As expected, age is associated with shorter TL.

3.2. Telomere length

During the study period, across all participants, TL (T/S ratio)

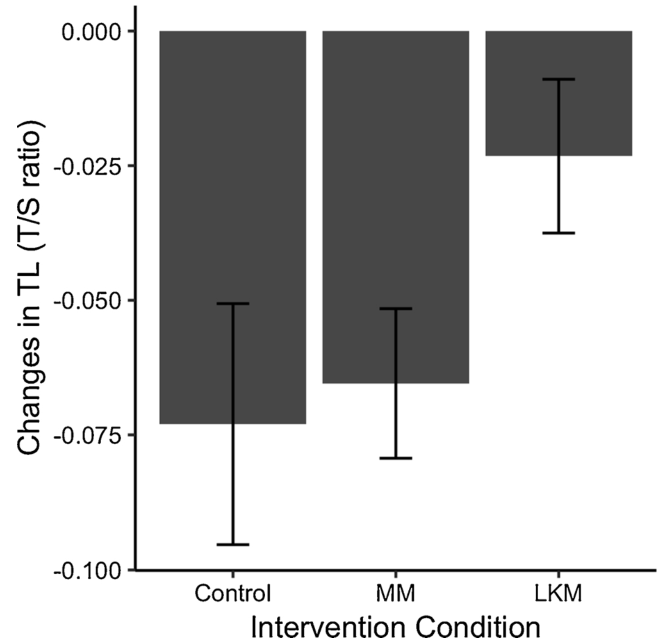

Fig. 1. Descriptive Mean and Standard Errors of Changes in TL per Experimental Conditions.

Table 3
Coefficients for Regression of changes in TL on Experimental Conditions Controlling for Covariates.

	B	SE_B	95% CI	p
Control (intercept)	−.070	.017	[-.103,-.036]	<.001
LKM	.048	.021	[.006,.089]	.024
MM	.019	.021	[-.022,.059]	.370
Time 1 TL	−.336	.046	[-.427,-.244]	<.001
Non-white	−.013	.021	[-.055,.029]	.547
Gender	−.016	.018	[-.051,.020]	.381
Age	−.003	.001	[-.005,-.001]	.003
Baseline BMI	.000	.001	[-.002,.003]	.742
BMI change	.002	.013	[-.024,.029]	.860

Note. B represents non-standardized coefficients. Variables include LKM (Loving kindness meditation; 1 = LKM, 0 = non-LKM), MM (Mindfulness meditation; 1 = MM, 0 = non-MM), time 1 TL (mean-centered), age (mean-centered), gender (0 = female, 1 = male), non-white (Caucasian = 0, Non-Caucasian = 1), baseline BMI, and BMI change.

Table 2
Correlations among independent, dependent variables, and covariates.

	M	*SD*	1	2	3	4	5	6	7	8	9	10	11
1. Time 1 TLs	1.05	0.19	–										
2. Time 2 TLs	1.00	0.17	.81***	–									
3. TL changes	−0.05	0.11	−.49***	.11	–								
4. Age	48.78	8.77	−.35***	−.42***	−.03	–							
5. Time 1 BMI	27.47	6.11	−.19*	−.13	.12	.01	–						
6. BMI changes	0.10	0.61	.02	.03	.02	−.04	−.09	–					
7. Non-white	0.19	0.39	−.01	−.00	.01	−.13	.20*	−.07	–				
8. Gender	0.30	0.46	−.06	−.06	.01	−.08	.04	.10	−.08	–			
9. Baseline PE	1.56	0.75	−.08	−.04	.07	.03	.02	.03	.20*	−.15	–		
10. Baseline NE	0.46	0.37	.05	.08	.04	.02	.00	.16	−.08	.05	−.11	–	
11. Meditation hours	8.87	7.47	−.07	−.05	.04	.25**	−.01	−.09	.05	.00	.18*	−.05	–
12. Meditation days	27.36	20.06	−.04	−.02	.04	.20*	−.06	−.07	.02	−.01	.15	−.05	.93***

Note. TL = Telomere Lengths, BMI = Body Mass Index, PE = Positive Emotions, NE = Negative Emotions.
*** $p < .001$.
** $p < .01$.
* $p < .05$.

Table 4
Condition-specific Tests of Null Hypothesis of No TL Change and Contrasts Between Experimental Conditions.

	B	SE_B	95% CI	p	p (adjusted)
Control vs. 0[a]	−.070	.017	[-.103,-.036]	.000	.000
LKM vs. 0	−.022	.016	[-.054,.010]	.177	.212
MM vs. 0	−.051	.015	[-.080, -.022]	.001	.003
LKM vs. Control[b]	.048	.021	[.006,.089]	.024	.048
MM vs. Control[c]	.019	.021	[-.022,.059]	.370	.370
LKM vs. MM	−.029	.019	[-.067,.009]	.131	.197

Note. B represents non-standardized coefficients. Model controlled for several covariates: baseline TL, gender, ethnicity, baseline BMI, BMI changes, and age.
[a] This contrast is the same as the test of “Control (intercept)” in Table 3.
[b] This contrast is the same as the test of “LKM” in Table 3.
[c] This contrast is the same as the test of “MM” in Table 3.

significantly decreased on average by .052 ($t[141] = 5.50$, $p < .001$). Fig. 1 shows the descriptive means and standard errors of TL changes by experimental conditions. Table 3 shows the model results for experimental conditions predicting ΔTL after controlling for mean-centered baseline TL and standard covariates. Due to the significant increase in BMI in the entire sample, we controlled for both mean-centered baseline BMI and BMI changes ($BMI_2 – BMI_1$).

In the full model, the intercept was significant and negative (B = -.070, SE = .017, 95%CI = [-.103,-.036], $p < .001$), indicating that TL significantly shortened in the control group. Compared to the control group, the LKM group has a significantly smaller decrease in TL (B = .048, SE = .021, 95%CI = [.006,.089], p = .024) whereas the MM group showed no difference relative to the control group (B = .019, SE = .021, 95%CI = [−.022,.059], p = .370). Changes in TL were also predicted by chronological age after controlling for other variables, suggesting that older participants showed more changes in TL. As stated previously, this pattern of significance was unchanged when post-intervention TL (instead of ΔTL) was used as the dependent variable (see Table S2 in the OSM).

To complete our understanding of group differences, we report in Table 4 six contrasts using the same model with the original and adjusted p values (Benjamini and Hochberg, 1995). These contrasts include three condition-specific tests of the null hypothesis of no TL change (i.e., each condition vs. 0) as well as all pairwise comparisons between conditions. Although three of these contrasts are redundant with Table 3, the overall pattern that emerges in Table 4 reveals that TL decreased significantly in the Control and MM conditions, but not in the LKM condition. Also, evident here is that change in TL in the MM group was not significantly different from either the Control group or LKM group. Taken together, this pattern of results suggests that although telomeres shortened overall for everyone, practicing LKM appears to have buffered that decrease, specifically compared to the Control group.

3.3. Sensitivity analyses

An ancillary sensitivity analysis showed that the effect of LKM remained after demographic covariates were removed from the full model (see Table S3 in the OSM). In addition, although baseline positive emotions differed significantly between the LKM and control conditions, baseline positive emotions had no significant effects on changes in TL, and controlling for them did not alter the pattern of significant effects (see Table S4 in the OSM).

3.4. Exploration of plausible mechanisms

Neither changes in weekly PE nor changes in weekly NE mediated the effects of experimental conditions on changes in TL (see section 3E in the OSM). Additionally, despite being different across the two meditation conditions, neither meditation frequency nor practice duration mediated the effects of experimental conditions on changes in TL (see Tables S5 and S6 in the OSM).

4. Discussion

The current study is the first randomized controlled trial to examine the differential effects of mindfulness meditation (MM) and loving-kindness meditation (LKM) on cellular aging in the context of daily life. Telomeres tended to shorten across all experimental conditions, significantly so in the mindfulness meditation group and the waitlist control group. However, the daily practice of loving-kindness meditation appeared to buffer against that attrition, with participants in the LKM group, on average, showing no significant telomere shortening over time and significantly less telomere shortening compared to those in the Control group. Whereas participants in the mindfulness group, on average, showed significant telomere shortening over time, those changes were intermediate between the LKM and waitlist control groups and not significantly different from either group.

The difference in telomere length between the Control and LKM groups was .048 T/S ratio after demographic covariates were considered. Based on comparison of T/S ratios and telomere length measured by Southern blot in a series of quality control samples from the same lab (Farzaneh-Far et al., 2010), we estimated this difference of .048 T/S ratio to be 115 basepairs. This TL decrease over the 12-week period appears to be large compared to studies of TL change with much longer time periods (Müezzinler et al., 2013). It is possible that this reflects short term dynamic change, or potential systematic differences in the collection and/or assay of baseline and follow-up samples. The fact that DNA extraction and assay were done as one batch (all samples from Time 1 and Time 2) argues against the latter concern, although we cannot completely rule out other potential unaccounted for systematic differences. Although it is unknown whether this effect remains longer than 3 weeks post-intervention, the current study demonstrated proof of concept for the malleability of TL changes, and that certain forms of meditation, in this case loving-kindness meditation, may buffer against telomere erosion.

The buffering effect of loving-kindness meditation on TL is consistent with previous studies that employed LKM in conjunction with other forms of meditation in their interventions (Carlson et al., 2015; Conklin et al., 2018). Similar to the current study, Carlson et al. (2015) found that a 6-week MSBR program (15–45 minutes of formal practice per day) may buffer the typical shortening of TL. Moreover, Conklin et al. (2018) found *increased* TL following an intensive meditation retreat (˜10 h of formal practice per day). Compared to less intensive and somewhat longer interventions such as in the current study and Carlson et al. (2015), intensive meditation retreats may exert a stronger replenishing effect on TL due to a variety of factors, including daily duration of meditation practice (˜10 h per day), the utilization of an experienced meditator sample, the combination of different meditation types, diet changes, and the associated reclusive and relaxing lifestyle. Although the effect of meditation is less drastic in the current study and non-intensive interventions in general, the realistic context of novices initiating a meditation practice in everyday life renders the present results more generalizable to the larger population.

Despite many methodological strengths, including a longitudinal, randomized controlled design, the collection of intensive emotion data, the distinction of two meditation practices, and a larger sample size than past published studies on meditation and telomere biology, the current study also has limitations. The study protocol was not preregistered, for example, and TL was a secondary outcome tested with non-directional hypotheses. In addition, LKM and MM are traditionally taught together as complementary approaches: focusing on and generating warm-hearted feelings toward a selected social target may rely on skills such as focused attention and open monitoring (especially of bodily state) trained via MM, whereas the compassionate, loving feelings built during LKM may aid a practitioner's acceptance of experiences during MM practice. In separating these two contemplative practices, the efficacy of both practices may have inadvertently been reduced. Despite this potential trade-off, practitioners of LKM appeared to be buffered from TL shortening. Theoretically, the two practices differ in mechanisms, with MM centering on attentional shifts to increase clarity (Shapiro et al., 2006) and LKM centering on emotional shifts to increase warmth and kindness. However, recent research (that incorporated data from the current study) has shown that both MM and LKM produced similar benefits for daily positive emotions (Fredrickson et al., 2017), and the present analyses found no evidence that changes in emotions (positive or negative) accounted for (statistically mediated) the effect of LKM on TL. Additionally, despite random assignment, our study groups unexpectedly emerged as unbalanced with respect to baseline positive emotions, specifically between LKM and waitlist control groups. However, baseline positive emotions also neither predicted changes in TL or, when controlled for, altered the effects of experimental conditions on changes in TL. The same held for the unexpected differences between the two meditation groups in practice time. These null findings suggest that mechanisms other than changes in daily emotions and practice time need to be investigated to better understand the underlying mechanisms that account for the effect of different types of meditation on TL changes.

Alternatively, it remains possible that differential emotions may indeed account for the effect of meditation condition on TL changes, whereas the end-of-day self-report assessment used in this study may have been insufficiently sensitive to the relevant fluctuations in subtle emotional states. To detect the differences in affective outcomes of the two types of meditation, research may need longer and more frequent meditation practice or to measure affect during or immediately after the meditation practice and through means other than self-report. Improved measurement accuracy would enable a more robust test of the hypothesized cognitive and affective mechanisms underlying group differences in telomere biology (Epel et al., 2009)

Participants were all midlife adults interested in or open to learning a meditation, which can limit the generalizability of the results to populations of other age groups and varying levels of interest in meditation. In addition, we did not conduct an intention-to-treat analysis due to the small number of participants ($n = 3$) who did not attend their assigned workshops. Similarly, MM and LKM were each taught by just one workshop instructor. Although the two instructors received similar evaluations from practitioners, we cannot rule out the possibility that the results were due to the unique pedagogical approaches of each teacher. Although no participants reported adverse effects arising from their meditation practice, we did not specifically probe for such responses. Finally, in this study, MM and LKM were taught in group-based, face-to-face workshop sessions that progressed over 6 weeks. The results therefore may not be generalizable to other instruction modalities (e.g., online, telephone, self-paced).

In addition, the results on TL may be confounded by immune cell redistribution. Specifically, because TL varies by cell type, it is possible that immune cell distributions may have changed between assessments during the study. We measured TL in PBMCs, which comprise many different cell types, including monocytes and lymphocytes (T-cells—-such as CD8 and CD4 cells, B-cells, and natural killer cells). Lymphocytes may temporarily redistribute in response to acute stress (Dhabhar, 2011), potentially leading to pseudo changes, whereby average TL increases due to an increase in cell types that have longer telomeres (Epel, 2012). It is also possible that the intervention itself changes cell distribution. Changes in cell types can result in shifts in telomere length in many other ways, and the field cannot yet assess TL changes for individual cells from archived samples, as in the case of this study. Therefore, one should interpret the differences in TL changes here with caution, treating them as evidence for "apparent" rather than true alterations in TL. Future studies, however, can incorporate a period of meditation or relaxation for all conditions before drawing blood to minimize the influence of acute stress response on cell redistribution. To further disentangle this alternative explanation, future research can use flow cytometry to assess cell distributions, measure TL in distinct immune cell types, and obtain multiple telomere-related measures such as telomerase activity and telomere-related gene expression to acquire convergent evidence for the actual improvements in telomeric functioning.

Declarations of interest

None.

Role of funding

This research was funded by National Institutes of Health (NIH) grant R01NR012899, supported by the NIH Common Fund, which is managed by the NIH Office of the Director/Office of Strategic Coordination. Khoa D. Le Nguyen was supported by the Royster Society Fellowship from the University of North Carolina at Chapel Hill. These funding agencies played no role in study design, data collection, data analysis, decision to publish, or preparation of the manuscript.

CRediT authorship contribution statement

Khoa D. Le Nguyen: Data curation, Formal analysis, Visualization, Writing - original draft, Writing - review & editing. **Jue Lin:** Formal analysis, Resources, Writing - review & editing. **Sara B. Algoe:** Conceptualization, Methodology, Writing - review & editing. **Mary M. Brantley:** Resources. **Sumi L. Kim:** Resources. **Jeffrey Brantley:** Resources. **Sharon Salzberg:** Resources. **Barbara L. Fredrickson:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing - review & editing.

Acknowledgement

We thank the laboratory of Dr. Elizabeth Blackburn for biological assay and current and former member of the UNC PEP Lab, including Aaron Bolton, Kelly Tan, Emily Stoke, Michael Prinzing, Jieni Zhou, Bailey Mcinnes, and Minnatulah Banawan for their contributions to study implementation and manuscript preparation. Special thanks go to Ann Firestine for superb research management. Finally, we deeply appreciate our study participants and meditation teachers who devoted time and energy across months to be involved in this research.

Online Supplemental Material

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.psyneuen.2019.05.020.

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