



SHORT COMMUNICATION

A meta-analytic review of the effects of mindfulness meditation on telomerase activity



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Summary The enzyme telomerase, through its influence on telomere length, is associated with health and mortality. Four pioneering randomized control trials, including a total of 190 participants, provided information on the effect of mindfulness meditation on telomerase. A meta-analytic effect size of $d = 0.46$ indicated that mindfulness meditation leads to increased telomerase activity in peripheral blood mononuclear cells. These results suggest the need for further large-scale trials investigating optimal implementation of mindfulness meditation to facilitate telomerase functioning.

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Shortened telomeres, and especially shortened immune cell telomeres, are associated with ill health and mortality (Epel et al., 2009; Willeit et al., 2011; Lin et al., 2012). Telomerase enzyme activity influences telomere length by facilitating the addition of DNA sequences onto telomeres during cell division (Blackburn, 2010). The potential of telomerase to influence telomere length has resulted in initial investigations of possible psychological, dietary, and exercise interventions that may influence telomerase activity and slow telomere shortening or even lengthen telomeres to promote health (Lin et al., 2012; Puterman and Epel, 2012).

In general, higher telomerase activity is associated with markers of better immune functioning, such as greater leukocyte telomere length, though this relationship is multifaceted, as illustrated by the findings of Wolkowitz et al.

(2011). Wolkowitz and colleagues found that among individuals with major depressive disorder, who tend to have shortened leukocyte telomeres, telomerase activity was higher than among control individuals; this heightened activity may have been due to compensatory telomerase activity to maintain telomere length during cellular stress, an interpretation bolstered by the finding in the same study that a relatively greater increase in telomerase activity during treatment for depression was associated with better response to antidepressant medication.

Several promising psychological interventions intended to facilitate telomere health have focused on mindfulness meditation. Mindfulness is a flexible state of consciousness that consists of non-evaluative awareness. Higher levels of mindfulness are associated with indices of better physical and mental health, including less experience of stress (Hölzel et al., 2011). Mindfulness meditation consists of practice in interactive processes of attention regulation, body awareness, emotion regulation, and changes in views of the self and others.

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Substantial evidence suggests that consistent practice of mindfulness increases mindfulness, reduces anxiety, depression, and stress (Grossman et al., 2004; Hofmann et al., 2010; Hölzel et al., 2011), and results in immune-function changes, such as increases in antibody titers to an influenza vaccine among participants in a mindfulness meditation intervention condition compared with those in a wait-list control group (Davidson et al., 2013) and increases in monocytes over time among mindfulness meditators (Carlson et al., 2007). It is noteworthy that shorter telomere length is associated with conditions such as psychiatric disorders, experience of stress, and poorer immune functioning (Lin et al., 2012; Puterman and Epel, 2012).

Here we review the initial investigations of the effect of mindfulness-meditation interventions on telomerase, with emphasis on interventions using randomized controlled trial designs. A ground-breaking non-randomized study investigating the effect of a program incorporating both mindfulness meditation and dietary and exercise lifestyle modifications for men with low-risk prostate cancer found that after three months the 24 participants for whom it was possible to assess pre and post telomerase activity showed a significant increase in telomerase. A recent five-year follow-up of 10 of the original participants showed that their telomere length had increased from baseline even though their telomerase activity had decreased somewhat compared to the baseline measurement (Ornish et al., 2013). A matched group of men, also with low-risk prostate cancer, showed a decrease in both telomere length and telomerase activity over the five-year period (Ornish et al., 2013). Another recent non-randomized trial compared individuals with extensive experience in loving-kindness meditation, an outward-focused mindful compassionate practice, to a matched control group and found a trend toward significance in greater telomere length for meditation practitioners compared to the matched control participants, with the trend reaching significance among women (Hoge et al., 2013).

Our review identified four randomized control trial studies investigating the impact of forms of mindfulness meditation on telomerase activity, but no randomized control trials investigating mindfulness training on actual telomere

length. We used meta-analytic procedures to generate an initial estimate of the effect of mindfulness mediation on telomerase.

1. Methods

We searched the databases Medline, PsychINFO, and Google Scholar for the terms telomere or telomerase and mindfulness or meditation, completing the search in September 2013. We also wrote to authors of intervention studies and authors of review articles focusing on the effect of lifestyle on telomerase to ask if they were aware of randomized control studies investigating the effect of mindfulness or meditation on telomerase. These searches resulted in records of 175 peer reviewed articles, which we screened. This screening identified four studies that met the inclusion criterion of employing a randomized control trial to test the effects of mindfulness meditation on telomerase activity. Each of these studies focused on telomerase activity in peripheral blood mononuclear cells, which are important in immune functioning.

We converted results to Cohen's *d*. The Comprehensive Meta-Analysis Program (Borenstein et al., 2005) calculated the overall weighted effect size, using a random effects model. The *Q* statistic assessed effect-size homogeneity across studies. The trim and fill method and fail-safe *N* assessed the impact of possibly missing studies.

2. Results

See Table 1 for information about each study. The combined weighted effect size (ES) for the impact of mindfulness meditation on telomerase was significant, $d_{adj} = 0.46$ ($p = .001$, 95% CI 0.18, 0.78) in a homogeneous set of studies ($Q [df = 3] = 0.95$, $p = .81$). Trim-and-fill indicated a publication bias, and correcting for one missing study outcome led to an overall ES of 0.41 (95% CI 0.17, 0.66). Fail-safe analysis showed that seven studies with a null ES would bring the combined ES down to a non-significant level. Because of the small number of effect sizes in the

Table 1 Effect of mindfulness meditation on telomerase.

Authors	<i>N</i>	Control Condition	Hours	Measure	Blind	Population	Loss	<i>d</i>	95% CI Lower	95% CI Upper
Daubenmier et al. (2012) ^a	47	Wait list	30	TRAP	Yes	Overweight/obese	CF	0.22	-0.35	.79
Ho et al. (2012) ^b	63	Wait list	60	Telo	Yes	Chronic fatigue	M	0.54	0.05	1.04
Jacobs et al. (2011) ^c	41	Wait list	567	TRAP	No	Meditators	Co	0.54	-0.09	1.26
Lavretsky et al. (2013) ^d	39	Relaxation	11	TRAP	No	Dementia carers	Co	0.53	-0.12	1.18

Hours = number of hours of meditation per person assigned during intervention, with or without the presence of a trainer.

Measure (of telomerase activity): TRAP = TRAPeze with ImageQuant 5.2; Telo = TeloTAGGG telomerase PCR ELISA with peroxidase-conjugated anti-digoxigenin antibody, tetramethyl benzidine, and colorimetric measures.

Blind = whether article indicated that assay technicians were blind to condition.

Loss (method of dealing with loss of participants): CF = carry forward intention-to-treat; M = "mean imputation"; Co = completer analysis.

Note: the Jacobs et al. (2011) study collected only post-intervention telomerase values; the other studies collected pre and post values. The Jacobs study excluded one outlier from analyses.

^a Mindfulness-Based Stress Reduction and Mindful Eating.

^b Mindfulness Meditation and Qigong Exercise.

^c Mindfulness and Loving Kindness Meditation.

^d Yogic Meditation.

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