Title
Meditation, Stress Processes, and Telomere Biology

Authors
Conklin, Quinn
Crosswell, Alexandra
Saron, Clifford
et al.

Publication Date
2018-11-02

DOI
10.31231/osf.io/p5ndr

Current Opinion in Psychology.

The aim of the issue is to provide a representative view of the current theory and research on mindfulness. We would be very keen to cover developments in research on the effects of **mindfulness meditation on telomere biology**, and we're wondering whether you might be willing to write on this subject based on your seminal work in this field.

- short review, in which you are free to express your own opinion on the subject.
- no more than **2000 words** of text (not including tables, figures, or references).
- cite up to 50 of the most interesting and relevant articles published recently in the field.
- due date for the submission is September 1, 2018.

Meditation, Stress Processes, and Telomere Biology

Quinn A. Conklin[1], Clifford D. Saron[1], Alexandra D. Crosswell[2], and Elissa S. Epel[2]

1) University of California, Davis

2) University of California, San Francisco

Corresponding authors:

Elissa S. Epel (Elissa.Epel@ucsf.edu) and Quinn A. Conklin (qconklin@ucdavis.edu)

Abstract

Both theoretical and empirical work support the notion that meditation training can promote healthier aging. At the cellular level, this includes longer telomeres, and adaptive levels of telomerase activity and telomere-related gene expression. A growing body of research suggests that meditation experience is related to better telomere profiles, but the psychological and biological mechanisms underlying these changes remain underspecified and untested, as do the contexts and boundary conditions in which these changes occur. Here we summarize studies investigating the effects of various meditation-based interventions on telomere biology, highlighting gaps that warrant further investigation. We then propose a model describing how meditation training may impact habitual stress processes and acute stress responses, as pathways to improved telomere biology.

Telomeres are DNA-protein complexes that cap and protect eukaryotic chromosomes. Telomeres are dynamic structures, regulated by an intricate system of proteins and other molecular components including telomerase, an enzyme capable of lengthening telomeres. When telomeres become too short, critical cellular events occur, such as cell death or inflammatory output and a state of prolonged senescence. Telomeres have been widely studied over the past decade as they have become easily measured in population-based studies. They reliably predict many diseases of aging [meta-analytic cites for CVD, diabetes, dementia], with evidence suggesting that telomere biology plays a small but causal role in disease processes. Specifically, genetic loading for short telomere length predicts degenerative diseases such as cardiovascular disease, and interestingly, genetic variation for longer telomeres predicting propensity for certain cancers, including glioma [Haycock].

Telomere length (TL) shortens slowly throughout life, though there is some degree of malleability in immune cell telomere length. Telomere length is associated with lifestyle factors [Lin, Epel & Blackburn 2012] and is shortened by long-term psychosocial adversity and stress exposures (early childhood adversity-meta, refugee displacement, caregiving [Damjanovic]). This link between telomere shortening and stress exposure raises the question of whether interventions that alter stress processes might improve telomere maintenance over time. We previously proposed a theoretical model exploring the impact of mindfulness meditation on telomere length (2009). In the decade since this model was posited, a small body of research has emerged that directly addresses the relationship between meditation practice and telomere-related outcomes (telomere length, telomerase activity, or telomere-related gene expression). Yet, very few studies have investigated the actual mechanisms that may link changes in mind states to changes in cellular health. Here we review the empirical work and propose an updated model describing how various meditation practices and training environments might influence habitual and acute stress processes, which in turn may impact telomere biology processes and, if sustained, improve long term telomere stability.

What we know so far:

Meditation-related changes in Telomerase Activity and Telomere Length. There have now been a total of 19 studies examining telomere health in relation to meditation, many of which are best described as pilot studies of varying quality. Two studies cross-sectionally compared experienced meditators to community controls, finding longer telomeres in meditators ([Alda] *n*=20; [Hoge] *n*= 13, in women only). The remaining 17 examined telomere-related outcomes in relation to interventions involving or emphasizing a meditation component (Table 1).

It was initially assumed that telomere length could not change within the weeks or months typical of meditation interventions, so most studies have measured telomerase activity as an indicator of telomere health. Of the ~~elven~~ eleven studies measuring telomerase activity, nine found intervention-related increases in telomerase [Kumar, Lavretsky, Rao, Ornish, Daubenmier, Lengacher, Tolahunase, Epel] or higher telomerase activity in the treatment group post-intervention [Jacobs], while two found no significant change in telomerase activity (cite those two). Need sentence about how many measured telomere length. By contrast, only three studies, which involved~~ing~~ interventions of higher intensity or greater duration than what?, showed increased telomere length [Conklin, Ornish 2013, Tolahunase], while the remaining six of what? found no change [Rima, Wang, Thimmapuram, Carlson, Duraimnai, Lengacher].

Interestingly, three out of the four studies that measured both telomere length and telomerase activity found intervention-related changes in one but not the other [Tolahunase, Lengacher, Ornish 2013, Conklin]. Since telomere length and telomerase activity are uncorrelated in cross sectional studies of healthy humans [Citation, Jue?], it may not be surprising that these two outcomes do not change simultaneously in intervention trials. It is possible that meditation training promotes initial changes in telomerase activity, which increase telomere length over a longer period of time, though the length of time needed to see these effects is unknown. Initial evidence suggests that changes can happen rapidly. For example, in intensive retreat studies of experienced meditators, telomerase increases have been seen in as short as one week [Epel 2016], while telomere length changes have been observed in as little as three weeks [Conklin]. ~~Yet, it~~It is unknown how long these increases persist. Generally speaking, telomere regulation is a dynamic system with complex temporal features that are not yet fully understood. Thus, truly

understanding the impact of meditation training on telomere health will require more frequent sampling and follow-up assessments. Advancing the field will also require studies designed to measure multiple indicators of telomere health using gold standard collection and measurement methods (e.g., drawing blood when one has no symptoms, using certain DNA extraction and storage methods, etc.) from various cell types that do not have shifting distribution of cell subtypes such as buccal cells, in addition to blood.

Moderators (or is it mediators?) of telomere outcomes. Although the predominant theory assumes that meditation training influences telomere biology by reducing psychological stress processes, very few of these studies included measures of stress to test this hypothesis. ~~However, s~~Several studies~~ome~~ did measure psychological factors that are likely to play a contributing role. For example, studies have found associations between increases in telomerase activity and improvements in mental health [Lavretsky] and declines in psychological distress [Ornish 2008; Daubenmier]. In a study of meditation retreat participants, Jacobs et al. [2011] found that improvements in perceived control, greater purpose in life, and decreases in neuroticism appeared to mediate the higher post-retreat telomerase activity levels. In a recent retreat study, we found that baseline levels of neuroticism and agreeableness predicted retreat-related increases in telomere length~~.~~

Interestingly, multiple studies have now found that changes in telomere outcomes in response to both brief [Bhasin] and intensive periods of practice [Epel 2016, Conklin] vary depending on the practitioners' level of prior meditation experience. These findings seem to suggest that experienced practitioners may have a more developed ability to derive benefit from periods of practice. They also underscore the importance of studying various stages of meditation training, as mechanisms and outcomes of interest may differ across the developmental trajectory.

Stress processes and their relation to telomere biology

In psychology, the "stress response" traditionally refers to a range of possible

cognitive, affective, behavioral, and physiological reactions to discrete stressful events or exposures (~~See Stress Typology~~ [Epel, Crosswell 2018]). This multisystem response is often referred to as the 'acute stress response' and includes psychological and physiology anticipatory elevations before the event happens, peak reactivity in response to the event, and recovery following the event. These acute stress responses are influenced by one's current and historical context, and characteristics of the specific stressor stimuli. A core tenet of models linking stress to health is that there are 'maladaptive' forms of this acute stress response that, if sustained, lead to long-term health problems [McEwen, 1998].

Acute stress reactivity refers to the magnitude of the immediate response to a stressor, as measured by changes in affective or physiological measures (cardiovascular, hormonal, immune) from pre-stressor to peak arousal. This peak often occurs during the stressor, though for some systems it may occur after the stressor has subsided, as is the case for cortisol. Greater peak reactivity is related to shorter telomeres in children [Kroenke et al., 2011, Gotlib et al., 2015], but findings in adults are mixed [Savolainen, 2015, Tomiyama 2012, Woody et al. 2017]. In the largest study, Steptoe et al (year) found that higher cortisol reactors had greater telomere attrition three years later. Another important feature of the acute stress response is **acute stress recovery**, or how quickly one returns to basal states after arousal. This phase may be even more important for long-term health outcomes, as prolonged ~~reactivity~~ heightened responses can lead to the increased wear and tear known as **allostatic load** [McEwen 1998]. Indeed, greater rumination following a psychosocial stressor has been linked to greater cortisol reactivity and slower recovery [Zoccola & Dickerson, 2011], which, in turn, are linked to shorter telomeres and lower telomerase activity [Puterman & Epel 2010].

Repeated exposures and perseverative cognitions are two mechanisms that extend the acute stress response ~~in to the territory of disease~~. Repeated exposures can lead to divergent paths for habituators and non-habituators [Peters & McEwen, 2015]. **Habituation** occurs when an individual's acute stress response ~~diminishes~~ increases in efficiency upon repeated exposure. This is thought to be crucial for adapting to challenging environments but can lead to decreased vigilance [Peters & McEwen, 2015]. Alternatively, those who do not habituate may experience anticipatory sensitization, whereby their acute stress response ~~of~~ is exacerbated with repeated exposures. This phenomenon is linked with perseverative cognitions,

such as **anticipatory stress**, or worry leading up to an event. Anticipatory threat appraisals have been highlighted as one key mechanism linking psychological stress and telomere attrition [O'Donovan 2010].

One fundamental principle of the acute stress response is that it is activated by the perception of threat, either to the physical or social self. Yet, the meaning and interpretation of stimuli (cognitive appraisals of the experience) are affected by **habitual mental filters** that vary by person and context. These filters include mental representations of the self (i.e., self-schema) and others (e.g., attachment figures), as well as measurable perceptions of one's environment (e.g. hypervigilance to negative stimuli or threats). They also include personality traits such as pessimism, neuroticism and hostility, which have been linked to prolonged stress reactivity and telomere attrition [Lin, Epel & Blackburn 2012]. Mental filters are shaped by life experience and influence how one sees and interprets the world. For example, having a history of childhood trauma leads one to anticipate negative events, and to have more maladaptive stress responses to acute stressors (e.g. greater 'threat' versus 'challenge' autonomic reactivity profiles; McLaughlin).

Individuals also have basal physiological states underlying their reactivity profiles. These **allostatic states** (multisystem physiological 'basal' states) refer to the baseline arousal states of the autonomic nervous system, neuroendocrine, and metabolic hormones, as well as the level of systemic inflammation from the immune system and tissues. These basal states are often elevated or dysregulated in individual experiencing chronic stress, putting them at a disadvantage when faced with acute stressors (since their system is already working at high capacity). These Individuals are also more likely to develop habitual processes that lead to maladaptive acute stress reactivity profiles [O'Donovan, 2012, 2013]. High basal levels of cortisol, inflammation, and oxidative stress ~~relate~~ are associated with ~~to~~ shorter telomere length [Epel & Prather, 2018].

Various forms of meditation have been shown to beneficially affect aspects psychology or physiology at every level of the acute stress response, (i.e., anticipation [Turan et al 2015], reactivity [Keng et al 2011, Creswell, Lindsay; Rosenkranz 2016], recovery [Crosswell 2017] and habituation [Goleman & Schwartz, 1976]), as well as basal levels of autonomic nervous system, metabolic hormones, chronic inflammation, and cortisol [Cole, Bower, ~~Bostock 2018,~~ though see ~~O'Leary, O'Neill, & Dockray 2016 and Matousek, Dobkin and Pruessner 2010~~].

Yet, these findings are often ~~mixed~~not consistent (e.g. . O'Leary, O'Neill, & Dockray 2016 and Matousek, Dobkin and Pruessner 2010). Given the diversity of meditation practices, unpacking ~~it may be fruitful to investigate~~ how different aspects meditation influence basal stress processes and components of the acute stress response may be important to understanding these mixed findings. ~~,~~ These linkages are ~~as shown in~~shown in ~~-~~**Figure 1** and discussed below.

Effects of meditation training on stress processes

Meditation practices can be conceived of as a variety of techniques developed to regulate a range of psychological processes, particularly those having to do with perceptions of reality and the self [Dahl, Lutz, Davidson, 2015]. As such, we expect various meditation techniques to target the mental filters that shape acute stress appraisals and responses, as well as the perseverative cognitions that extend stress reactivity in to disease states.

One contemporary classification system organizes meditation techniques in to 'families' of practice based on the cognitive mechanisms they are believed to target [Dahl, Lutz, and Davidson 2015]. The attentional family describes a class of practices used to train the self-regulation of **attention**, so that it can be applied at will. Often, interoceptive and sensory stimuli (e.g., sensations of the breath) are used as the object of attentional training. This process of orienting attention to bodily sensations can disrupt self-referential processing [Barsalou] and bring clarity and granularity to one's emotional experiences, likely contributing to improved emotion regulation. Together these processes may enable greater control over one's emotional reactions to acute stimuli and may also bring awareness to aspects of unconscious affect and embodied emotions that contribute to prolonged~~chronic~~ stress arousal. Training attention to one's~~'~~ present-moment experience has also been shown to reduce elaborative processing of stimuli [Slagter et al. 2007] and to inhibit habitual responding [Zanesco, 2018]. These changes may lead to a more efficient and flexible use of attentional resources that promotes less catastrophic and more accurate appraisals of experience, as well as more adaptive responses.

Other cognitive processes thought to improve with attention training are meta-awareness and dereification (also conceptualized as orthogonal dimensions of

mindfulness [Lutz]). **Meta-awareness** describes the ability to observe and monitor one's internal processes of thinking and feeling [Dahl 2015]. **Dereification** occurs when thoughts, feelings and perceptions, are observed as temporary mental phenomena rather than accurate reflections of reality [Lutz 2015, Dahl 2015]. Together, these faculties may help to disrupt negative self-concepts and perseverative cognitions, and to promote the reappraisal of potentially threatening stimuli.

Furthermore, d~~D~~ereification is also a more explicit target of the deconstructive family, a set of self-inquiry practices used to foster insight into the processes of perception, emotion, and cognition. The goal of these practices is often to deconstruct maladaptive internal models of self, others, and the world [Dahl 2015].

Finally, the constructive family of practices are intended to cultivate cognitive and affective patterns that foster well-being.

perspective taking and reappraisal

An ~~kind~~ attitude of **self-compassion**, inherent in most mindfulness interventions, appears to have potent effects in attenuating stress processes such as XXX (citations, stress cognitions? Cortisol?). Self-compassion and decreases in experiential avoidance can break the cycle of anticipatory anxiety, maladaptive peak reactivity, and prolonged recovery~~, to be a more positive stress profile characterized by greater recovery~~. It may also lead to greater habituation upon next exposure.

The boundaries between these families of practices are not clear cut, and some practices may target multiple cognitive mechanisms involved with both basal states of perception and acute stress responding. Given the multiple mechanisms through which meditation training may affect habitual and acute stress processes, and the interactions between these processes, it will be difficult to map specific mechanisms of meditation to stress processes to telomere biology. This diversity and nonlinearity of mechanisms may help explain why different types of meditation interventions, as well as other mind-body interventions such as yoga and qigong, have been found to have positive effects on telomere biology

Meditation training contexts: safety and support

While traditional stress-health models link stress arousal to worse health through repeated activation of the acute stress systems (e.g. McEwen, 1998), the Generalized Unsafety Theory of Stress (GUTS [Brosschot, Verkuil, Thayer]) posits that it is a consistent lack of perceived safety, rather than exposure to frequent stressors, that activates and prolonged stress-related physiology ~~, ultimately causing biological damage~~ [Brosschot, Verkuil, Thayer]. This framework assumes that the stress-response is active by default and is only inhibited by learned safety cues. To suppress the default response, one needs to learn or re-learn safety cues. Thus, making fundamental shifts in perceived and unconscious stress and allostatic strain may require immersion in safety cues, until they become believed and habitual. Meditation training may have unique effects by increasing perceptions of safety—safety within the context of the self, in social exchanges, and by providing physically safe environments.

Meditation teachers ideally model a supportive and nonjudgmental figure—a role model who can be trusted. This relationship may target social stress by creating feelings of safety and activating schemas of interconnectedness. Similarly, interacting with a community of individuals who share and a support a common goal—the *sangha,* as they might be referred to in Buddhist traditions—may also contribute to a more benevolent and compassionate view of others....

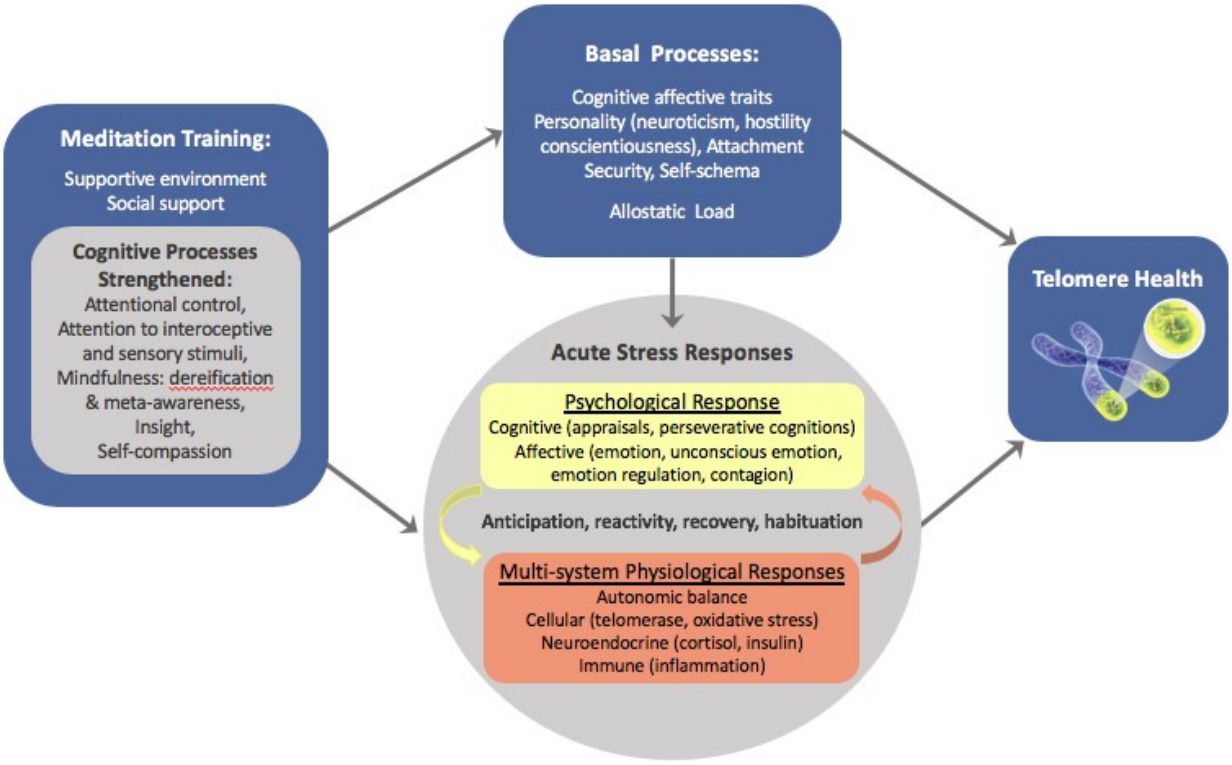
Meditation training often occurs in the context of a highly supportive environment. Residential retreats are the most extreme and unique example, where one is sequestered from real world demands and threats and taken care of in terms of basic needs. This may be a particularly beneficial training format for individuals with greater unconscious generalized unsafety, with risk factors such as early trauma, insecure attachment, and high neuroticism—the latter indicated by our recent retreat study [Conklin].

Conclusion

Recent research gives reason to believe that meditation training can improve

telomere maintenance and health. Yet, this literature is still too sparse to fully understand how and under what conditions these effects are achieved, or how long they might last. We proposed here that changes in basal psychological and physiological functioning, and changes in acute stress responses, are potential and thus far untested mechanistic pathways from meditation training to telomere biology alterations. As measuring telomere processes and length becomes easier, the next generation of meditation intervention studies will be able to determine more definitively if and how telomere biology is impacted. ~~in a meaningful way.~~ This will involve ~~testing the potential mechanism described here, as well as~~ a more systematic investigation of the different dimensions of various meditation interventions, including styles of practice, duration, intensity~~,~~, and training environments ~~and social support~~. There is still much to learn ~~relationships outlined in Figure 1 are likely complex and multidetermined, yet there is still much we can learn~~ about the specificity of ~~meditation-stress-biology mechanisms.~~ how meditation influences biological functioning.

Figure 1: Theoretical model of how meditation training may impact telomere biology via stress processes



Only some of the mechanistic pathways proposed have been tested. For example, there is evidence for the link between stress appraisals and telomere length [O'Donovan 2010], and for the ability of meditation training to enhance positive reappraisals [cite], yet no study has simultaneously assessed the full mediational pathway—of whether an intervention changes stress appraisals and subsequently telomere biology. Similarly, there is evidence that meditation training reduces rumination [cite], but no studies have specifically studied association between telomere length and rumination in general, or in relation to meditation training.

References

Papers to review in Table

1. Alda, M., Puebla-Guedea, M., Rodero, B., Demarzo, M., Montero-Marin, J., Roca, M., García-Campayo, J., 2016. Zen meditation, length of telomeres, and the role of experiential avoidance and compassion. Mindfulness 7, 651–659. http://doi.org/10.1007/s12671-016-0500-5

   Only study to measure median telomere length and proportion of short telomeres

2. Bhasin, M.K., Dusek, J.A., Chang, B.-H., Joseph, M.G., Denninger, J.W., Fricchione, G.L., Benson, H., Libermann, T.A., 2013. Relaxation response induces temporal transcriptome changes in energy metabolism, insulin secretion and inflammatory pathways. PLoS ONE 8, e62817. http://doi.org/10.1371/journal.pone.0062817 (could potentially leave this one out of table if we don't include gene-only citations)
3. Carlson, L.E., Beattie, T.L., Giese-Davis, J., Faris, P., Tamagawa, R., Fick, L.J., Degelman, E.S., Speca, M., 2015. Mindfulness-based cancer recovery and supportive-expressive therapy maintain telomere length relative to controls in distressed breast cancer survivors. Cancer 121, 476–484. http://doi.org/10.1002/cncr.29063
4. Conklin, Q.A., King, B.G., Zanesco, A.P., Lin, J., Hamidi, A.B., Pokorny, J.J., Álvarez-López, M.J., Cosín-Tomáse, M., Huang, C., Kaliman, P., Epel, E.S., Saron, C.D., 2018. Insight meditation and telomere biology: The effects of intensive retreat and the moderating role of personality. Brain. Behav. Immun. https://doi.org/10.1016/j.bbi.2018.03.003

   [First study to measure telomere length, telomerase and telomere related genes in a pre-post design]

5. Daubenmier, J., Lin, J., Blackburn, E., Hecht, F.M., Kristeller, J., Maninger, N., Kuwata, M., Bacchetti, P., Havel, P.J., Epel, E., 2012. Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study. Psychoneuroendocr. 37, 917–928. http://doi.org/10.1016/j.psyneuen.2011.10.008
6. Duraimani, S., Schneider, R.H., Randall, O.S., Nidich, S.I., Xu, S., Ketete, M., Rainforth, M.A., Gaylord-King, C., Salerno, J.W., Fagan, J., 2015. Effects of lifestyle modification on telomerase gene expression in hypertensive patients: A pilot trial of stress reduction and health education programs in African Americans. PLoS ONE 10, e0142689. http://doi.org/10.1371/journal.pone.0142689 (could potentially leave this one

out of table if we don't include gene-only citations)

7. Epel, E.S., Puterman, E., Lin, J., Blackburn, E.H., Lum, P.Y., Beckmann, N.D., Zhu, J., Lee, E., Gilbert, A., Rissman, R.A., Tanzi, R.E., Schadt, E.E., 2016. Meditation and vacation effects have an impact on disease-associated molecular phenotypes. Transl. Psychiatry. 6, e880. http://doi.org/10.1038/tp.2016.164

   [Best controlled study to date]

8. Hoge, E.A., Chen, M.M., Orr, E., Metcalf, C.A., Fischer, L.E., Pollack, M.H., DeVivo, I., Simon, N.M., 2013. Loving-kindness meditation practice associated with longer telomeres in women. Brain Behav. Immun. 32, 159–163. http://doi.org/10.1016/j.bbi.2013.04.005
9. Jacobs, T.L., Epel, E.S., Lin, J., Blackburn, E.H., Wolkowitz, O.M., Bridwell, D.A., Zanesco, A.P., Aichele, S.R., Sahdra, B.K., MacLean, K.A., King, B.G., Shaver, P.R., Rosenberg, E.L., Ferrer, E., Wallace, B.A., Saron, C.D., 2011. Intensive meditation training, immune cell telomerase activity, and psychological mediators. Psychoneuroendocr. 36, 664–681.
10. Lavretsky, H., Epel, E.S., Siddarth, P., Nazarian, N., Cyr, N.S., Khalsa, D.S., Lin, J., Blackburn, E., Irwin, M.R., 2013. A pilot study of yogic meditation for family dementia caregivers with depressive symptoms: Effects on mental health, cognition, and telomerase activity. Int. J. Geriatr. Psychiatry 28, 57–65. http://doi.org/10.1002/gps.3790
11. Lengacher, C.A., Reich, R.R., Kip, K.E., Barta, M., Ramesar, S., Paterson, C.L., Moscoso, M.S., Carranza, I., Budhrani, P.H., Kim, S.J., Park, H.Y., Jacobsen, P.B., Schell, M.J., Jim, H.S.L., Post-White, J., Farias, J.R., Park, J.Y., 2014. Influence of mindfulness-based stress reduction (MBSR) on telomerase activity in women with breast cancer (BC). Biol. Res. Nurs. 16, 438–447. http://doi.org/10.1177/1099800413519495
12. Ornish, D., Lin, J., Chan, J.M., Epel, E., Kemp, C., Weidner, G., Marlin, R., Frenda, S.J., Magbanua, M.J.M., Daubenmier, J., Estay, I., Hills, N.K., Chainani-Wu, N., Carroll, P.R., Blackburn, E.H., 2013. Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study. Lancet Oncol. 14, 1112–1120. http://doi.org/10.1016/S1470-2045(13)70366-8
13. Ornish, D., Lin, J., Daubenmier, J., Weidner, G., Epel, E., Kemp, C., Magbanua, M.J.M., Marlin, R., Yglecias, L., Carroll, P.R., Blackburn, E.H., 2008. Increased telomerase activity and comprehensive lifestyle changes: A pilot study. Lancet Oncol. 9, 1048–1057. http://doi.org/10.1016/S1470-2045(08)70234-1
14. Rao, K.S., Chakraharti, S.K., Dongare, V.S., Chetana, K., Ramirez, C.M., Koka, P.S., Deb, K.D., 2015. Antiaging effects of an intensive mind and body therapeutic program through enhancement of telomerase activity and adult stem cell counts. J. Stem Cells 10, 107–125.

[Need to include an annotation here discussing the quality of the study]

15. Tolahunase, M., Sagar, R., Dada, R., 2017. Impact of yoga and meditation on cellular aging in apparently healthy individuals: A prospective, open-label single-arm exploratory study. Oxid. Med. Cell. Longev. 2017, 1–9. http://doi.org/10.1155/2017/7928981
16. Wang, X., Sundquist, K., Hedelius, A., Palmér, K., Memon, A.A., Sundquist, J., 2017. Leukocyte telomere length and depression, anxiety and stress and adjustment disorders in primary health care patients. BMC Psychiatry 17, 148. https://doi.org/10.1186/s12888-017-1308-0
17. Thimmapuram, J., Pargament, R., Sibliss, K., Grim, R., Risques, R., Toorens, E., 2017. Effect of heartfulness meditation on burnout, emotional wellness, and telomere length in health care professionals. J. Community Hosp. Intern. Med. Perspect. 7, 21–27. https://doi.org/10.1080/20009666.2016.1270806
18. Rima, D., Shiv, B.K., Bhavna, C., Shilpa, B., Saima, K., 2016. Oxidative Stress Induced Damage to Paternal Genome and Impact of Meditation and Yoga - Can it Reduce Incidence of Childhood Cancer? Asian Pac. J. Cancer Prev. 17, 4517–4525.

Other potential Refs

Brosschot, J.F., Verkuil, B., Thayer, J.F., 2018. Generalized unsafety theory of stress: Unsafe environments and conditions, and the default stress response. Int. J. Environ. Res. Public Health 15, 1–27. https://doi.org/10.3390/ijerph15030464

Epel, E.S., Crosswell, A.D., Mayer, S.E., Prather, A.A., Slavich, G.M., Puterman, E., Mendes, W.B., 2018. More than a feeling: A unified view of stress measurement for population science. Front. Neuroendocrinol. 49, 146–169. https://doi.org/10.1016/j.yfrne.2018.03.001

O'Leary, K., O'Neill, S., & Dockray, S. (2016). A systematic review of the effects of mindfulness interventions on cortisol. *Journal of Health Psychology*, *21*(9), 2108–2121. http://doi.org/10.1177/1359105315569095

1. Blackburn, E.H., 2005. Telomeres and telomerase: Their mechanisms of action and the effects of altering their functions. FEBS Lett. 579, 859–862. http://doi.org/10.1016/j.febslet.2004.11.036
2. Blackburn, E.H., Epel, E.S., Lin, J., 2015. Human telomere biology: A contributory and interactive factor in aging, disease risks, and protection. Science 350, 1193–1198. http://doi.org/10.1126/science.aab3389

3. Dahl, C.J., Lutz, A., Davidson, R.J., 2015. Reconstructing and deconstructing the self: Cognitive mechanisms in meditation practice. Trends Cogn. Sci. 19, 515–523. http://doi.org/10.1016/j.tics.2015.07.001

4. Dhabhar, F.S., Malarkey, W.B., Neri, E., McEwen, B.S., 2012. Stress-induced redistribution of immune cells—From barracks to boulevards to battlefields: A tale of three hormones. Psychoneuroendocr. 37, 1345–1368. http://doi.org/10.1016/j.psyneuen.2012.05.008

5. Epel, E., 2012. How "reversible" is telomeric aging? Cancer Prev. Res. 5, 1163–1168. http://doi.org/10.1158/1940-6207.CAPR-12-0370

6. Epel, E.S., 2009. Telomeres in a life-span perspective: A new "psychobiomarker?" Curr. Dir. Psychol. Sci. 18, 6–10. http://doi.org/10.1111/j.1467-8721.2009.01596.

7. Epel, E.S., Blackburn, E.H., Lin, J., Dhabhar, F.S., Adler, N.E., Morrow, J.D., Cawthon, R.M., 2004. Accelerated telomere shortening in response to life stress. Proc. Natl. Acad. Sci. 101, 17312–17315. http://doi.org/10.1073/pnas.0407162101

8. Epel, E.S., Lin, J., Dhabhar, F.S., Wolkowitz, O.M., Puterman, E., Karan, L., Blackburn, E.H., 2010. Dynamics of telomerase activity in response to acute psychological stress. Brain Behav. Immun. 24, 531–539. http://doi.org/10.1016/j.bbi.2009.11.018

9. Goyal, M., Singh, S., Sibinga, E.M.S., Gould, N.F., Rowland-Seymour, A., Sharma, R., Berger, Z., Sleicher, D., Maron, D.D., Shihab, H.M., Ranasinghe, P.D., Linn, S., Saha, S., Bass, E.B., Haythornthwaite, J.A., 2014. Meditation programs for psychological stress and well-being: A systematic review and meta-analysis. JAMA Intern. Med. 174, 357–368. http://doi.org/10.1001/jamainternmed.2013.13018

10. Lin, J., Epel, E., Blackburn, E., 2012. Telomeres and lifestyle factors: roles in cellular aging. Mutat. Res. 730, 85–9. https://doi.org/10.1016/j.mrfmmm.2011.08.003

11. Lutz, A., Jha, A.P., Dunne, J.D., Saron, C.D., 2015. Investigating the phenomenological matrix of mindfulness-related practices from a neurocognitive perspective. Am. Psychol. 70, 632–658. http://doi.org/10.1037/a0039585

12. Pace, T.W.W., Negi, L.T., Adame, D.D., Cole, S.P., Sivilli, T.I., Brown, T.D., Issa, M.J., Raison, C.L., 2009. Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. Psychoneuroendocr. 34, 87–98. http://doi.org/10.1016/j.psyneuen.2008.08.011

13. Puterman, E., Epel, E., 2012. An intricate dance: Life experience, multisystem resiliency, and rate of telomere decline throughout the lifespan. Soc. Personal. Psychol. Compass 6, 807–825. http://doi.org/10.1111/j.1751-9004.2012.00465.

14. Rosenkranz, M.A., Davidson, R.J., MacCoon, D.G., Sheridan, J.F., Kalin, N.H., Lutz, A., 2013. A comparison of mindfulness-based stress reduction and an active control in modulation of neurogenic inflammation. Brain Behav. Immun. 27, 174–184. http://doi.org/10.1016/j.bbi.2012.10.013

15. Shalev, I., Entringer, S., Wadhwa, P.D., Wolkowitz, O.M., Puterman, E., Lin, J., Epel, E.S., 2013. Stress and telomere biology: A lifespan perspective. Psychoneuroendocr. 38, 1835–1842. http://doi.org/10.1016/j.psyneuen.2013.03.010

16. Tomiyama, A.J., O'Donovan, A., Lin, J., Puterman, E., Lazaro, A., Chan, J., Dhabhar, F.S., Wolkowitz, O., Kirschbaum, C., Blackburn, E., Epel, E., 2012.

Does cellular aging relate to patterns of allostasis?: An examination of basal and stress reactive HPA axis activity and telomere length. Physiol. Behav. 106, 40–45. http://doi.org/10.1016/j.physbeh.2011.11.016

17. Turan, B., Foltz, C., Cavanagh, J.F., Wallace, B.A., Cullen, M., Rosenberg, E.L., Jennings, P.A., Ekman, P., Kemeny, M.E., 2015. Anticipatory sensitization to repeated stressors: The role of initial cortisol reactivity and meditation/emotion skills training. Psychoneuroendocr. 52, 229–238. http://doi.org/10.1016/j.psyneuen.2014.11.014

18. Zalli, A., Carvalho, L.A., Lin, J., Hamer, M., Erusalimsky, J.D., Blackburn, E.H., Steptoe, A., 2014. Shorter telomeres with high telomerase activity are associated with raised allostatic load and impoverished psychosocial resources. Proc. Natl. Acad. Sci. 111, 4519–4524. http://doi.org/10.1073/pnas.1322145111

19. Zanesco AP, King BG, MacLean KA, Saron CD: **Cognitive aging and long-term maintenance of attentional improvements following meditation training**. *J Cogn Enhanc* 2018, **NA**:NA.

20. Schutte, N.S., Palanisamy, S.K.A., McFarlane, J.R., 2016. The relationship between positive psychological characteristics and longer telomeres. Psychol. Health 31, 1466–1480. http://doi.org/10.1080/08870446.2016.1226308

Potential Refs for Methodological Issues

21. Susser, E., Verhulst, S., Kark, J.D., Factor-Litvak, P.R., Keyes, K., Magnus, P., Aviv, A., 2016. Non-dynamic association of depressive and anxiety disorders with leukocyte telomere length? Am. J. Psychiatry 173, 1147. https://doi.org/10.1176/appi.ajp.2016.16060747

22. Verhoeven, J. E., Lin, J., Révész, D., Wolkowitz, O. M., & Penninx, B. W. (2016). Unresolved Issues in Longitudinal Telomere Length Research: Response to Susser et al. *American Journal of Psychiatry*, *173*(11), 1147-1149.

23. Lin, J., Cheon, J., Brown, R., Coccia, M., Puterman, E., Aschbacher, K., Sinclair, E., Epel, E., Blackburn, E.H., 2016. Systematic and cell type-specific telomere length changes in subsets of lymphocytes. J. Immunol. Res. 2016, 1–9. http://doi.org/10.1155/2016/5371050

24. Lin, J., Epel, E., Cheon, J., Kroenke, C., Sinclair, E., Bigos, M., Wolkowitz, O., Mellon, S., Blackburn, E., 2010. Analyses and comparisons of telomerase activity and telomere length in human T and B cells: Insights for epidemiology of telomere maintenance. J. Immunol. Methods 352, 71–80. http://doi.org/10.1016/j.jim.2009.09.012