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Review Article

The effect of meditation on telomerase and stem cell

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ABSTRACT

Meditation has garnered increasing interest due to its potential effects on cellular aging processes, particularly telomere and stem cells. This narrative review aims to synthesize existing research on how meditation affects telomeres and stem cells. Meditation significantly influences telomere through stress reduction, immune system, inflammation, and oxidative stress modulation. Meditation has been shown to reduce stress, improve circadian rhythms, and modulate the hypothalamus-pituitary-adrenal (HPA) axis, thereby decreasing cortisol levels and promoting telomere maintenance. Melatonin, elevated through meditation, further supports telomere health by reducing oxidative stress and inflammation. Meditation also affects the activity of genes associated with inflammation and stress response, contributing to telomere integrity. Through increasing antioxidant defenses and reducing oxidative damage, meditation also reduces oxidative stress that can damage telomeres. In the context of stem cells, meditation may also increase telomerase activity (TA), which plays a role in maintaining telomere length (TL) and supporting stem cell function essential for tissue regeneration. Despite promising findings, gaps remain in understanding the precise mechanisms through which meditation modulates telomere and stem cells. Future research should further elucidate the mechanisms involved and explore the long-term implications of meditation on cellular aging processes.

Keywords: Meditation, Stem cell, TA, TL

INTRODUCTION

Accelerated cellular aging is significantly associated with phenomenal complex lifestyle diseases, including cardiovascular diseases and diabetes mellitus.[1,2] Several cardinal biomarkers are identified to address cellular aging, including DNA damage, TL shortening, and oxidative stress.[3] Telomeres are protective caps at the end of chromosomes, crucial for maintaining genomic stability. Telomerase, an enzyme crucial for maintaining TL, is linked to aging and cellular senescence.[4] At the same time, stem cells are essential for tissue regeneration and maintenance throughout life.[5]

The two are intertwined in discussing TA and stem cells. TA and expression are distinguishing features of stem cells.[6] Most adult stem cells exhibit TA at considerably lower levels, which is adequate to decelerate telomeres' shortening and extend their ability to replicate.[7] TL's shortening (or attrition) is linked to the diminished regenerative ability of stem cells and their niche cells in organs with high turnover, contributing to disease development.[8,9] Moreover, functional or longer telomeres

are crucial for developing embryonic or induced pluripotent stem cell pluripotency. This suggests that TL could provide a valuable marker for evaluating stem cell pluripotency.[10] Thus, telomere shortening is the hallmark of stem cell senescence.[11]

Lifestyle intervention effects on TL and TA have been rigorously studied. While dietary modification and aerobic exercise are beneficial to maintain or improve telomere health, research has suggested other lifestyle intervention types.[12,13] Meditation, another lifestyle intervention, has garnered increasing interest in scientific research during the past decade due to its potential effects on cellular aging processes by affecting TA and stem cell function. As of June 2024, many studies have investigated the association between meditation and TA, TL, and stem cell activity.[14-16]

Numerous studies have demonstrated that meditation-based intervention can contribute to the elongation of telomeres and the augmentation of TA.[17] Studies indicate that mindfulness meditation can directly influence TA, leading to increased telomerase levels in peripheral blood mononuclear cells. This increase in TA is significant as it plays a crucial role in maintaining TL, associated with cellular longevity and overall health. Research has shown that meditation interventions to reduce chronic stress and foster positive emotional states can contribute to maintaining TL, cognitive function, and psychosocial wellbeing.

Moreover, the effects of meditation on TA have been observed in various settings, including intensive retreats and real-world environments. Individuals participating in a one-month retreat with intense meditation training exhibited increased TL compared to experienced meditators who did not partake in the intensive retreat, underscoring the potential impact of training intensity on telomere dynamics. Furthermore, studies have indicated that meditation practices like loving-kindness meditation may be linked to longer telomeres, suggesting a potential association between specific meditation techniques and cellular aging processes.

However, while evidence provides valuable insights into the connection between meditation and TA, there are still gaps in the literature that necessitate further exploration. More studies are required to understand how meditation influences TA and the cellular aging processes, which could offer crucial information for developing targeted interventions to promote healthy aging.

This literature review aims to synthesize existing research on how meditation affects telomerase and stem cell activity. By examining various forms of meditation and focusing on the psychological and biological mechanisms linking meditation practice to telomerase and stem cell activity, this review seeks to provide a comprehensive understanding of the current state of knowledge and identify areas requiring further investigation.[18]

MECHANISMS ON HOW MEDITATION AFFECTS TELOMERE

Telomeres are chromosomal regions with fragile structures that are difficult to replicate, leading to telomere shortening. Various biological systems and factors, such as stress hormones, circadian rhythms, oxidative stress, and inflammatory mediators, highly regulate telomerase. Changes from psychological stress to physiological neuroendocrine changes, and down to the cellular and molecular levels, are influenced by a variety of interconnected and mutually reinforcing processes through positive feedforward loops. The pathways involved still need to be studied in depth. They have three prominent roles: stress mediators (glucocorticoids), oxidative stress, and inflammation. The cellular and molecular mechanisms have been reviewed in Lin and Epel's study. Based on this review, we propose the mechanism framework in Figure 1.

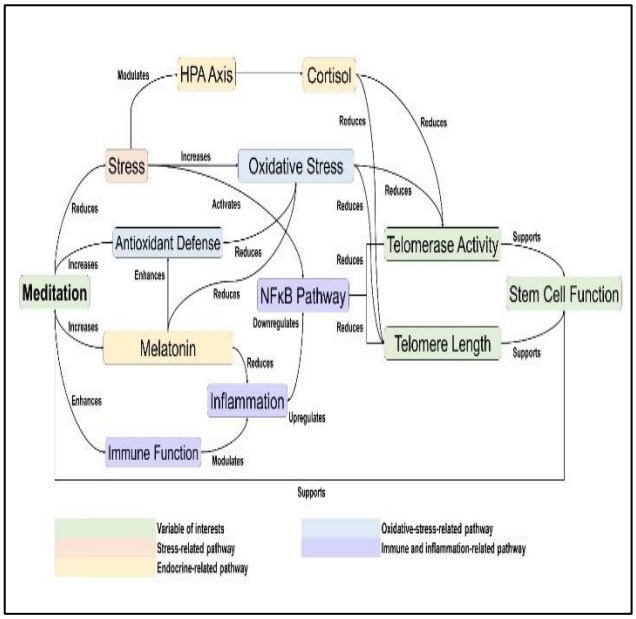

Figure 1: Proposed mechanism on how meditation affects variable of interests.

Endocrine-related mechanism

Meditation, stress, and telomere

Meditation's impact on telomere appears significantly mediated through endocrinological mechanisms, particularly stress reduction and improvement in circadian rhythm. Research consistently shows that meditation lowers stress levels and enhances psychological well-being.[37] The underlying mechanism proposed is modulation of the HPA axis.[38] It is posited that those who attain the Samadhi stage through meditation will experience a general sense of well-being, reducing stress levels. The decrease in stress levels, in turn, prompts changes in the brain through the HPA axis.[29] While studies have indicated that meditation may

influence the HPA-axis, the precise mechanism through which this occurs remains unclear. The HPA axis is a neuroendocrine system that regulates the synthesis and secretion of hormones involved in the stress response, including corticotropin-releasing hormone (CRH), adrenocorticotropin hormone (ACTH), and cortisol.

Previously, studies have demonstrated that stress-related health problems result in telomere shortening due to cellular aging. Decreased cortisol levels (a stress biomarker) have been associated with telomere lengthening (TL). These findings demonstrate a negative correlation between TL and perceived stress and cortisol levels. Additionally, repeated exposure to stress has been shown to increase cortisol reactivity, indicative of an increased growth rate and energy requirements associated with rapid cell division. At this stage, an allostatic load and exposure to high cortisol levels lead to the shortening of TL.

Based on in vitro studies, stress has an inverse correlation with total telomerase production and cortisol response, indicating that individuals who experience higher psychophysiological stress reactions (characterized by high cortisol levels) have a decreased ability to induce TA. Previous studies by Choi et al also obtained similar findings with exogenous hydrocortisone administration.[46] Glucocorticoids are thought to influence telomerase regulation by limiting the maximal activity of the immune system, modulating inflammatory gene transcription, and inhibiting lymphocyte proliferation and immune cell activity.

The limit of stress discussed in studies encompasses not only acute stress but also chronic stress, which can manifest prenatally or in early life. Chronic stress has been found to suppress the basal activity of telomerase, as evidenced by the findings of Epel et al studies. In a review, De Punder et al concluded that this effect is thought to be due to decreased nuclear and total TA, which is caused by increased levels of oxidative stress induced by chronic stress.[35] In contrast, Zalli et al reported that chronic stress was associated with shorter TL and higher basal TA. The authors proposed that this phenomenon indicates a chronic low-grade inflammation, in which chronic stress induces immune cell proliferation, resulting in increased basal TA, but cannot maintain TL under chronic stress conditions, causing shorter TL.

Although some studies have identified the effect of meditation on the HPA axis, other studies have yielded contradictory findings. For instance, the study by Parks et al demonstrated no correlation between TL and nocturnal cortisol levels. Savolainen et al discovered no linear correlation between leukocyte TL and HPA axis activity in an elderly population. This discrepancy may be related to the type of cells studied, which differed across studies. Notably, most studies that reported positive findings on the effects of meditation on TL employed peripheral blood mononuclear cells (PBMCs). In contrast, the opposite results were observed in whole blood (predominantly composed of short-lived granulocytes) and leukocytes. These findings indicate that cortisol may influence TA in specific cell types. Choi et al observed the most substantial effect of cortisol on the telomerase of CD8+ cells.[46] Further research is necessary to confirm this hypothesis, allowing future studies to determine the most appropriate cell type for investigating the impact of cortisol on telomerase.[19]

Meditation, stress, and melatonin

Melatonin, a hormone produced primarily by the pineal gland, is essential for regulating the sleep-wake cycle and possesses antioxidant properties. Research has demonstrated that yogic practices can stimulate the endogenous secretion of melatonin, thereby enhancing an individual's sense of well-being. Furthermore, the elevation of melatonin levels through meditation can positively affect telomere health. Melatonin is suggested to protect telomeres by reducing oxidative stress and inflammation, both of which contribute to telomere shortening. Consequently, the increase in melatonin induced by meditation may indirectly support telomere integrity by mitigating oxidative damage and inflammatory processes. Additionally, meditation's stress-reducing effects are significant in the context of melatonin, telomere health, and overall well-being. Chronic stress accelerates telomere shortening and contributes to various age-related diseases. Meditation has been demonstrated to mitigate the adverse effects of stress on telomeres by reducing stress levels and promoting relaxation. By modulating the hypothalamic-pituitary-adrenal (HPA) axis and reducing cortisol levels, meditation fosters a physiological environment conducive to maintaining TL and cellular health.[20]

Immunology-related mechanism

Research has examined the cellular and molecular mechanisms by which meditation affects the immune system and how they connect to telomere health. Rathore et al demonstrated that meditation-based therapies help to maintain genomic stability by conserving TL and improving innate immunity. This shows that meditation may contribute to general cellular health by protecting genetic material and boosting immunological function.[21]

Studies have observed significant impacts of meditation on various physiological systems necessary for immunological control. Meditation can reduce the detrimental effects of stress on the immune system by boosting immunoglobulin A (IgA) and natural killer cells. A scoping review found that meditation can increase cell-mediated immunity, making it a helpful preventive measure against illnesses requiring immunity, emphasizing meditation's immunomodulatory effects on the body's defense mechanisms. Furthermore, a systematic review and meta-analysis found that meditation can modulate immune and inflammatory

indicators, possibly via genetic pathways, indicating that meditation may affect the immune system by influencing genetic mechanisms that regulate immune responses.

A mechanistic model for meditation as a preventive and therapeutic modality has been proposed, emphasizing its ability to dampen pro-inflammatory responses at the cellular level. This model suggests meditation may affect immune function by modulating inflammatory pathways. Sapozhnikov study on the effect of integrated meditation practices on immune responses in examining stress highlights the potential of meditation in modulating immune changes associated with stress.[22]

One of the molecular mechanisms underlying meditation's immune-modulating effects is its impact on the levels of interferon-gamma, thereby restoring immune balance. Meditation can alter INF-γ levels, which function as a buffer to correct any imbalances caused by an overabundance or a deficiency of immune response expression.[23]

Meditation, inflammation, and telomere

The inflammatory response is closely associated with immune function. There are several proteins and cytokines involved in an inflammatory response. Immune cells are responsible for the release of inflammatory cytokines, either pro-inflammatory or anti-inflammatory ones. The synthesis of cytokines is mediated by nuclear factor kappa B (NFκB), indicating the role of NFκB in initiating the inflammatory response. Interleukin 1 (IL-1), IL-6, IL-8, and tumor necrosis factor (TNF)-α, are pro-inflammatory cytokines often used as a marker of inflammation, along with c-reactive protein (CRP), an acute phase inflammatory protein which synthesis is influenced by IL-6. Along with inflammation, the level of NFκB activity, CRP, and pro-inflammatory cytokines are increased.[24]

Meditation's impact on the NF-κB pathway is crucial, as this pathway is found to regulate numerous genes involved in the inflammatory response. The NF-κB pathway regulates pro-inflammatory cytokines and chemokines, arachidonic acid cascade enzymes, and adhesion molecules involved in inflammatory response. Furthermore, the downregulation of the NF-κB pathway in meditators was found to be a key element to the molecular mechanism of inflammatory response.[25]

Various signalling pathways are associated with telomere dysfunction. However, besides the p38 MAPK signalling pathway and other identified pathways, the NFκB pathway was found to play a vital part in the process. Numerous evidence has been linking the role of the NFκB inflammatory signalling pathway in the TL and/or TA change. An in vivo study involving chronic low-grade inflammation mouse model describes that chronic inflammation exacerbates telomere dysfunction. In patients with Duchenne muscular dystrophy, continuous activation of the NFκB pathway leads to the telomere shortening of the muscle satellite cell.[26] Additionally, activation of the NFκB pathway may lead to the up-regulation of hTERT, which after the administration of NFκB inhibitor was significantly down-regulated, indicating a positive correlation between NFκB expression and TA.[27]

While it is plausible that inflammation can lead to telomere dysfunction, in contrast, studies have considered that there is a cause-and-effect phenomenon in which shortened telomeres induce an inflammatory cascade. The two are also found to be coexisting and represent a vicious cycle.[3] Regardless of whether telomere shortening or the inflammatory process occurs first, it is possible to break the vicious cycle that results in telomere dysfunction through meditation.[28]

Meditation has decreased IL-6, TNF-α, CRP, and NFκB. While many studies have supported the findings, the detailed mechanism has yet to be uncovered. Aside from these findings, meditation has been found to modify gene expressions involved in the modulation of chromatin and inflammatory response, including TNF pathway, impairment in the expression of histone deacetylase genes, and receptor-interacting serine-threonine kinase-2 and cyclooxygenase-2. A recent study discovered that 61 differentially methylated sites were observed following a day of intense meditation practice, which influenced the methylome of PBMCs in experienced meditators. The methylation sites were enriched in genes primarily linked to immune cell metabolism and aging and binding sites for various transcription factors involved in immune response and inflammation. Additionally, the TBKBP1 gene, involved in the TNF-α/NFκB pathway, and TNFSF13B, which codes for a TNF family cytokine, were enriched during inflammation. One day of meditation retreat is associated with more significant methylation and suppression of TBKBP1 and TNFSF13B gene, indicating the link between meditation and reduced inflammation through the NFκB and TNF pathways.[29]

Another protein involved in the inflammatory pathway is brain-derived neurotrophic factor (BDNF). This protein is involved in complex inflammation, immunity, and stress response regulation.[30] Meditation is also found to improve the BDNF levels. The basal levels of BDNF predict an increase in bulk TL. Multiple mechanistic reasons were proposed by Cahn et al for the observed rise in BDNF levels following meditation. First, like intensive learning regimens that enhance neuroplasticity by raising BDNF signalling, meditation activates attentional engagement and modulations of frontal brain circuitry that engage neuroplastic brain mechanisms. Second, because deep breathing, yoga, and meditation raise the vagal tone and activate the BDNF receptor TrkB, they may also impact the autonomic nervous system. Finally, these effects might also be influenced by how meditation practices reduce stress reactions. Therefore, based on available evidence, there is a possibility of maintaining

telomere health through the modulation of inflammation through meditation practice.[31]

Meditation, oxidative stress, and telomere

Oxidative stress is when oxidant levels exceed antioxidant levels, creating an imbalance within the body. Reactive oxygen species (ROS) are oxidants that can damage proteins, lipids, and nucleic acids within cells. Conversely, the body produces antioxidants endogenously through antioxidant enzymes, including glutathione peroxidases, catalase, peroxidases, and peroxiredoxin, or obtains them exogenously through dietary sources.[32]

Some models have been put forth to elucidate the mechanisms through which oxidative stress induces alterations in telomeres. Nevertheless, no consensus has been reached on a universally accepted model, and numerous questions remain unanswered. Indeed, it remains unclear whether oxidative stress induces changes in telomeres through direct or indirect pathways. A review by Barnes et al provides a comprehensive overview of the models related to oxidative stress and telomere changes. However, the oxidative DNA damage model is the most widely discussed.[33]

The oxidative DNA damage model posits that when ROS interact with DNA, this reaction can result in the oxidation of over 100 different bases, including purines and pyrimidines, as well as the formation of single-strand breaks and apurinic/apyrimidinic sites.[14] Guanine, the natural base most susceptible to oxidation, can produce 8-oxo guanine (or 8-oxoG), which is more sensitive to oxidation. Nevertheless, whether this oxidative damage results from heightened susceptibility to oxidative damage or diminished telomere repair efforts remains unclear. Further research is necessary to elucidate the mechanistic pathway through which telomeres are altered by oxidative stress, even within this model.[34]

The potential of meditation to influence oxidative stress levels through various cellular and molecular mechanisms has been increasingly recognized. Several studies have demonstrated meditation's efficacy in reducing oxidative stress and enhancing antioxidant defense mechanisms. For example, research has demonstrated that meditation practices can result in a reduced redox state, which is advantageous for reducing oxidative stress levels.[35] Meditation has been linked to decreased cortisol and elevated melatonin levels, which are vital for regulating oxidative stress.[8]

Research has demonstrated that meditation can enhance superoxide dismutase (SOD) activity, mitigate lipid peroxidation, and function as an antioxidant therapy at the cellular level. These findings indicate that meditation may directly influence the cellular antioxidant defense system, thereby mitigating oxidative stress. Asana, pranayama, and meditation have been demonstrated to enhance oxygen flow to cells, reduce stress levels by modulating the HPA axis, and potentially impact TL.[36] Furthermore, evidence suggests that meditation practices are associated with lower levels of a marker of oxidative stress, such as lipid peroxidation, indicating a potential role for meditation in maintaining cellular health and reducing oxidative damage.[37] In relation to pranayama, a recent systematic review revealed that breathing exercises were effective in improving various oxidative stress markers, particularly malondialdehyde, SOD, and glutathione. Meditation was observed to induce the conversion of SOD to hydrogen peroxide through the catalysis of oxygen reduction. This hydrogen peroxide was then converted to water by glutathione, effectively reducing oxygen free radicals. Effect more pronounced in group that performed breathing exercises.[38]

Concerning the molecular mechanisms involved, there is evidence that meditation is associated with alterations in gene expression related to cellular metabolism and oxidative stress pathways.[39] It has been proposed that meditation training may influence telomeric regulation by affecting acute and habitual stress processes, which could potentially impact cellular aging and oxidative stress.[40] Additionally, evidence suggests that meditation upregulates the genes' expression in maintaining TL, which may contribute to controlling cellular aging and reducing oxidative stress.[41]

MEDITATION EFFECTS ON TELOMERE

Various studies have explored the relationship between meditation, TA, and TL to understand how mindfulness practices may influence cellular aging processes. Meditation has been shown to alter relative TLs, with a greater effect observed in women. This significant finding can potentially be used as a biomarker associated with longevity.[42] Epel et al proposed that specific forms of meditation, including mindfulness meditation, transcendental meditation, mantra meditation, tai chi, and cognitive behavioral stress management, could positively impact TL by reducing cognitive stress, enhancing positive mental states, and promoting hormonal factors supporting telomere maintenance. In a review by Conklin et al only two of the nine studies measuring TL that involved interventions of relatively high intensity or duration demonstrated increased TL in the treatment group.[43] Conversely, the remaining seven studies found no significant change in TL. The results suggest that meditation may directly influence cellular aging by affecting stress responses and psychological well-being.[44]

Studies like Alda et al have suggested that Zen meditation, in particular, is linked to longer leukocyte TL, indicating a potential association between mindfulness practices and cellular aging processes. Zen meditation is potentially associated with longer TL and reduced cellular aging through mechanisms involving reduced experiential avoidance and enhanced self-compassion. The group of Zen meditation experts had a

significantly longer median TL (10.82 kb) compared to a matched healthy comparison group (9.94 kb). The meditators also had a significantly lower percentage of short telomeres (5.22 kb) than the non-meditators (4.80 kb). Moreover, Thimmapuram et al demonstrated increased TL in healthcare professionals practicing heartfulness meditation, even with shorter daily meditation durations (less than 30 minutes) in real-world settings, suggesting that while longer durations are expected to be more beneficial, incorporating meditation into short daily routines may also positively impact telomere maintenance. Additionally, Carlson et al explored how practices like asana, pranayama, and meditation could influence telomere stability through the regulation of telomere metabolism and contribute to genomic stability and reduction in telomere attrition, which could positively impact telomere stability.[45]

Research by Sung et al found that participants in a high-intensity Insight meditation retreat (10 hours a day) experienced increased TL compared to meditation-experienced individuals who did not engage in the intensive program, highlighting the potential influence of training intensity on telomere maintenance. Interestingly, this study also found that personality traits predicted the changes in TL, indicating that the depth and rigor of meditation may affect its impact on cellular aging markers. Furthermore, Sheikh-Wu et al emphasized the interconnectedness between telomeres, cognition, mood, and physical function, suggesting that meditation and mindfulness practices aimed at reducing chronic stress and enhancing positive arousal could help maintain TL and overall well-being, underscoring the holistic benefits of meditation beyond cellular aging, extending to cognitive and emotional health.[24,46]

Meditation has also been found to influence TA, a critical cellular aging biomarker. A review by Conklin et al highlighted a growing body of research investigating the connection between meditation practice and telomere-related outcomes, such as TL and TA. Nine of the eleven studies measuring TA found intervention-related increases or higher TA in the treatment group following meditation interventions. Two studies found no significant changes in TA. Four studies assessed both TA and TL concurrently, each reporting significant changes in one measure but not the other. They suggest that TA and TL have different kinetics and fluctuate on different time scales.[47]

The evidence shows a promising relationship between mindfulness practices and cellular aging processes measured by telomere activity. Meditation may play a role in maintaining TL and supporting overall cellular health by reducing stress, promoting positive mental states, and potentially influencing hormonal factors. The intensity, duration, and type of meditation may all contribute to its effects on telomeres, emphasizing the need for further exploration to fully understand the underlying mechanisms of these relationships.[48]

MECHANISMS ON HOW MEDITATION AFFECTS STEM CELL

From telomere to stem cell

TL has been closely linked to stem cell pluripotency and function in the context of stem cells. Telomeres play a critical role in regulating the replicative capacity of stem cells, which are essential for tissue regeneration and maintenance. Studies have demonstrated that TL homeostasis is crucial for determining the proliferative potential of stem cells and ensuring tissue homeostasis. This balance between telomere elongation and trimming is essential for maintaining telomere stability in stem cells, highlighting the significance of telomeres in stem cell biology.

Telomerase, the enzyme responsible for maintaining TL, has been a critical focus in understanding the dynamics of telomeres in stem cells. The regulation of TA is intricately linked to the maintenance of TL. It is essential for the long-term survival and function of stem cells. TA ensures genomic stability and cellular proliferation in stem cell populations. Telomerase is crucial for maintaining TL, especially in stem cells that support self-renewal and differentiation. By enhancing TA, meditation may improve cellular resilience under stress conditions, thus promoting longevity and optimal cell function. Stem cells, susceptible to telomere shortening and senescence, benefit significantly from meditation-induced increases in TA. By preserving TL, stem cells can sustain their replicative capacity and contribute to tissue regeneration and repair processes.

Given the established role of telomeres in regulating stem cells, it is plausible to suggest that telomere structure and function alterations may indirectly impact stem cell biology. The potential for meditation to modulate telomere integrity could, therefore, have implications for stem cell maintenance, including their proliferative capacity and availability.[49]

Meditation and stem cell

Meditation has been a subject of interest in understanding its potential effects on stem cell activity, differentiation, and trafficking. Stem cells play a crucial role in tissue regeneration, repair, and maintenance; thus, exploring how practices like meditation may influence these processes is essential. Research has indicated that stem cell trafficking involves complex mechanisms that various factors, including signalling pathways, cell surface interactions, and tissue-specific environments, can influence. Understanding the dynamics of stem cell trafficking is crucial for developing targeted interventions that could optimize stem cell mobilization and homing, as discussed in Suárez-Álvarez et al study.[51]

Studies such as Kucia et al have highlighted the pivotal role of the SDF-1-CXCR4 axis in regulating the

trafficking of various types of stem cells in the body, including both non-malignant and malignant stem cells, emphasizing the importance of understanding the molecular mechanisms involved in stem cell movement.[52] Small-molecular inhibitors of CXCR4 and other compounds can increase the mobilization of HSCs and nonhematopoietic stem cells into the peripheral blood. Further study by Fyfe-Johnson et al found a marked increase in the expression of CXCR4 on the endogenous progenitor cells after an eight-week manualized relaxation response meditation intervention. The result suggests that interventions targeting this axis, potentially influenced by meditation practices, could impact stem cell trafficking dynamics.[53]

Moreover, Kraitchman et al suggested that defective trafficking of stem cells could be a significant mechanism in diseases like endometriosis, underscoring the importance of understanding how external interventions, such as meditation, could potentially modulate stem cell movement to mitigate disease processes.[54] Similarly, Williams et al demonstrated that FLT3 ligand administration could influence the trafficking of hematopoietic stem cells (HSCs) through interactions with CXCR4 and the marrow niche, indicating the potential for external factors to regulate stem cell trafficking.[30]

Smith-Berdan et al highlighted the regulation of HSC trafficking by complex mechanisms involving endothelial cells and vascular niches.[33] Endothelial and perivascular cells, such as mesenchymal stem cells and osteoblasts, play essential roles in HSC maintenance and mobilization. The Slit2-Robo4 signalling pathway has been shown to promote vascular stability by blocking Arf6 activity, and Robo4 is a vascular-specific receptor that inhibits endothelial migration. Multiple adhesion molecules, such as selectins, integrins, and CD44, are involved in HSC homing and engraftment. In addition, chemokines and cytokines, such as CXCL12 and SCF, regulate HSC mobilization from the bone marrow to peripheral blood in response to physiological and pathological stimuli. Overall, the regulation of HSC trafficking is a complex process that involves multiple cell types and molecular signals, and further research is needed to understand the mechanisms involved completely. Meditation-based practices, one of which is meditation, have long been suspected to initiate the mobilization of hematopoietic stem cells and very small embryonic-like stem cells (VSEL) to the peripheral circulation. The mobilization of these stem cells was dependent on the participant's age, exercise intensity, and exercise status.

Meditation has also been shown to affect stem cell differentiation. Mindfulness-based interventions, including mindfulness meditation, have increased populations of endogenous progenitor cells in patients with systolic hypertension, indicating a potential for arterial repair.[29] A mindfulness meditation intervention has also been shown to improve physical and psychological symptoms in hematopoietic stem cell transplant patients. Additionally, a short, intensive mind and body therapy program was found to upregulate hematopoiesis and adult stem cell numbers while controlling genes that regulate age-related complications.[50]

Overall, from available evidence, while the direct impact of meditation on stem cell activity, differentiation, and trafficking requires further investigation, existing research suggests that external factors can influence these processes. Understanding the intricate mechanisms involved in stem cell dynamics and how interventions like meditation modulate these processes could pave the way for novel therapeutic approaches targeting stem cell behavior.

FUTURE PERSPECTIVE

Future research on the effects of meditation on TL and stem cell activity should prioritize long-term, longitudinal studies across diverse populations to observe sustained impacts and generalize findings. These studies should include participants from various age groups, ethnicities, and health conditions to identify subgroups that may benefit most from meditation practices. Additionally, in-depth mechanistic studies are essential to elucidate the precise pathways through which meditation influences TA, TL, and stem cell dynamics. Understanding the molecular and genetic changes induced by meditation, particularly its modulation of the HPA axis, inflammatory pathways, and oxidative stress, will provide valuable insights.

Moreover, future research should evaluate the comparative effectiveness of different meditation techniques, such as mindfulness meditation, loving-kindness meditation, and yoga, considering factors like intensity, duration, and frequency of practice. Investigating the synergistic effects of meditation combined with other lifestyle interventions, such as dietary modifications, aerobic exercise, and stress management, could offer a comprehensive approach to promoting healthy aging. Translational research is also necessary to develop meditation-based interventions for clinical applications, particularly for patients with age-related diseases, cardiovascular conditions, and chronic stress-related disorders. Integrating technology, such as mobile applications and wearable devices, can facilitate large-scale studies by providing accessible platforms for monitoring practice adherence and physiological changes, enhancing data collection and participant engagement.

CONCLUSION

Meditation appears to impact telomere and stem cells, potentially influencing cellular aging, regeneration, and overall physiological well-being. Research indicates that meditation can enhance TA, improve TL, and positively

affect stem cell dynamics through mechanisms involving stress reduction, immune system, inflammation, and oxidative stress. These findings underscore the potential of meditation as a valuable intervention for promoting healthy aging and mitigating age-related diseases.

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REFERENCES

1. Boccardi V, Paolisso G, Mecocci P. Nutrition and lifestyle in healthy aging: the telomerase challenge. Aging. 2016;8(1):12-5.
2. Jackson AS, Sui X, Hébert JR, Church TS, Blair SN. Role of Lifestyle and Aging on the Longitudinal Change in Cardiorespiratory Fitness. Arch Intern Med. 2009;169(19):1781-7.
3. Correia-Melo C, Hewitt G, Passos JF. Telomeres, oxidative stress and inflammatory factors: partners in cellular senescence? Longev Heal. 2014;3(1):1.
4. Armstrong L, Saretzki G, Peters H, Wappler I, Evans J, Hole N, et al. Overexpression of Telomerase Confers Growth Advantage, Stress Resistance, and Enhanced Differentiation of ESCs Toward the Hematopoietic Lineage. Stem Cells. 2005;23(4):516-29.
5. Nurkovic J, Volarevic V, Lako M, Armstrong L, Arsenijevic N, Stojkovic M. Aging of Stem and Progenitor Cells: Mechanisms, Impact on Therapeutic Potential, and Rejuvenation. Rejuvenation Res. 2016;19(1):3-12.
6. Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, et al. Embryonic stem cell lines derived from human blastocysts. Science. 1998;282(5391):1145-7.
7. Allsopp RC, Morin GB, DePinho R, Harley CB, Weissman IL. Telomerase is required to slow telomere shortening and extend replicative lifespan of HSCs during serial transplantation. Blood. 2003;102(2):517-20.
8. Hiyama E, Hiyama K. Telomere and telomerase in stem cells. Br J Cancer. 2007;96(7):1020-4.
9. Lupatov AY, Yarygin KN. Telomeres and Telomerase in the Control of Stem Cells. Biomedicines. 2022;10(10):2335.
10. Huang J, Wang F, Okuka M, Liu N, Ji G, Ye X, et al. Association of telomere length with authentic pluripotency of ES/iPS cells. Cell Res. 2011;21(5):779.
11. Fathi E, Charoudeh HN, Sanaat Z, Farahzadi R. Telomere shortening as a hallmark of stem cell senescence. Stem Cell Investig. 2019;6:7.
12. Galiè S, Canudas S, Muralidharan J, García-Gavilán J, Bulló M, Salas-Salvadó J. Impact of Nutrition on Telomere Health: Systematic Review of Observational Cohort Studies and Randomized Clinical Trials. Adv Nutr. 2020;11(3):576-601.
13. Song S, Lee E, Kim H. Does Exercise Affect Telomere Length? A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Medicina (Mex). 2022;58(2):242.
14. Bossert L, Arzberger K, Dorok F, Kern J, Stickler C, Wunderlich M, et al. The Effects of Mindfulness-Based Interventions on Telomere Length and Telomerase Activity: A Systematic Review and Meta-Analysis. Mindfulness. 2023;14(3):495-509.
15. Dasanayaka NN, Sirisena ND, Samaranayake N. The effects of meditation on length of telomeres in healthy individuals: a systematic review. Syst Rev. 2021;10(1):151.
16. Dasanayaka NN, Sirisena ND, Samaranayake N. Impact of Meditation-Based Lifestyle Practices on Mindfulness, Wellbeing, and Plasma Telomerase Levels: A Case-Control Study. Front Psychol. 2022;13:846085.
17. Dasanayaka NN, Sirisena ND, Samaranayake N. Improving Mindfulness, Quality of Life, and Controlling Cellular Aging through Meditation. In: Well-Being Across the Globe-New Perspectives-Concepts, Correlates and Geography. IntechOpen; 2023.
18. Duraimani S, Schneider RH, Randall OS, Nidich SI, Xu S, Ketete M, et al. Effects of Lifestyle Modification on Telomerase Gene Expression in Hypertensive Patients: A Pilot Trial of Stress Reduction and Health Education Programs in African Americans. Eller K, editor. PLOS One. 2015;10(11):e0142689.
19. Lavretsky H, Epel ES, Siddarth P, Nazarian N, Cyr NSt, Khalsa DS, et al. 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. 2013;28(1):57-65.
20. Mendioroz M, Puebla-Guedea M, Montero-Marín J, Urdánoz-Casado A, Blanco-Luquin I, Roldán M, et al. Telomere length correlates with subtelomeric DNA methylation in long-term mindfulness practitioners. Sci Rep. 2020;10(1):4564.
21. Rathore M, Abraham J. Implication of asana, pranayama and meditation on telomere stability. Int J Yoga. 2018;11(3):186-6.
22. Sapozhnikov D. Promise of Mindfulness-Based Interventions as Therapies to Prevent Cognitive Decline. McGill Sci Undergrad Res J. 2015;10(1):49-54.
23. Schutte NS, Malouff JM. A meta-analytic review of the effects of mindfulness meditation on telomerase activity. Psychoneuroendocrinology. 2014;42:45-8.
24. Sheikh-Wu SF, Liang Z, Downs CA. The Relationship Between Telomeres, Cognition, Mood, and Physical Function: A Systematic Review. Biol Res Nurs. 2023;25(2):22739.
25. Shen H, Chen M, Cui D. Biological mechanism study of meditation and its application in mental disorders. Gen Psychiatry. 2020;33(4):e100214.
26. Sung MK, Koh E, Kang Y, Lee JH, Park JY, Kim JY, et al. Three months-longitudinal changes in relative telomere length, blood chemistries, and self-report questionnaires in meditation practitioners

compared to novice individuals during midlife. Medicine (Baltimore). 2022;101(41):e30930.
27. Thimmapuram J, Pargament R, Sibliss K, Grim R, Risques R, Toorens E. Effect of heartfulness meditation on burnout, emotional wellness, and telomere length in health care professionals. J Community Hosp Intern Med Perspect. 2017;7(1):21-7.
28. Tiwari A, Chan CLW, Ho RTH, Tsao GSW, Deng W, Hong AWL, et al. Effect of a qigong intervention program on telomerase activity and psychological stress in abused Chinese women: a randomized, wait-list controlled trial. BMC Complement Altern Med. 2014;14(1):300.
29. Tolahunase M, Sagar R, Dada R. 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;2017:7928981.
30. Williams-Orlando C. Loving-kindness Meditation in Psychology. Altern Complement Ther. 2016;22(3):111-6.
31. Epel ES, Daubenmier J, Moskowitz JT, Folkman S, Blackburn E. Can Meditation Slow Rate of Cellular Aging? Cognitive Stress, Mindfulness, and Telomeres. Ann N Y Acad Sci. 2009;1172(1):34-53.
32. Conklin QA, Crosswell AD, Saron CD, Epel ES. Meditation, stress processes, and telomere biology. Curr Opin Psychol. 2019;28:92-101.
33. Sfeir A, Kosiyatrakul ST, Hockemeyer D, MacRae SL, Karlseder J, Schildkraut CL, et al. Mammalian Telomeres Resemble Fragile Sites and Require TRF1 for Efficient Replication. Cell. 2009;138(1):90-103.
34. Bryan TM. G-Quadruplexes at Telomeres: Friend or Foe? Molecules. 2020;25(16):3686.
35. De Punder K, Heim C, Wadhwa PD, Entringer S. Stress and immunosenescence: The role of telomerase. Psychoneuroendocrinology. 2019;101:87-100.
36. Lin J, Epel E. Stress and telomere shortening: Insights from cellular mechanisms. Ageing Res Rev. 2022;73:101507.
37. Lavretsky H, Epel ES, Siddarth P, Nazarian N, Cyr NSt, Khalsa DS, et al. 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. 2013;28(1):57-65.
38. Pascoe MC, Thompson DR, Ski CF. Meditation and Endocrine Health and Wellbeing. Trends Endocrinol Metab. 2020;31(7):469-77.
39. Tang YY, Hölzel BK, Posner MI. The neuroscience of mindfulness meditation. Nat Rev Neurosci. 2015;16(4):213-25.
40. Epel ES, Blackburn EH, Lin J, Dhabhar FS, Adler NE, Morrow JD, et al. Accelerated telomere shortening in response to life stress. Proc Natl Acad Sci. 2004;101(49):17312-5.
41. Shalev I. Early life stress and telomere length: Investigating the connection and possible mechanisms. BioEssays. 2012;34(11):943-52.
42. Conklin QA, King BG, Zanesco AP, Lin J, Hamidi AB, Pokorny JJ, et al. Insight meditation and telomere biology: The effects of intensive retreat and the moderating role of personality. Brain Behav Immun. 2018;70:233-45.
43. Tomiyama AJ, O'Donovan A, Lin J, Puterman E, Lazaro A, Chan J, et al. Does cellular aging relate to patterns of allostasis? An e`xamination of basal and stress reactive HPA axis activity and telomere length. Physiol Behav. 2012;106(1):40-5.
44. Savolainen K, Eriksson JG, Kajantie E, Lahti J, Räikkönen K. Telomere length and hypothalamic–pituitary–adrenal axis response to stress in elderly adults. Psychoneuroendocrinology. 2015;53:179-84.
45. Nelson BW, Allen NB, Laurent H. Infant HPA axis as a potential mechanism linking maternal mental health and infant telomere length. Psychoneuroendocrinology. 2018;88:38-46.
46. Choi J, Fauce SR, Effros RB. Reduced telomerase activity in human T lymphocytes exposed to cortisol. Brain Behav Immun. 2008;22(4):600-5.
47. Belsky J, Shalev I. Contextual adversity, telomere erosion, pubertal development, and health: Two models of accelerated aging, or one? Dev Psychopathol. 2016;28(4pt2):1367-83.
48. Barnes PJ, Adcock IM. Glucocorticoid resistance in inflammatory diseases. The Lancet. 2009;373(9678):1905-17.
49. Bauer ME. Stress, glucocorticoids and ageing of the immune system. Stress. 2005;8(1):69-83.
50. Epel ES, Lin J, Wilhelm FH, Wolkowitz OM, Cawthon R, Adler NE, et al. Cell aging in relation to stress arousal and cardiovascular disease risk factors. Psychoneuroendocrinology. 2006;31(3):277-87.
51. Suárez-Álvarez B, López-Vázquez A, López-Larrea C. Mobilization and Homing of Hematopoietic Stem Cells. 2012: 152–170.
52. Kucia M, Reca R, Miekus K, Wanzeck J, Wojakowski W, Janowska-Wieczorek A, et al. Trafficking of Normal Stem Cells and Metastasis of Cancer Stem Cells Involve Similar Mechanisms: Pivotal Role of the SDF-1–CXCR4 Axis. STEM CELLS. 2005;23(7):879–94.
53. Fyfe-Johnson A, Taylor D, Zierold C, Dusek J. OA04.01. Effects of relaxation response intervention on endogenous progenitor cells in a hypertensive population. BMC Complement Altern Med. 2012;12(S1):13–13.
54. Kraitchman DL, Tatsumi M, Gilson WD, Ishimori T, Kedziorek D, Walczak P, et al. Dynamic Imaging of Allogeneic Mesenchymal Stem Cells Trafficking to Myocardial Infarction. Circulation. 2005;112(10):1451–61.

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