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Can meditation slow rate of cellular aging? Cognitive stress, mindfulness, and telomeres

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Abstract

Understanding the malleable determinants of cellular aging is critical to understanding human longevity. Telomeres may provide a pathway for exploring this question. Telomeres are the protective caps at the ends of chromosomes. The length of telomeres offers insight into mitotic cell and possibly organismal longevity. Telomere length has now been linked to chronic stress exposure and depression. This raises the question of how might cellular aging be modulated by psychological functioning.

We consider two psychological processes or states that are in opposition to one another--threat cognition and mindfulness--and their effects on cellular aging. Psychological stress cognitions, particularly appraisals of threat and ruminative thoughts, can lead to prolonged states of reactivity. In contrast, mindfulness meditation techniques appear to shift cognitive appraisals from threat to challenge, decrease ruminative thought, and reduce stress arousal. Mindfulness may also directly increase positive arousal states.

We review data linking telomere length to cognitive stress and stress arousal and present new data linking cognitive appraisal to telomere length. Given the pattern of associations revealed so far, we propose that some forms of meditation may have salutary effects on telomere length by reducing cognitive stress and stress arousal and increasing positive states of mind and hormonal factors that may promote telomere maintenance. Aspects of this model are currently being tested in ongoing trials of mindfulness meditation.

Keywords

meditation; mindfulness; stress; appraisal; rumination; telomere length; telomerase

Introduction

Chronological age is the ultimate predictor of disease and death. However, tremendous individual variability is found in onset of morbidity and mortality. Therefore, it is of great scientific and clinical interest to identify markers of biological age, as well as factors that influence them. Telomere length (TL) appears to be such an indicator. TL shortens with

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chronological age, predicts risk factors for cardiovascular disease (CVD) independent of age, and is shortened in people with age-related diseases, including atherosclerosis and diabetes.[1] Stress appears to influence the rate of telomere shortening.[2] Here we examine links between TL, stress arousal, and stress cognitions, and consider how mindfulness meditation might alter these pathways, as well as have direct effects independent of stress pathways.

There are specific types of stress cognitions that lead to greater stress arousal and thus may impact cell longevity. Threat appraisals enhance negative emotional responses to a stressor by construing it as a threat to oneself and amplifying the significance of the stressor. In addition to the content of an appraisal, the process of rumination about negative appraisals prolongs the stress arousal, and can induce distress about the emotional response itself. These two types of stress cognition then trigger negative emotional responses tied to specific forms of physiological arousal (high catabolic, low anabolic profiles) which can impair telomere length.

Mindfulness is a psychological process that acts on specific parts of this cognitive content and process, disrupting the stress pathways and possibly having direct salutary effects on physiological arousal systems. Based on a combination of empirical data and speculation, we propose that these processes, stress cognition and mindfulness, may be linked to cellular aging, shown in Figure 1. Below we offer a selective review on the literatures of cell aging (telomeres and telomerase), stress cognition (threat appraisals and rumination) and their effects on arousal relevant to telomere maintenance, and lastly, the potential impact of mindfulness and meditation on these stress processes.

Cellular aging and ‘bodily aging.’

Telomeres provide a unique model for understanding cell aging and senescence. Telomeres are the protective nucleoprotein structures capping the ends of eukaryotic chromosomes, consisting of a simple repeat sequence (TTAGGG)$_n$. When cells divide, the end of the telomere cap may not be replicated because the DNA polymerase does not function properly at the end of a DNA strand.[3] Therefore telomeres tend to shorten with mitosis so that cells in older organisms have on average shorter telomeres than cells in younger organisms.

Telomerase is a ribonucleoprotein reverse transcriptase cellular enzyme that counteracts TL shortening and adds telomeric DNA to shortened telomeres. Telomerase thus forestalls shortened telomeres from signaling the cell to cease dividing or to die. Telomerase promotes cell longevity even in the face of critically shortened telomeres.[4] Conversely, cells with short telomeres without telomerase are at highest risk of fusions, senescence, and apoptosis.[5, 6] Thus, it is in part the interaction between short telomeres and low telomerase activity that appears to increase the risk of cell death.[7]

Cell aging, disease, and death

Telomere shortening and replicative senescence is thought to be indicative of bodily aging. Several genetic premature aging syndromes are characterized by cell sencescence (Werner Syndrome, Progeria Hutchinson Guilford, and ataxia teleangiecstasia); at least when subject’s cells are examined in vitro, and are characterized by signs of accelerated aging and early mortality.[8] There is a proliferation of research in this area, and many studies show that TL is linked to a variety of disease states. Shorter TL is related to aspects of cardiovascular disease, such as plaques,[9] heart attacks[10] greater calcific aortic valve stenosis [11], vascular dementia [12] and degenerative conditions such as osteoarthritis[13] and osteoporosis.[14] It has also been related to diabetes[15, 16] and general risk factors for chronic disease, including

obesity and insulin resistance.[16, 17] Lastly, TL in leukocytes predicted earlier mortality in a community sample, and in samples with Alzheimer's disease and history of stroke.[18-20]

Psychological stress and cell aging

Given the role of telomere maintenance to cell longevity and apparently human longevity, it is important to find the nexus of how psychological function might affect this longevity system. We first examined whether young healthy women under chronic stress had shorter telomeres than those with low levels of life stress. We found that objective stress (years of caregiving) and perceptions of life stress were both related to shorter telomere length.[21] We have found similar relationships with dementia caregivers and controls (unpublished data). Others have since found shortened telomeres in major depression,[22] and in those with lower socioeconomic status.[23] Thus, stressful life circumstances, stress appraisals, and severe distress, appear to be related to greater telomere shortening.

It is nevertheless difficult to predict who is most vulnerable to telomere shortening when exposed to similar conditions of chronic stress. Here we briefly review some of the important psychological (cognitive and emotional) aspects of stress, and then physiological stress mediators that are likely related to cell aging as well. We note, however, that psychological function is only one of many factors influencing telomere length in adulthood, and a lifespan approach may be the best way to understand telomere length at any one moment in time [24].

Cognitive stress

Given the huge individual variance in perception and reaction to common stressful events, the process of coping with challenge is an important mediator of emotional reactions[25] and presumably physiological reactivity.

Appraisal

A prevailing model for understanding what makes a situation stressful is Lazarus and Folkman's (1984) Stress and Coping Theory.[26] Situations where a goal that matters to the person is at stake and the demands of the situation outweigh the person's resources for coping with it can cause feelings of 'stress'. We may feel 'stressed' when a situation harms or threatens important goals ("threat appraisals"). In contrast, in a stressful situation, a person might see the possibility of doing well at coping and thus perceive the stressor as a challenge ("challenge appraisals"). Here, we focus on threat appraisals, which according to our model is the harmful type of stress, linked to cell aging.

Appraisal and coping

Cognitive appraisal in turn affects choice of coping strategy. Coping refers to constantly changing (moment to moment) cognitive and behavioral efforts to manage the demands of a stressful situation.[26] A key aspect of the appraisal process is the evaluation of personal control over the outcome. Situations in which there is the possibility of control usually call for behaviorally active, problem-focused coping strategies; situations in which nothing can be done usually call for cognitive strategies that help the person accept the situation or regulate their emotional responses to it.[27, 28] Accurate appraisals are important to enact effective coping (e. g., to prevent mismatches such as attempting to exert control over an uncontrollable situation).

In our original study on stress and cell aging among maternal caregivers, we examined perceptions of life stress, using the Perceived Stress Scale (PSS),[29] among healthy women (n = 65), some caring for a child with a chronic condition and others caring for healthy

children. As reported elsewhere, the full scale score assessing stress-related feelings and thoughts over the last month was significantly related to shorter TL ($r = -0.31$), after covarying age and body mass index.[2] Here we examine which aspects of stress perception on the PSS are linked to TL. Three of the 10 items were significantly related to TL, and these items represent the three core components of perceived stress: the two cognitive components, which include the perception that demands outweigh coping resources and a loss of control, represented by the question "difficulties were piling up so high I could not overcome them,' ($r = -0.40$, $p < .002$)' and "feeling unable to control important things in life" ($r = -0.28$, $p < .05$); and the face-valid emotional component of stress represented by the question "feeling nervous or stressed," ($r = -0.40$, $p < .002$). This item analysis suggests that specific stress cognitions may be related to TL, at least in this sample of women.

Appraisal and emotion under acute and chronic stress

Appraisals also drive emotional states. Threat appraisals drive negative emotions (such as fear and anxiety), whereas challenge appraisals can foster both negative (e.g., anxiety) and positive emotions (e.g., feeling energized and elated).[26, 30] According to Stress and Coping Theory, [26] the coping process begins when an event is appraised as threatening or challenging. These appraisals prompt both emotional states and coping efforts. If the event is resolved favorably, a positive emotional state (e.g., relief, satisfaction) ensues. If the event is resolved unfavorably or if it remains unresolved, a negative emotional state results (e.g., anger, guilt, anxiety) and the coping process continues through reappraisal and continued rounds of coping.

Chronic stress and positive coping

Many people in modern societies are dealing with at least one, if not multiple, chronic life stressor, such as financial, relationship, work or caregiving stressors. What are the coping mechanisms people use to maintain positive affect and a positive outlook? In dealing with chronic stressors, the negative emotion associated with unfavorable resolution can in some cases motivate positive changes. Negative states motivate meaning-focused coping processes such as those that draw on important goals and values, [31-33] including goal-directed problem-focused coping, positive reappraisal, benefit finding and benefit reminding about a specific situation, [34] and infusion of ordinary events with meaning.[35] These coping processes result in positive emotion, which serve important coping functions: they provide a psychological 'time-out' from the distress associated with chronic stress and help motivate and sustain ongoing efforts to cope with the negative effects of the chronic stressor.[36]

Chronic stress and cognitive shifts (thriving)

There appears to be such a strong drive to experience positive emotions, such that people facing chronic adversity may be driven to reorganize their outlook on life. In the course of coping with chronic stress, people often develop cognitive shifts or changes in one's mental filter that promotes positive appraisals. These are distinct from acute stress appraisals and coping strategies. We call these cognitive shifts psychological thriving.[37] Thriving includes a range of positive appraisals such as greater appreciation of life, or self growth (new skills and feeling empowered). These changes are not tied to specific situations, but rather serve as meta-cognitions about one's life. These shifts may stay with a person (i.e., become ingrained schemas) and affect future appraisals as well. We suspect that psychological thriving shifts situational appraisals of everyday minor stressors toward challenge appraisals, and decreases rumination. In this way, psychological thriving may promote a state of enhanced allostasis, a state where one has lower basal stress arousal, more efficient reactivity peaks, quicker recovery, and greater anabolic functioning after stress, as described in detail elsewhere.[37, 38]

We do not know which individual or situation factors, in the course of chronic stress, cause some people to engage in positive coping, while others remain more fixed in their thinking. It is possible that mindfulness training can help foster positive coping and eventually psychological thriving.

New data: Cognitive appraisal and cell aging—an empirical test

Here, we report a preliminary test of one aspect of this model, the link between acute stress appraisals and telomere length. We asked whether acute appraisals to a standardized stressor are linked to telomere length. In the maternal caregiver study described above, we also examined response to an acute laboratory psychosocial stressor, an adapted form of the Trier Social Stress Test (TSST).[39] Before the stressor, we measured thoughts and emotions linked to threat and challenge appraisals based on theory and research.[27, 40, 41] Participants rated how much they felt each of 6 emotions, including worried, anxious, or fearful (threat emotions) and eager, confident, and hopeful (challenge emotions). They also rated expectations for the task, including anticipated success, difficulty of the task, perceptions of control over the task, and effort they would need to exert.

An exploratory factor analysis was performed requesting two factors, with a varimax rotation. All items loaded on one of two factors, with loadings of .59 or higher, accounting for 51% of the total variance, supporting the existence of threat and challenge appraisal factors. The threat factor (Eigenvalue of 2.8) included the threat emotions and scoring high on expected difficulty. The challenge factor (Eigenvalue of 2.4) included scoring high on challenge emotions, high anticipated success, high perceived control, and expecting to exert high effort. Factor scores were created and examined independently and as a ratio of challenge to threat, in case relative levels of appraisal mattered. There were no correlations between TL with challenge (−.07) or threat (r = .00) factors, suggesting that neither type of appraisal alone is associated with telomere shortening. However, the ratio of challenge to threat was significantly correlated with longer telomeres ($r = .26$, $p < .05$), suggesting that appraising a standardized stressor as more challenging than threatening may be related to longer TL. Appraisals are complex, even with a short lab stressor. In response to the upcoming laboratory stressor, people made both challenge and threat appraisals. Given the correlation between appraisal ratio and TL, and that telomere length is a ‘cumulative’ measure, one that changes slowly over years, it appears that the predominant appraisal, determined by the relative balance of appraisals, is likely related to habitual ways of responding to small daily stressors.

Stress arousal

The neuroendocrine system and autonomic nervous system which regulate the stress response are important physiological mediators between emotional stress and illness. Chronic stress can depress levels of heart rate variability or vagal tone, an index of the counterregulatory response to sympathetic arousal. For example, low vagal tone has been related to work stress[42], depression[43] and low socioeconomic status.[44]

Chronic stress can lead to dysregulation of the hypothalamic pituitary axis, which can take many forms, such as a blunted diurnal rhythm of cortisol or elevated basal levels.[45, 46] Flattened rhythm in turn can predict various indicators of physical and mental health, such as coronary calcification[47] and metastatic breast cancer progression.[48] Chronic stress can suppress levels of certain anabolic hormones, such as DHEA or insulin like growth factor [49] and can increase levels of insulin and visceral fat [50]. Anabolic hormones such as testosterone appear to suppress or counterregulate the catabolic and sympathetic stress response [51] thus playing an important role in endocrine balance. Lastly, acute and chronic

stress appear to increase levels of oxidative stress.[52] These relationships between stress and neuroendocrine balance have been reviewed extensively elsewhere.[49, 53-55]

Cognitive appraisal and arousal

Strong positive and negative emotions associated with appraisals can induce changes in physiological arousal systems. A primary construct for understanding appraisal and arousal is perceived control. Perceptions of control help determine whether a situation is appraised as a threat or challenge, and these appraisals in turn are primary determinants of physiological stress responses. Classic stress research has shown that feeling a lack of control over a stressor, including a sense of unpredictability and uncertainty, stimulates cortisol reactivity.[56] A meta-analysis across studies of psychological laboratory stressors showed that conditions of social evaluative threat (perceptions that ego relevant aspects of one's identity will be negatively judged) and low control, are potent stimulants of the adrenal gland, with additive effects for both.[57]

Little research has examined positive emotions and physiology, and no research to our knowledge has compared high vs. low arousal positive states. Positive emotional states may promote a more salutary pattern of arousal. High arousal positive states, such as sports competition, vicariously experiencing winning, or experiencing challenge appraisals while successfully coping with an acute stressor, may activate certain anabolic hormones such as testosterone and DHEA-S.[58-60] Lower arousal emotions, such as feeling composed, calm and peaceful are associated with greater vagal tone (parasympathetic activity) [61] and possibly to higher DHEA.[62] Low DHEA at baseline has also been related to greater subsequent threat appraisals and negative affect in response to a stressor, suggesting it promotes affective vulnerability to acute stress.[63] Thus, there are likely bidirectional relationships between neuroendocrine balance of anabolic and catabolic hormones, and appraisals. We suggest that the anabolic (mainly androgens and vagal tone) response to positive states, both high arousal states (challenge) and low arousal states (relaxation) may be one key to the effects of mindfulness on physical health (See Figure 1, Positive states).

Rumination and stress arousal

When a coping outcome is appraised as unfavorable and the goal remains highly valued, people feel more negative affect and may engage in rumination, repetitive thought that is not goal directed. Depressive rumination, a negative self-focus on assumed basic faults, can prolong negative mood and over time predict depression.[64] Negative affect and rumination may further lead to prolonged cardiovascular recovery.[65-67] State rumination has been related to higher salivary cortisol after acute stress.[68]

Stress arousal and cell aging

As yet few studies attempt to link cell aging to stress arousal. In our initial study of healthy young women, those with shorter telomeres excreted higher levels of both cortisol and epinephrine in their urine overnight, [69] suggesting chronically elevated stress response system activity. When examining telomerase, we found that low telomerase was related to greater basal hemodynamic arousal (heart rate, blood pressure), lower heart rate variability, and greater sympathetic reactivity to lab stress.[69] Low telomerase was related to lower resting vagal tone and a greater dip in vagal tone in response to an acute lab stressor independent of resting vagal tone.

Endocrine and biochemical milieu can affect rate of telomere shortening with each cell division. Oxidative stress, characterized by excess free radicals, shortens telomeres, whereas telomerase can rebuild and thus lengthen the telomere. Further, in vitro evidence in various cell lines suggests that certain anabolic hormones, including growth hormone, [70] IGF-1,[71-73]

and estrogen, [74, 75] can promote telomerase activity. In contrast, insulin and insulin resistance are related to telomere shortness.[17] These same pathways may be affected by chronic stress and meditation, discussed further below.

Mindfulness Meditation

Here we review meditation techniques theorized to positively modulate stress-related cognitive processes and arousal with implications for cellular aging. We first outline the theoretical claims and practice of mindfulness meditation, in particular, based on a large body of theory and research in this area, and examine other forms of meditation when applicable. We then review research linking mindfulness states, mindfulness meditation, and other types of meditation to aspects of stress cognition, coping, and emotional reactivity. Lastly, we review research linking meditation to stress arousal.

Definitions of mindfulness

At the outset, we note the Buddhist origins of mindfulness meditation techniques and acknowledge that scientific understandings of mindfulness have developed largely independent of Buddhist paradigms, theory, and goals (for a discussion on this issue, see [76, 77]). Mindfulness meditation has been adapted to Western secular contexts to treat patients with a variety of physical and psychological conditions and research to date has predominantly focused on its efficacy to improve these conditions and examine underlying mechanisms. In contrast, in Buddhist settings, mindfulness is one aspect of a set of integrated spiritual practices, beliefs, and teachings aimed at achieving insight into the nature and cause of suffering and realizing spiritual freedom.[77] These differing goals and contexts have implications for the understanding of mindfulness and so we emphasize the importance of not mistaking secular, therapeutic conceptualizations of mindfulness, as we focus on here, for Buddhist conceptualizations. Notwithstanding these issues, we would argue that the adaptation of mindfulness to Western contexts retains at least some of its essential ingredients and appears to be beneficial. Thus, it is within this larger context that we aim to review the scientific literature on mindfulness. We specifically focus on the relation of mindfulness to stress related cognitions, affect, and coping processes using Stress and Coping theory as a framework to propose mechanisms through which mindfulness, and other forms of meditation, may positively impact stress arousal and cellular aging.

Mindfulness is considered an inherent aspect of consciousness that can be enhanced through a variety of mental training techniques collectively referred to as mindfulness meditation. Mindfulness, translated from the Pali word *sati* (Sanskrit: *smrti*), literally means “to remember.” In the traditional Buddhist context, it means to adhere to an object of consciousness with a clear mental focus in a given moment [78]. This simple definition contrasts with the multidimensional conceptualization of mindfulness by contemporary Western scientists. Although scientists have yet to agree on a precise definition,[76, 79-81] the most commonly cited one belongs to pioneer Jon Kabat-Zinn, who defined it as “paying attention in a particular way: on purpose, in the present moment and non-judgmentally” [82] (p.4). Kabat-Zinn adds an attitudinal dimension to the state of mindfulnesss, that of nonjudgmentalness. Other researchers following his lead have described the attitude as one of curiosity and acceptance[80] or kindness, compassion, and patience. [83] Thus, in addition to characterizing mindfulness as a form of attention regulation as in the Buddhist definition, scientists emphasize the importance of the cognitive and emotional manner in which attention is deployed.

The practice of mindfulness

Instructions for the formal practice of mindfulness meditation entail purposefully directing attention to one's experience in the present moment with an attitude of open curiosity and acceptance.[80] An upright sitting posture with minimal movement is encouraged (with eyes either open or closed) to allow the body to relax and the mind to remain alert. Attention is directed to a pre-determined object, usually localized sensations involving respiration, such as those at the tip of the nose (external objects can also be used, such as a picture). Novice practitioners usually report that after a short period of time, they become distracted by thoughts, feelings, sounds, or physical sensations and their focus on the intended object is lost. At this point, the instruction is to notice these experiences ("distractions") fully without judgment, to "let them go," and return attention back to its intended object. Instructions for attending to "distractions" vary - from silently applying a specific label to the object (e.g., anger, anticipation, sound) to applying the general term "thinking" to any thought, to not making any mental notation whatsoever. Labeling an experience is believed to strengthen recognition of it and this may be particularly helpful for some individuals or when experiencing intense distractions. The process of becoming distracted and returning the attention is repeated over and over again during formal mindfulness practice. The goal is to increase awareness of present-moment experience to increasingly subtle levels and to strengthen stability of attention. The goal is not to ignore or "get rid" of thought in order to have a "blank" mind, but to notice with full attention whatever arises. In this sense, there are no distractions; whatever is noticed in the field of awareness can be observed. Interestingly, it can be painful to observe thoughts one wishes to avoid, so in this sense, the practice cultivates a willingness to experience discomfort and reduces attempts to escape it. At the other extreme, the goal is not to indulge in pleasant thought or achieve a pleasant experience (although this may occur), but to remain aware of each experience as it occurs.

Mindfulness and metacognition

A fundamental shift in the relation to thought and other objects of awareness is considered a pivotal, key mechanism of mindfulness training. This metacognitive process has been referred to as *decentering* and *reperceiving*, processes which have been similarly defined.[79, 84] Here we use the term reperceiving, which is defined as a "shift in perspective in that what was previously 'subject' becomes 'object'" (p. 378); or, in other words, consciousness becomes awareness of thought rather than thought itself. This shift in perspective is hypothesized to lead to the realization that "I am not that thought" allowing for greater flexibility in how to respond to thought or any experience when it occurs. This insight is argued to have manifold salutary effects on psychological functioning further elaborated below.[81] We feel this is a key process for defusing stress cognitions, as described in detail below (under appraisal and rumination sections).

Mindful states of consciousness are not confined to formal meditation practice, but are thought to carry over into daily activities. Additionally, as mindfulness is considered an innate capacity of human consciousness, individuals without formal training are thought to vary in the extent to which they are mindful. As such, self-report measures of dispositional mindfulness have been developed using non-meditators [85, 86]. Effects of mindfulness training have most commonly been studied a) in the context of an eight-week group intervention program, Mindfulness-Based Stress Reduction (MBSR) [87] or variations of this program tailored to meet the needs of specific populations, b) using brief inductions of mindfulness in laboratory settings, or c) comparing experienced meditators to controls, findings of which are highlighted below.

Mindfulness and attention

As noted, a central aspect of mindfulness training involves the self-regulation of attention. In support, recent studies find improved performance on attention-related behavioral tasks after mindfulness training. Jha and colleagues found improved ability to orient attention in response to an environmental cue, enhancing response accuracy and reaction time on a computerized task among MBSR participants compared to meditation-naïve participants.[88] The researchers also found individuals who completed a one-month mindfulness-based residential retreat increased accuracy of a target location when no prior cue was presented compared to controls, indicating an enhanced vigilant state of alertness. These findings suggest that mindfulness enhances attention-related responsiveness to environmental cues and ability to maintain alertness.

In line with these findings, two studies have shown that meditation training is associated with inhibition of habitual responding on the classic Stroop task, in which participants are asked to name the colored text of a word rather than the word itself (e.g., the correct response to the word ‘red’ appearing in blue-colored font is ‘blue’). [89, 90] Although a contrived laboratory task, the findings support the suggestion that automatic, “top-down” information processing is reduced following certain forms of meditation practice. One implication of the ‘deautomatization’ of thought is that it should lead to enhanced ability to notice nuanced details of experience from a fresh perspective and inhibit reliance on memories, expectations, and schemas during information processing.[91]

Meditation training has further been shown to reduce elaborative processing of previous stimuli thereby increasing attentional resources to present-moment experience.[92] The distribution of attentional resources as measured by performance on an attentional-blink task improved after a 3-month intensive mindfulness-based meditation retreat compared to controls.[92] Scalp-recorded brain potentials showed reduced brain-resource allocation to the first target embedded in a rapid stream of stimuli enabling increased identification of the second target.

Enhanced attention-related processes are hypothesized to improve early detection of potential stressors and increase the probability that effective coping will be implemented in a timely manner (Teasdale et al, 1995). Increased awareness of present-moment experience may also disrupt ruminative thought processes that play a role in prolonged stress reactivity and vulnerability to mental illness (Teasdale et al, 1995).

In addition, training in present-moment awareness appears to increase interoceptive processes, which involve awareness of visceral signals and subtle emotional feelings thought to be important in emotion regulation.[93] Using functional magnetic resonance imaging, increased neural activity of brain regions involved in processing present-moment experience was found following eight weeks of mindfulness training compared to controls.[94] Specifically, viscerosomatic brain areas showed greater activation (including the insula, secondary somatosensory cortex and infereior parietal lobule) when meditators compared to novices were asked to maintain an experiential momentary experience vs. a narrative self-focus after presentation of personality traits.[94] In a study of long-term mindfulness meditation practitioners, magnetic resonance imaging revealed greater cortical thickness in brain regions associated with interoception, including the right anterior insula, compared to controls.[95] These studies provide neural evidence that mindfulness meditation cultivates interoceptive awareness, which is thought to play a key role in maintaining present moment awareness and regulating emotions.

Mindfulness and cognitive appraisal

In regards to cognitive appraisals, to the extent mindfulness reduces identification with self-related cognition and goals through enhanced attention to present-moment experience and reperceiving, situations may be appraised as less threatening. Heppner and Kernis [96] argue that individuals who report greater dispositional mindfulness are less likely to interpret ambiguous behavior by others as reflecting hostile intent, and report less anger and desire to retaliate. In a mindfulness meditation induction experiment (as described in Heppner et al, 2007, citing unpublished analyses), participants exposed to a brief mindfulness practice (mindful eating of a raisin) displayed less aggressive behavior following social rejection compared to control participants. They suggest these participants may have experienced reduced reactivity to social threat because they attributed less hostile intent to the actor. In a study of relationship stress among romantic couples, those with higher dispositional mindfulness reported relatively more positive perceptions of their partner and relationship after discussing a conflict in a laboratory setting.[97] A randomized waitlist-controlled trial of an abbreviated MBSR program conducted among adults at their work-site, found reductions in global appraisals of life stress (using the Perceived Stress Scale) compared to control group participants.[98]

These studies support the notion that mindfulness facilitates interpretation of situations as less threatening, perhaps due to less activation of self-relevant concerns, so that events are responded to more thoughtfully, rather than reacted to through automatic filters of cognitive and emotional processes. Mindfulness is argued to promote “cognitive balance,” the ability to see clearly beyond assumptions, preventing common and habitual cognitive distortions.[99]

Mindfulness may also improve coping with events that are appraised as threatening in which there is little possibility of control. Mindfulness may serve to increase a sense of control, not simply by reacting more “coolly,” (with attenuated cycles of negative thoughts and emotions), but by lessening one’s perceived need to be in control, especially when situations are determined to be uncontrollable. In one controlled mindfulness-based meditation intervention of 28 healthy participants, those in the treatment group reported both increases in sense of control over life and increased willingness to let go of control efforts (greater use of acceptance/yielding to cope with stressors).[100]

Mindfulness training also improves the ability of patients to cope with a variety of chronic disease-related stressors that often afford limited opportunities for control. A meta-analysis of 20 studies examining effects of MBSR in patients with chronic illnesses (including cancer, fibromyalgia, and chronic pain) as well as those seeking to reduce stress, found a moderate effect size (Cohen’s d = ~.50) across observational, waitlist-controlled, and active-controlled studies.[101] Improvements in psychological functioning (e.g., anxiety and depressive symptoms, copying style) were observed in addition to improvements in physical health symptoms, including pain and physical impairment and function. Large, well-controlled studies that assess the active ingredients of mindfulness are still needed, yet the accumulated studies offer encouragement that MBSR is helpful in enhancing patients’ ability to cope with a wide range of chronic illnesses.

Other types of meditation and appraisal

Several other forms of meditation have been shown to reduce threat appraisals and enhance adaptive coping. A randomized controlled trial of mantra meditation (repeating a spiritually-related word or phrase throughout the day, including a focus on noticing and interrupting stressful thoughts) showed an increase in positive reappraisal, the tendency to reframe situations in a more positive light.[102] Robins, McCain et al. 2006 conducted an uncontrolled study of Tai Chi, a form of moving meditation focusing on breath, in a sample of 59

participants with HIV. Although they found no changes in other types of coping, there was a significant increase in positive reappraisal.[103]

Lastly, a randomized study of Cognitive Behavioral Stress Management (CBSM) which incorporates a variety of somatic and cognitive techniques including meditation, progressive muscle relaxation, cognitive restructuring, assertiveness training, and anger management, examined responses to a standardized laboratory stressor (TSST, described above). They found that those in CBSM made fewer stress appraisals, both threat and challenge, and experienced greater expected control. These appraisals mediated lower cortisol responses to the stressor.[104] A similar study followed 28 students, randomized to CBSM or a waitlist control group, and measured stress appraisals before a naturalistic stressor (an exam). Compared to the control group, those who received CBSM were less likely to appraise the exam as threatening (although equally likely to appraise it as challenging, thus changing the appraisal ratio), and had marginally greater perceived competence.[105] These studies show that forms of meditation practice and stress reduction other than mindfulness also reduce stress-related cognitions, partly by shifting appraisals of events from threatening to positive and/or challenging.

Mindfulness and ruminative thought

One key way in which mindfulness may protect one from the negative effects of stress is by decreasing rumination. Increasing awareness of present-moment experience may disrupt ruminative thought processes that play a role in prolonged stress reactivity. [106] The typical "instructions" for mindfulness meditation, to notice thoughts and let them go, target "the discursive mind " – the tendency to revisit the same thoughts repeatedly. As thoughts and feelings are experienced as transient mental events occurring within a wider context of awareness, attenuation of automatic identification and reactivity to them may occur. Over time, this more objective perspective on mental content, referred to as "meta-cognitive awareness," may interrupt ruminative thinking, increase the ability to evaluate the accuracy of thoughts, and allow greater freedom of choice in responding to thoughts and emotions.[84]

The practice of changing how one relates to thoughts and emotions contrasts with cognitive behavioral therapies that emphasize changing the content of thoughts. Mindfulness practice involves first allowing awareness of thought and then becoming less engaged or attached to the thoughts themselves before attempting to evaluate their accuracy.[99] This type of non-reactivity to inner experiences such as negative thoughts is one factor of a multi-factorial self-report measure of mindfulness.[86]

There are several studies that examine mindfulness and rumination. Mindfulness, as an individual difference variable, is related to less rumination.[107, 108] Conversely, mindfulness is negatively related to the more trait-like automatic habit of negative thinking,[108] suggesting that it may prevent tonic dysphoria and low self esteem, in addition to playing a role in coping with stressors. A recent randomized trial suggests that mindfulness training reduces ruminative thought and distraction to a larger extent than somatic relaxation. This reduction in rumination is thought to be key to reducing distress.[109]

Mindfulness may also influence the secondary response to negative emotions that perpetuates the cycle of negative thoughts (distress about distress). Mindfulness-Based Cognitive Therapy (MBCT), based on the MBSR program, specifically targets rumination and negative thought patterns associated with depression. A primary goal of the MBCT intervention developed for people with a history of depression is to shift the way participants relate to depressive thoughts and emotions, a process referred to as "decentering," in that thoughts are experienced more objectively as passing events in the mind rather than accurate reflections of reality. The program has been found to be effective for reducing depression

relapse in currently non-depressed patients in randomized usual-care controlled trials.[84, 110] Using semi-structured interview techniques to elicit memories of mildly depressive situations, the researchers found that mindfulness training increased the ability of participants to view their depressive thoughts and emotions with greater discrimination, evaluate the appropriateness of their thoughts and feelings, and gain greater perspective that their thoughts were self-generated rather than accurate reflections of reality.

Mindfulness and emotional reactivity

Mindfulness is theorized to enhance emotion regulation skills by increasing awareness of emotions, increasing the willingness to tolerate and accept distressing or uncomfortable emotions, and reducing emotional reactivity to provocative events and emotions themselves.[111]

The proposal that mindfulness improves affect regulation through enhanced awareness of emotional processes is supported by three studies on reactivity to emotional stimuli. In one study, participants were asked to label emotions expressed on human faces while undergoing functional magnetic resonance imaging (fMRI). Individuals scoring higher on a measure of trait mindfulness showed enhanced prefrontal cortical regulation of affect and reduced bilateral amygdala activity (typically associated with negative affective states) during affect labeling compared to a control labeling task.[112] Furthermore, those with high vs. low trait mindfulness showed strong negative associations between areas of prefrontal cortex and right amygdala activity. These findings point to neural substrates that may underlie aspects of the "*reperceiving*" process in which consciousness is shifted from identification with emotion to conscious awareness of emotion. The effect of this cognitive shift may be to disrupt or inhibit automatic affective responses, reducing their intensity and duration.[112, 113]

Brief mindfulness-based meditation training has been shown to reduce reactivity to emotional stimuli and increase willingness to be exposed to or tolerate negative stimuli. Participants who participated in a 15-minute focused breathing exercise akin to exercises taught in MBSR, reported less negative affect in response to images known to elicit negative emotions compared to two control groups instructed to either let their minds wander for 15 minutes or worry about certain aspects of their lives.[111] The mindfulness participants also continued to report moderate levels of positive affect throughout exposure to emotionally neutral images and were more willing to view additional negative images compared to the control groups.

In a randomized waitlist-controlled MBSR trial among employees, Davidson and colleagues (2003) found an increased pattern of left-sided anterior brain activation, known to be associated with state and trait positive affect, in response to positive and negative mood inductions in MBSR participants compared to waitlist group from pre to post intervention. Left-sided anterior activation has been associated with quicker emotional recovery following a negative event.[114] These studies indirectly support the idea that mindfulness promotes adaptive regulation of emotion.

In addition, mindfulness is linked to greater emotional well-being across studies with differing methodologies, including correlations of self-report levels of mindfulness with self-report emotional well-being, mindfulness induction experiments conducted in laboratories, and clinical trial interventions, as reviewed by Brown et al (2007). Trait levels of mindfulness have been associated with fewer emotional disturbances (e.g., depressive and anxiety symptoms), greater affective balance – high positive affect and low negative affect, and less difficulties with emotional regulation.[85, 86] In a 2-week experience-sampling study, reports of greater state mindfulness were associated with affective balance (higher positive affect and lower negative affect), independent of trait mindfulness.[85]

Mindfulness is also although thought to increase intensity and frequency of positive and pro-social emotions, including empathy, kindness and compassion for self and others (Wallace and Shapiro, 2006). A randomized study of mindfulness-based stress reduction demonstrated increased scores on a measure of empathy, the capacity to notice and feel what another is feeling.[115]

In summary, the early research reviewed above suggests that mindfulness appears to reduce stress cognitions – both the negative content of threat appraisals, the ruminative process of revisiting negative thoughts, as well as the secondary response of feeling distress about feeling distress.

Meditation and Stress arousal

In addition to mitigating stress-related cognitions and emotions, some types of meditation appear to reduce markers of stress arousal, both through the HPA axis, increasing vagal tone, and reducing markers of sympathetic arousal. Transcendental meditation (TM), a concentrative technique that uses silent repetition of a word or phrase as the object of awareness, has been the most extensively studied meditative technique. It appears to reduce systolic and diastolic blood pressure to levels comparable to pharmacologic treatment[116] and improves heart rate variability compared to an active control group.[117] It also appears to lower basal cortisol and lead to greater cortisol peaks in response to an acute stressor,[118-120] a profile that might be described as enhanced allostasis.[38, 121] TM and a similar type of concentrative meditation (the relaxation response technique) are also characterized by decreased oxygen consumption,[122, 123] carbon dioxide elimination,[124, 125] and salutary EEG patterns (theta and alpha activation).[126]

Little research has evaluated specifically the effects of mindfulness meditation on HPA axis arousal or autonomic activity[127] although similar effects as those found with transcendental meditation and the relaxation response could be predicted to occur. In one uncontrolled MBSR intervention study, cancer patients consistently showed decreased daily average cortisol values after one year of follow-up .[128] In a second study, lower cortisol responses to mental stress were observed after five days of practicing an integrated mind-body meditation approach incorporating mindfulness compared to a randomized relaxation control group.[129] However, one caveat is that mindfulness includes acknowledgement of distressing thoughts and feelings, which may initially increase arousal and emotional activity, but viewed as a developmental process, may progressively lead to decreased reactivity through enhanced awareness, tolerance of discomfort, and acceptance. Thus, for beginners, and periodically for experienced practitioners, mindfulness meditation is expected to produce increases in physiologic arousal.[130]

Several randomized controlled trials have demonstrated the effectiveness of CBSM on reducing peripheral stress arousal. CBSM training reduced urinary free cortisol and epinephrine in clinical samples.[131, 132] In one study of healthy participants, CBSM led to lower cortisol reactivity in response to a standardized laboratory stressor within 2 weeks[104] and, to a lesser extent, four months after the intervention.[133] To the extent that mindfulness or other forms of meditation promote the ability to buffer oneself from social evaluative threat -- recognizing that negative social judgments or reflected appraisals of the self (what one thinks others think about oneself) do not necessarily represent reality or a threat to one's self-worth, practitioners should indeed become less stress reactive.

Although concentrative and mindfulness meditation techniques may reduce HPA axis and autonomic arousal, the brain appears to respond to specific types of meditation in ways that may represent an adaptive attentional state to appraise stimuli. An fMRI study of meditation practitioners (who practiced Kundalini meditation in which focused attention on respiration

is linked to silent repetition of a phrase found increased activation of localized neural structures involved in attention (frontal and parietal cortex) and control of the autonomic nervous system (pregenual anterior cingulate, amygdala, midbrain, and hypothalamus) compared to a control nonmeditative condition.[134] These data suggest that as some meditation practices produce deep physical relaxation evidenced by reductions in autonomic and HPA arousal, these practitioners were engaged in an active attentional state of autonomic control, countering the notion that meditation is a state of mental as well as physical relaxation.

Further evidence suggests that meditation effects are not simply the result of volitionally reduced peripheral arousal. Results of a study comparing neural correlates of mindfulness meditation and respiratory biofeedback found that while some regions are engaged by both tasks, mindfulness meditation activates additional neural regions (e.g., right anterior insula).[135] Thus, while some forms of meditation engage attentional resources to induce a hypometablic state benefical for managing stress-related arousal, they also appear to modulate cognitive and emotional processes involved in the appraisal of stress, such as interoception.

Positive arousal

Several meditation studies have measured markers of positive health, such as anabolic hormones, and these may have relevance for cellular aging. As discussed above and reviewed elsewhere, several stress reduction interventions have induced increased heart rate variability and increased anabolic hormones such as DHEA.[136] Several uncontrolled studies of TM show healthier profiles of arousal, including greater levels of DHEA-S.[120, 137]

Meditation, oxidative stress, and health

Across controlled studies, mindfulness meditation appears to improve physical health symptoms and functioning across a variety of disorders, and increases measures of mental health, including reduced negative affect and increased quality of life.[138, 139] It is thought that these positive effects are mediated in part by reductions in psychological and physiological stress. TM has been linked to reduced cardiovascular disease risk factors and in controlled trials, has reduced blood pressure[116] and carotid artery atherosclerosis [140] as reviewed by Walton and colleagues.[141] [2893]

Oxidative stress may be an important mediator between stress and disease. It is linked to cardiovascular disease, as well as telomere shortening. Although few studies have examined oxidative stress balance, two initial studies found that meditation practitioners (TM and Zen) had lower levels of a marker of oxidative stress (lipid peroxidation).[142, 143]

Summary and Significance

Stress cognitions are important for survival, but if they are based on distorted perceptions, they may promote excessive stress arousal, creating a harmful milieu for cellular longevity. During the longevity conference that these proceedings are based upon, H.H. the Dalai Lama explained that emotions based on reason and analysis, tend to drive meaningful behavior. In contrast, emotions based on ‘false projections’ or fear-based beliefs are harmful to longevity. Here, as shown in Figure 1, we speculate that certain types of meditation can increase awareness of present moment experience leading to positive cognitions, primarily by increasing meta-cognitive awareness of thought, a sense of control (and decreased need to control), and increased acceptance of emotional experience. These cognitive states and skills reduce cognitive stress and thus ability for more accurate appraisals, reducing exaggerated threat appraisals and rumination, and distress about distress. These positive

states are thus stress-buffering. Increasing positive states and decreasing stress cognitions may in turn slow the rate of cellular aging.

There is some indirect support of aspects of this hypothesis involving stress cognitions. In our previous study, perceived life stress -- primarily an inability to cope with demands and feeling a lack of control, and higher nocturnal stress hormones (cortisol and catecholamines) were related to shorter telomere length.[2] Trait negative mood was related to lower telomerase activity, a precursor of telomere shortening.[144] Here we presented preliminary data from the same sample linking telomere length to higher proportions of challenge appraisals relative to threat appraisals in response to a standardized stressor. The results suggest that the relative balance of threat to challenge cognitions may be important in buffering against the long term wear and tear effects of stressors. To the extent that meditation mitigates stress-related cognitions and propagation of negative emotions and negative stress arousal, a longstanding practice of mindfulness or other forms of meditation may indeed decelerate cellular aging.

We also speculate about the physiological mechanisms. Above we have reviewed data linking stress arousal and oxidative stress to telomere shortness. Meditative practices appear to improve the endocrine balance toward positive arousal (high DHEA, lower cortisol) and decrease oxidative stress. Thus, meditation practices may promote mitotic cell longevity both through decreasing stress hormones and oxidative stress and increasing hormones that may protect the telomere. There is much evidence of neuroendocrine and physical health benefits from TM, which has a longer history of study than MBSR. The newer studies of mindfulness meditation are promising, and offer insight into specific cognitive processes of how it may serve as an antidote to cognitive stress states.

This field of stress induced cell aging is young, our model is highly speculative, and there are considerable gaps in our knowledge of the potential effects of meditation on cell aging. Several laboratories are working on diverse aspects of this model, which will soon allow it to be evaluated in light of the empirical data.

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Figure 1. Model of Mindfulness Meditation Effects on Telomere Length through Positive and Stressful Cognitive States

This speculative model has support for some relationships, as reviewed throughout this paper, but the full model remains to be tested. The dotted arrows represent inverse relationships. Positive cognitions are linked to affective balance (higher positive affect and lower negative affect) whereas stress cognitions are linked to greater negative affect. Positive cognitions and emotions may promote greater vagal tone, androgens, and growth hormone (GH) axis activity, whereas stress cognitions and negative affect lead to high cortisol, insulin, and oxidative stress. Mindfulness may promote positive arousal directly and/or through positive cognitions, and may inhibit negative arousal directly and/or through dampening stress cognitions. Lastly, the positive pathway and the negative stress pathway tend to counter-regulate each other (arrows not shown), and have opposite effects on telomere maintenance. Specifically, we pose that positive arousal promotes and stress arousal prevents telomere maintenance.