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Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study

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Summary
Background: Psychological distress and metabolic dysregulation are associated with markers of accelerated cellular aging, including reduced telomerase activity and shortened telomere length. We examined whether participation in a mindfulness-based intervention, and, secondarily, improvements in psychological distress, eating behavior, and metabolic factors are associated with increases in telomerase activity in peripheral blood mononuclear cells (PBMCs).
Methods: We enrolled 47 overweight/obese women in a randomized waitlist-controlled pilot trial ($n = 47$) of a mindfulness-based intervention for stress eating and examined changes in telomerase activity from pre- to post-intervention. In secondary analyses, changes in telomerase activity across the sample were examined in relation to pre- to post-intervention changes in psychological distress, eating behavior, and metabolic factors (weight, serum cortisol, fasting glucose and insulin, and insulin resistance).
Results: Both groups increased in mean telomerase activity over 4 months in intent-to-treat and treatment efficacy analyses ($p < 0.001$). Nonsignificant trends showed that greater attendance

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was associated with increases in telomerase, and telomerase increases were 18% higher among 'as treated' participants compared to controls. Across groups, changes in chronic stress, anxiety, dietary restraint, dietary fat intake, cortisol, and glucose were negatively correlated with changes in telomerase activity. In exploratory analyses, decreases in dietary fat intake partially mediated the association between dietary restraint and telomerase activity with marginal significance.

Conclusions: While there was no clear effect of the intervention on telomerase activity, there was a striking pattern of correlations between improvements in psychological distress, eating behavior, and metabolic health and increases in telomerase activity. These findings suggest that telomerase activity may be in part regulated by levels of both psychological and metabolic stress.

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1. Introduction

Chronic stress and overeating are prevalent in modern societies and can lead to metabolic dysregulation. Chronic stress can promote overeating, which, in turn, can elevate cortisol, glucose, and insulin levels, cause weight gain, and increase inflammatory and oxidative stress processes (Epel, 2009). Growing evidence suggests that these biological factors work together to accelerate cellular aging by inhibiting the telomere maintenance system.

Telomere length in immune cells provide a window into the aging of the immune system (Andrews et al., 2010). Telomeres are DNA—protein complexes at the end of linear chromosomes, required for the complete replication of DNA and chromosome stability. Intact telomeres protect chromosomes from nuclease degradation, end-to-end fusion, and cellular senescence. The cellular enzyme, telomerase, adds telomeric repeat sequences to the chromosomal DNA ends, preserving not only telomere length but also healthy cell function and long-term immune function (Blackburn, 2000). An aged immune system, as indicated by shorter telomere length (TL) and lower telomerase activity, secretes pro-inflammatory cytokines (Effros, 2007) and is predictive of earlier cell mortality and mortality in people (Bakaysa et al., 2007; Cawthon et al., 2003; Honig et al., 2006; Kimura et al., 2008; Martin-Ruiz et al., 2006). However, cells containing chromosomes with shortened telomeres can remain genetically stable if telomerase activity is high (Blackburn, 2000). Recently, telomerase was found to be expressed at low levels in PBMCs and to be a dynamic enzyme capable of immediate and short term changes (Broccoli et al., 1995; Weng et al., 1996). Thus, PBMC telomerase can be measured over short time periods (hours or weeks), unlike telomere length, which is thought to take months to years for changes to be detectable (Epel et al., 2010). Studying telomerase activity provides a unique opportunity to examine how lifestyle and metabolic factors affect the aging process, and further, if modulating lifestyle retards cellular aging processes.

Emerging research suggests that an unhealthy lifestyle, including psychological distress, poor nutrition, and physical inactivity, is associated with either lower telomerase or shorter TL. Chronic psychological stress and mood disorders are linked to shorter telomere length (Damjanovic et al., 2007; Epel et al., 2004; Lung et al., 2007; Puterman et al., 2010; Simon et al., 2006) and dampened telomerase activity (Epel et al., 2004). Conversely, longer leukocyte telomeres are related to a more healthy diet, including greater intake of antioxidants (multivitamins, vitamins C, E, D) (Richards et al., 2007; Xu et al., 2009); less processed meat consumption (Nettleton et al., 2008); greater frequency or intensity of exercise (Cherkas et al., 2008; Puterman et al., 2010; Werner et al., 2009); and a healthy lifestyle index consisting of greater intake of fruits and vegetables, less dietary fat and cigarette smoking, and greater exercise (Mirabello et al., 2009). Further, dietary restraint, a set of attitudes and behaviors reflecting a preoccupation with weight and unsuccessful attempts to restrict calorie intake that can result in episodic overeating, has been related to shorter TL (Kiefer et al., 2008).

Metabolic factors, including a greater body mass index (BMI), abdominal fat, and increased circulating glucose levels, have been related to shorter TL and lower telomerase activity (Epel et al., 2006; Valdes et al., 2005). Increases in body mass index, and in particular, insulin resistance, predict telomere shortening over a 10—13 year period (Gardner et al., 2005). Further, higher levels of nocturnal cortisol excretion, an indicator of chronic stress, are related to shorter TL (Epel et al., 2006). In vitro, exposure to high levels of cortisol dampens telomerase activity (Choi et al., 2008).

These studies suggest that lifestyle and metabolic factors are related to the telomerase/telomere length maintenance system. However, it is not clear whether reducing psychological distress and improving health behaviors can improve cell aging. No controlled studies have yet examined the effects of lifestyle interventions on TL; however, two studies have examined associations of behavioral interventions with telomerase activity. In one study, men diagnosed with early stage prostate cancer participating in a 3-month intensive lifestyle change program involving diet, exercise, stress management, and group support had increased telomerase levels in PBMCs from pre- to post-intervention (Ornish et al., 2008). However, this study lacked a randomized control group. In a second study, telomerase was examined at the end of a randomized controlled trial of a 3-month residential meditation program. The meditation group had higher post-intervention telomerase than the waitlist control group, and increases in psychological well-being (increased perceived control and purpose in life and decreased negative affectivity) were related to higher post-intervention telomerase in the treatment but not control group (Jacobs et al., 2011). No studies, to our knowledge, have examined the effects of