THESIS

EFFECTS OF A MINDFULNESS-BASED INTERVENTION ON DEPRESSIVE SYMPTOMS, STRESS EATING, AND TELOMERE LENGTH IN ADOLESCENTS AT-RISK FOR ADULT OBESITY

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ABSTRACT

EFFECTS OF A MINDFULNESS-BASED INTERVENTION ON DEPRESSIVE SYMPTOMS, STRESS EATING, AND TELOMERE LENGTH IN ADOLESCENTS AT-RISK FOR ADULT OBESITY

Rates of adolescent obesity and cardiometabolic diseases such as type 2 diabetes are increasing. Recent studies suggest that depression symptoms may be one contributor to obesity and cardiometabolic diseases through stress-related behavioral mechanisms (e.g., stress-eating) and physiological mechanisms (e.g. shortened telomeres). From an allostatic load framework, depression symptoms affect the biological system, potentially exerting sustained damage on stress physiology, and thus, contributing to cardiometabolic disease risk. Mindfulness-based interventions (MBIs) have demonstrated favorable impacts for lowering depression symptoms and lowering symptoms of stress-related eating patterns, yet these effects have not been well studied in adolescents. In the current randomized controlled pilot study, I conducted secondary analyses to explore the effects of a six-session MBI group on lowering depression symptoms, reducing stress-eating, and preserving telomere length, compared to a six-session health education (HE) control group, in 25 adolescent girls (n=14; 56%) and boys (n=11; 44%) at-risk for adult obesity (body mass index [BMI] z-score M=1.56, SD=.55). At baseline/prior to the intervention and again, at an 18-month follow-up, perceived stress and depression symptoms were assessed with validated surveys, stress-eating by laboratory test meal, and average telomere length from whole blood. Dispositional mindfulness by questionnaire, BMI from fasting weight and height, and fasting blood glucose levels were also measured at the same intervals. Analyses of covariance were used to test group condition as a predictor of baseline to 18-month change scores, controlling for the respective baseline level of the outcome variable. Results showed that adolescents who were randomized to the MBI group had less change in stress-eating from baseline to 18-months than those randomized to HE (*M*=-49.44, *SD*=81.47 kcal vs. *M*=217.42, *SD*=84.88 kcal, Cohen's *d*=.74, *p*=.04). There were no other significant between-condition effects. There were moderate, favorable non-significant effects of MBI, compared to HE, for perceived stress (*d*=.45, *p*=.21) and depression symptoms (*d*=.50, *p*=.23). There was no significant effect on telomere length (*d*=.05, *p*=.91). Changes in dispositional mindfulness, BMI, and fasting blood glucose levels were small and also non-significant. Findings from the current project suggest that a relatively brief, MBI group reduces stress-eating in adolescents at-risk for adult obesity over a year and a half later. To what extent MBI, delivered alone or in combination with additional supports, ultimately affects allostatic load and cardiometabolic health remains to be tested in a larger trial.

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INTRODUCTION

In recent years, there has been a rise in the prevalence of obesity and cardiometabolic diseases such as type 2 diabetes among adolescents (Dabelea, Hamman, & Knowler, 2017). An estimated 18.5% of adolescents in the United States have a body mass index (BMI; kg/m^2) equal or exceeding the 95th percentile for age and sex as of 2016 (Hales, Fryar, Carroll, Freedman, & Ogden., 2018). Depression symptoms have increasingly become recognized as one likely contributor to the development of obesity and cardiometabolic disease (Dallman, 2010; Milaneschi, Simmons, Rossum, & Penninx., 2018). Depression may contribute to the development of excess weight gain and adverse cardiometabolic outcomes through stress-related behavioral and physiological mechanisms; yet, this association also likely works in the reverse direction, particularly in adults, such that having obesity and cardiometabolic disease promotes psychological difficulties due to the burden and stigma of having obesity and/or an obesity-related chronic disease (Filho, Lima, Vasconcelos, Freitas de Lucena, Maes, & Macedo, 2018; Maner, Dittmann, Meltzer, & McNulty, 2017). From a developmental pathophysiological framework, alterations in stress-related behaviors (e.g., stress-eating) and stress-related physiology (e.g., allostatic load) offer possible pathways through which depression contributes to markers of cardiometabolic disease risk (e.g., BMI, blood glucose; **Figure 1**; Fitzpatrick et al., 2007; Manoliu et al., 2017; Pariante & Lightman, 2008). Adolescence is a particularly important window to understand and potentially intervene to alter stress-related mechanisms and cardiometabolic health trajectories.

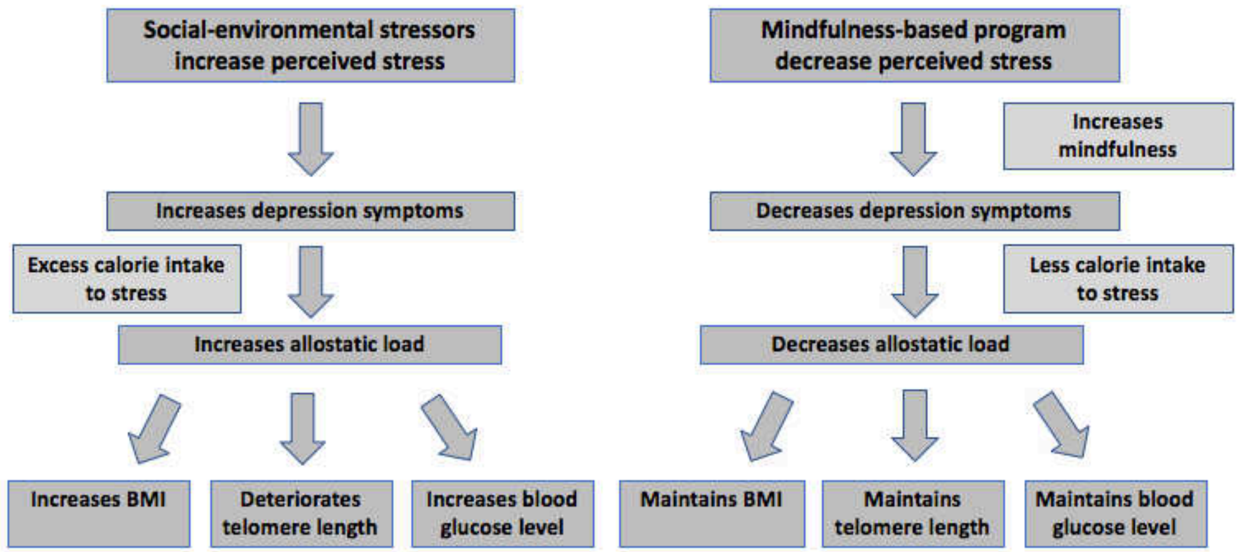

Figure 1. Guiding conceptual model for the study

Stressors resulting from relationships, conditions at home, school/academic factors, and within peer groups are of particular relevance to adolescents, who are already undergoing a variety of hormonal changes as a result of puberty, which taken together, all significantly increase susceptibility to environmental stressors during this age span (Bos, Rooij, Miers, Bokhorst, & Westenberg, 2014; Romeo, 2013). Given such heightened sensitivity, many psychopathologies, including major depressive disorder (MDD), initially develop during adolescence, which then persist into adulthood if untreated (Juster, McEwen, & Lupien, 2010). This sensitive period for psychopathology may be a result of both adolescents' increased susceptibility to environmental stressors and adolescents' growing and adapting stress response system. Adolescents are experiencing key changes to their stress response system, which render them particularly susceptible to environmental stress; adolescents' stress response can be fundamentally altered by the amount of stress they perceive during this time period. Yet, there is also the strong potential that intervening to reduce adolescents' perceived stress might serve to lessen depression symptoms and in turn, ameliorate cardiometabolic risk (Juster, McEwen, & Lupien, 2010).

Allostatic load offers one conceptual biological framework to describe how the body responds to various stressors. Broadly, allostatic load describes the body's adapting of internal conditions in response to the external environment (Juster, McEwen, & Lupien, 2010). For example, allostatic load describes how the body produces adrenaline in response to a stressful environmental stimulus and increases heart rate and blood pressure to better oxygenate the brain and muscles so as to respond to the environmental stimuli. Sustained, chronic environmental stress can result in psychological problems, including depression, and result in abnormal allostatic load. Allostatic load can be measured by a variety of different neuroendocrine (cortisol), immune (pro and anti-inflammatory agents), metabolic (insulin), cardiovascular (blood pressure), and anthropometric biomarkers (body mass index; BMI kg/m^2) (Juster, McEwen, & Lupien, 2010). Abnormal allostatic load would be indicated by elevated levels of cortisol, inflammatory agents, insulin, blood pressure, and above-average BMI scores.

One particularly important biomarker with long-term health implications are telomeres, regions of non-coding DNA that cap the ends of chromosomes to protect them from degradation, that shorten with age (Blackburn, 1991; Blackburn, Epel, & Lin et al., 2015). Telomeres can be adversely impacted by abnormal allostatic loads (Tomiyama et al., 2012). Given telomeres' importance to protecting genomic stability and how they can be adversely impacted by abnormal allostatic loads, telomere length dynamics may be an especially representative biomarker of long-term, overall health (Blackburn, Epel, & Lin et al., 2015). During early childhood, telomere length sharply decreases as a result of rapid cell division (Epel, 2009; Zeichner et al., 1999). This period of shortening begins to taper off starting in late childhood/adolescence and plateaus at early to middle adulthood (Epel, 2009; Zeichner et al., 1999). Adolescence is a formative time, both for finalizing development during puberty and in formation of stress response systems (Epel, 2009; Zeichner et al., 1999). The influences of stress on allostatic load and telomere length, adolescent's increased susceptibility to environmental stress, and lack of fully developed stress management systems, place adolescents at a particular risk of accelerated telomere attrition. Any additional telomere attrition resulting from abnormal allostatic load levels during adolescence can therefore have a huge impact on long-term health because shorter telomere lengths in adults have been associated with increased risk of cancer, diabetes, heart disease, and earlier mortality (Epel, Daubenmier, Moskowitz, Folkman, & Blackburn., 2009; Ma et al., 2011; Weischer, Bojesen, Cawthorn, Frieberg, Hansen, & Nordestgaard, 2012; Zhao et al., 2014). Alternatively, stress-reduction interventions in adolescents at-risk for adult obesity and cardiometabolic disease may alleviate allostatic load, better preserve telomere length, and decrease risk of adverse health outcomes in adulthood.

Mindfulness-based interventions (MBIs) may be particularly well-suited to intervene in adolescence to improve perceived stress, stress-related behaviors including stress-eating, and slow deterioration of telomere length. Mindfulness can be described as awareness of and attention to the present moment in a non-judgmental way (Kabat-Zinn, 1994). Mindful attention and awareness can be directed toward environmental factors (e.g., sounds, sights) or intrinsic factors (e.g., breath, body sensations). Through increasing general, dispositional mindfulness, MBIs have been used to lower depression and anxiety symptoms in adults (Makki, Ajmal, & Bajwa, 2018; Matousek, Dobkin, & Pruessner, 2010). Studies have shown that a standard program developed for adults, mindfulness-based stress reduction (MBSR), also may have a significant impact on improving stress physiology. For instance, MBSR programs have been found to lower secretion of both blood and salivary levels of cortisol, a key hormone in the body's physiological response to stress and in allostatic load models (Matousek, Dobkin, &

Pruesner, 2010). These findings have been observed both at post-intervention and a longer-term follow-up and some, but not all, studies have utilized a control group. MBIs have also been specifically employed to treat stress-related eating behaviors, including disordered eating such as binge or emotional eating, and excess weight in adults (Matousek, Dobkin, & Pruesner, 2010; Katterman, Kleinman, Hood, Nackers, & Corsica, 2014). MBIs are thought to address disordered eating behaviors through the development of enhanced internal awareness, increased self-acceptance, cognitive flexibility, increased compassion, and a generally improved capacity to cope with emotions (Katterman, Kleinman, Hood, Nackers & Corsica, 2014). These mechanisms would be expected to provide individuals with a greater awareness of internal feelings, including hunger and satiety, which may facilitate more effective self-regulation of eating in response to appetitive cues (Annameier et al., 2018). Additionally, increased ability to cope with difficult emotions would be anticipated to lessen disordered eating and stress-eating as a method to cope with negative affect (Pearson et al., 2018).

Preliminary literature shows that MBIs, ranging in length from 6-10 weeks, are as effective as cognitive-behavioral therapy (CBT) groups for addressing binge and emotional eating behaviors, but show less robust results for weight loss outcomes as compared to CBT, dietary education, and other control groups (Katterman, Kleinman, Hood, Nackers, & Corsica, 2014). Results from randomized control trials demonstrate that mindfulness may be just as effective as CBT in managing/reducing binge and emotional eating behaviors, and results from such interventions persist up to 4 months post intervention (Kristeller, Wolever, & Sheets, 2014). Although the mechanisms are not fully understood, one possibility is that MBIs work to increase dispositional mindfulness and lessen perceived stress, thereby minimizing stress-eating and alleviating allostatic load to ultimately decrease cardiometabolic risk (Epel, Lin, Wilhelm et al, 2006; Epel et al., 2009).

Building from the existing literature on stress, cellular aging, and cardiometabolic diseases (Epel, Lin, Wilhelm et al, 2006; Epel et al., 2009), the current project is guided by a model in which social-environmental stressors are proposed to increase perceived stress and heighten depressive symptoms in adolescents. In turn, depressive symptoms result in increased stress-eating that leads to excess calorie and high-fat/high-sugar intake (Mooreville et al., 2014). Such eating patterns increase metabolic demands on the body resulting in increases to allostatic load, which promote shorter telomere lengths (Epel, Blackburn, Lin, Dhabhar, Adler, Morrow, & Cawthon., 2004; Epel, Daubenmier, Moskowitz, Folkman, & Blackburn., 2009; Tomiyama et al., 2012). By intervening during adolescence through mindfulness-based stress management strategies, we anticipate that general, trait mindfulness will increase, perceived stress, depressive symptoms, and stress-eating will decrease, and alleviating allostatic load will manifest as preserved telomere length. This process is expected to result in weight stabilization and lessening of cardiometabolic disease risk.

Current Research

In the current master's thesis study, I conducted secondary analyses of a randomized controlled pilot study in which adolescents at-risk for excess weight gain participated in a mindfulness-based group intervention or a health education (HE) control group. As previously reported, the main results were that a mindfulness-based group was feasible and acceptable to adolescent girls and boys at-risk for adult obesity (Shomaker et al., 2019). In secondary analyses, adolescents randomized to MBI displayed decreased food reward sensitivity, referring to the propensity to find food rewarding relative to other reinforcers, and they tended to show decreased stress-eating at six-months follow-up (Shomaker et al., 2019). Percent body fat decreased 2-3% over six-months in both conditions, with no between-condition difference in adiposity or BMI indices (Shomaker et al., 2019).

Drawing on the guiding conceptual framework, the aim of this thesis study was to explore the following questions: 1) Did participation in MBI have a longer-term/sustained impact on increasing dispositional mindfulness and reducing perceived stress, depression symptoms, and stress-eating? 2) Did participation in MBI lead to better maintenance of telomere length? and 3) To explore if changes among mindfulness, perceived stress, depression, stress-eating, and telomere length were related in the sample overall or within conditions. The hypotheses were that those randomized to MBI would show more mindfulness, less perceived stress, less depressive symptoms, less stress-eating, and less telomere attrition over an 18-month follow-up period, as compared to adolescents who were randomized to health education. We anticipated that changes in these factors would correspond. We also expected stabilization to both BMI (weight stabilization) and fasting glucose levels (cardiometablic disease risk factor).

METHOD

Participants and Procedure

In this study, we utilized a convenience sampling technique to recruit volunteers. Recruitment entailed sending letters to families with adolescents within a 60-mile radius of Fort Collins, Colorado. Additionally, flyers were distributed in local schools, community clinics, and agencies alongside advertisements in newspaper, radio, and on social media within the local community. Informational sessions were held at local schools and community events. Adolescent volunteers were recruited to take part in a group program to lower stress and promote healthy weight gain (Shomaker et al., under review). Inclusion criteria were: (i) age 12-17 years, (ii) at-risk for adult obesity as determined by either being above-average weight (BMI $\geq 70^{th}$ percentile for age/sex) or having two biological parents with reported obesity (BMI ≥ 30 kg/m^2), and (iii) good general health determined as parental report on a health history interview. Exclusionary criteria were: (i) psychiatric symptoms that would impede compliance and necessitate treatment (e.g., suicidal behavior), (ii) major medical problem (e.g., type 1 or 2 diabetes, musculoskeletal problems), (iii) medication affecting weight, mood, and/or eating (e.g., antidepressants, insulin sensitizers, stimulants), (iv) current weight loss treatment or psychotherapy, and (v) pregnancy in females.

Intervention Groups

After a screening to determine eligibility and to collect baseline assessments, 54 participants were randomized to take part in either the Learning to BREATHE MBI group or a HE didactic control group program. Both conditions met for six one-hour weekly sessions during after-school hours from May 2015 to March 2017 (spread over five separate cohorts).

Learning to BREATHE (MBI)

In the current study, Learning to BREATHE was delivered as a six-week MBI curriculum derived from MBSR (Kabat-Zinn, 1991) and adapted for adolescents. Experiential activities and guided discussions to teach standard mindfulness skills were designed to reduce stress, depression, overeating, and prevent the onset of diabetes in adolescents (Broderick, 2013). Examples included breath awareness, body scanning, mindful eating, sitting meditation, loving-kindness practice, and gentle yoga. Brief (~10 minutes/day) homework was assigned for practicing skills in daily life. Adolescents were given meditation audio-recordings, a yoga mat, meditation cushion, homework log, and worksheets. They reported homework completion to facilitators at sessions 2-6. The intervention was co-facilitated by Master's graduate students in Marriage and Family Therapy who attended a workshop with the developer and reviewed/practiced material with the lead investigator, a licensed clinical psychologist. Facilitators received weekly supervision on audio-recorded sessions.

Health Education (HE)

HE was drawn from a didactic program, "Hey Durham" (Bravender, 2005). Group sessions incorporated handouts, videos, and presentations. As in our previous trials (Shomaker, et al., 2016; Shomaker, et al., 2017), sessions covered six topics: alcohol/drug use, nutrition/body image, domestic violence, gang violence/non-violent conflict resolution, sun safety, and major depression/signs of suicide. No direct counseling was provided. HE was co-facilitated by Master's graduate students in Food Science and Human Nutrition, Public Health, and Prevention Science.

Outcome Measures

Measures evaluated in this study were assessed at two time points: (i) baseline prior to the intervention and (ii) 18-month follow-up. All assessments were administered at both intervals, unless otherwise noted.

Trait Mindfulness

Adolescents completed the Mindful Attention Awareness Scale (MAAS) to measure general trait or dispositional mindfulness. This 15-item survey contains items rated on a 1 (almost always) to 6 (almost never) Likert scale (Brown & Ryan., 2003). The total score is the sum of all items (Total Score possible range: 15-90) with higher scores reflecting a more positive valence and greater trait mindfulness. Studies have shown that the MAAS can be reliably administered to adolescents, that higher scores on the MAAS correlate with better mental health indicators, and that trait mindfulness scores can be significantly improved directly following MBSR and sustained at 12-month follow up (Brown, West, Loverich, & Biegel, 2011; Shapiro, Brown, Thoresen, & Plante, 2010).

Perceived Stress

The 10-item Perceived Stress Scale was administered to measure adolescents' perceptions of stress (Kupst et al., 2015). The total score is calculated as the sum of all items, with each item rated on a 5-point Likert scale and higher values reflecting greater stress (Total Score possible range: 0-50; Cohen et. al., 1983).

Depression Symptoms

To evaluate symptoms of depression over the past two weeks, the 20-item Center for Epidemiologic Studies-Depression Scale (CES-D) was utilized. The CES-D items range from 0-3, with 0 representing no symptom at all and 3 representing nearly every day (Radloff, 1977). The CES-D total score is calculated as the sum of all items (Total score range: 0-60), and there is support for convergent validity with interview-based measures of depression in adolescents (Garrison, Addy, Jackson, McKeown, & Waller, 1991).

Laboratory Stress-Eating Paradigm

To assess stress-eating, participants were given a lunch-item test meal following exposure to the Trier Social Stress Test for Children (TSST-C). The TSST-C is a validated platform to induce a subjective and physiological stress response in a laboratory setting (Yim, Quas, & Cahill., 2010). The participant is required to give a speech and to take a mental arithmetic test challenge in front of an interviewer who gives no feedback or encouragement (Yim, Quas, & Cahill., 2010). Following the TSST-C, the participant was offered a meal comprised of ~4,500 kcal and instructed to eat as they normally would prior to the researcher leaving the room. Each food item was weighed to the nearest 0.1 gram before and after being served so as to determine total kcal consumed in response to stress. Participants observed an overnight fast prior to the visit and were served a standardized breakfast shake in the morning prior to the blood draw. Thus, the test meal represented a midday meal.

Blood Collection for Telomere Length Analysis and Fasting Glucose

Following an overnight 12-hour fast, a fasting blood sample was collected from adolescents by a trained phlebotomist. Whole blood was stored in a Thermo scientific (-80° C) freezer. DNA was then isolated from blood samples, and telomere length was analyzed using QPCR (polymerase chain reaction) assay. The QPCR method has been empirically validated to be just as reliable as the southern blot method for telomere length analysis (Cawthon., 2009). Fasting blood also was evaluated for glucose using a STAT Plus Glucose Lactate Analyser immediately after blood was drawn.

Statistical Plan

Descriptive information about the study sample was evaluated to check for problems with skew or kurtosis and to correct for outliers. Retention at 18-months was described and baseline characteristics were evaluated as predictors of attrition. To address the main aims, univariate analyses of covariance (ANCOVAs) were used to explore the effect of condition (MBI vs. HE) on change from baseline to 18-month in dispositional mindfulness, perceived stress, depression symptoms, stress-eating, telomere length, BMI, and fasting glucose, controlling for the respective baseline level of the outcome. We also conducted correlational analyses to explore the bivariate relations among baseline to 18-month changes in mindfulness, perceived stress, depression, stress-eating, telomere length, BMI, and fasting glucose by condition. Because the sample was a small pilot, we primarily expected to observe patterns as opposed to statistical significance, defined as $p < .05$. We report both statistical significance and trend-level associations, defined as $p < .10$. We also estimated effect sizes with Cohen's *d*, with .20 a small effect size, .50 a moderate effect size, and .80 or higher a large effect. Once primary data collection has been completed for the total sample (up to 54 participants), a full analysis will be conducted that will consider additional covariates.

RESULTS

Descriptive Information

Of the 54 total adolescents originally randomized to an MBI group (*n* = 29) or HE group (*n* = 25), 39 have completed 18-month follow-ups, to date. We anticipate that an additional 12 adolescents will complete 18-month follow-ups within the next 3-6 months.

Twenty-five adolescents (MBI: *n* = 13; HE: *n* = 12) have had telomere length assessed at baseline and 18-month follow-up, and this subset was used in the current analyses. We examined baseline characteristics in the current cohort of 25 youth in comparison to the 29 adolescents who were not studied, either because they have not yet completed an 18-month follow-up (*n* = 15) or because they were missing telomere data (*n* = 14). There were no significant differences in any baseline characteristic. There was only one trend-level difference, such that adolescents in the current cohort tended to have higher trait mindfulness (Mean ± SD 62.32 ± 14.96) compared to adolescents who were not studied (54.96 ± 13.85, $t = 1.86$, $p = .07$).

Within the *n* = 25 subset evaluated in the current project, we were missing a small amount of data for trait mindfulness (*n* = 1; HE group at 18-months) and BMI/weight status (*n* = 1; HE group at 18-month follow-up).

Baseline and follow-up characteristics by MBI and HE conditions are displayed for descriptive purposes in **Table 1**.

Table 1. Baseline characteristics of current telomere study participants by (MBI) or health education (HE) group assignment

Characteristic	MBI (*n*=13)		HE (*n*=12)	
	Baseline	18-months	Baseline	18-months
Demographic				
Age, years	13.77 (1.53)	15.36 (1.56)	14.65 (1.90)	16.24 (1.94)
Race/ethnicity, *n* (%)				
White	61.5%		83.3%	
Hispanic	30.8%		16.7%	
Asian	7.7%		0%	
Anthropometric				
BMI, kg/m^2	26.38 (3.63)	27.54 (5.25)	27.68 (5.93)	29.63 (8.02)
BMI z score	1.57 (0.50)	1.45 (0.7)	1.55 (0.62)	1.43 (0.67)
BMI percentile	91.88 (9.65)	88.2 (14.95)	90.91 (8.8)	88.34 (12.47)
Body fat, %	35.4% (6.7)	34.3% (10.1)	31.6% (6.7)	30.7% (9.2)
Weight Status, *n* (%)				
Lean (BMI<85)	23.1%	30.8%	25.0%	27.3%
Overweight (BMI 85-94)	7.7%	15.4%	33.3%	27.3%
Obese (BMI ≥95)	69.2%	53.9%	41.7%	45.4%
Stress-Eating, kcal	713 (227)	705 (280)	853 (441)	1025 (353)
Trait mindfulness	61.69 (15.98)	67.54 (15.26)	63.00 (14.44)	65.82 (11.47)

Note: Values depicted are means (standard errors) of measurements taken at baseline and 18-month follow up.

Group Condition Effects

A summary of all within and between-group condition effects are displayed in **Table 2**. Accounting for baseline mindfulness, general dispositional mindfulness exhibited no change, on average, from baseline to 18-months within either condition, and there was no significant between-group difference in mindfulness change from baseline to 18-months (Figure 1a; Cohen's d = .28). Accounting for baseline perceived stress, perceived stress significantly decreased, on average, from baseline to 18-months within the MBI condition only (95% CI: -8.33, -0.10), but did not significantly change within HE; however, the between-group difference in change in perceived stress from baseline to 18-months did not reach statistical significance although this represented a moderate effect (Figure 2b; Cohen's d = .45). Accounting for baseline depressive symptoms, depressive symptoms exhibited no statistically significant change from baseline to 18-months within either condition, and the between-group differences was also non-significant and moderate in size (Figure 2c; Cohen's d = .50).

Table 2. Summary of analyses of covariance (ANCOVAs) examining group condition as a predictor of changes in outcomes from baseline to 18-month follow-up

Characteristic	MBI	HE	*p*-value Between-Conditions
Trait Mindfulness	5.30 (2.98)	1.92 (3.24)	.45
Perceived Stress	-4.22 (1.99)	-.51 (2.07)	.21
Depressive Symptoms	-1.76 (2.56)	2.82 (2.66)	.23
Kcal Consumed	-49.44 (81.47)	217.42 (84.88)*	.04
Fasting Glucose, mg/dL	5.91 (2.45)	8.37 (2.45)	.49
BMI, kg/m^2	1.33 (.64)	1.77 (.67)	.64
BMI, z	-.13 (.10)	-.02 (.10)	.44
BMI, percentile	-2.99 (1.49)	-1.26 (1.62)	.44
Telomere Length, µg/mL	-.02 (.05)	-.03 (.05)	.91

Note: Values depicted are means (standard errors) of the change scores, and control for the baseline level of the change score/outcome. *Refers to significant within-condition change, $p < .05$.

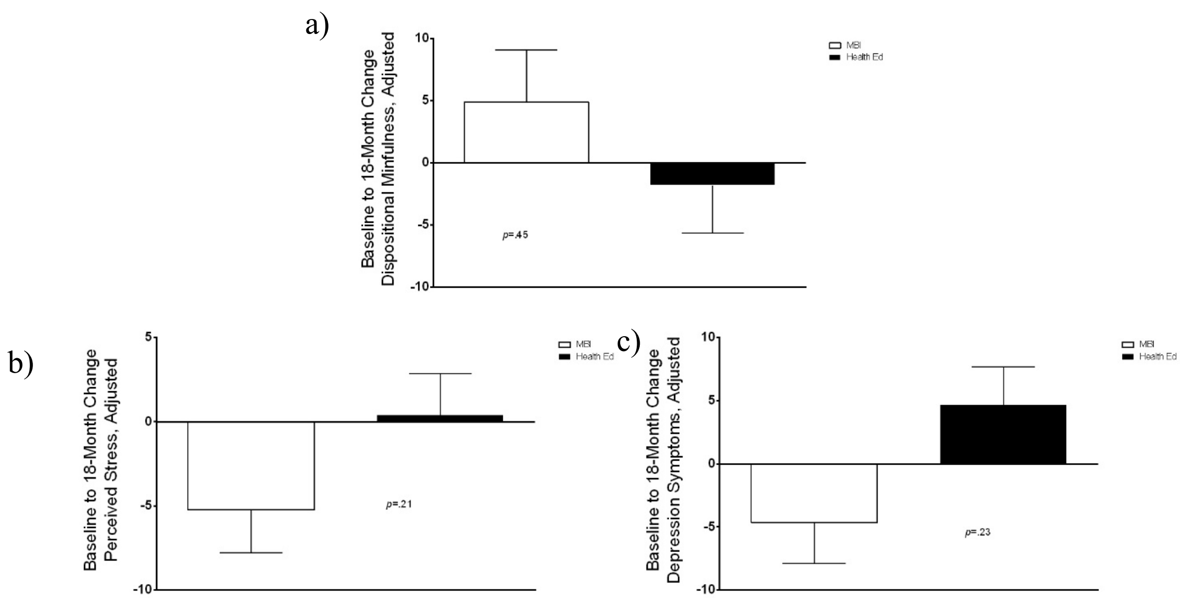

Figure 2. Baseline to 18-month change in (a) dispositional mindfulness, (b) perceived stress, and (c) depressive symptoms

Accounting for baseline telomere length, telomere length exhibited no change from baseline to 18-months within either condition, with no between-group difference (Figure 3a; Cohen's d = .05). Likewise, BMI was stable from baseline to 18-months within both conditions, with no statistically significant between-group difference (Figure 3b; Cohen's d = .16). Accounting for baseline stress-eating, stress-eating significantly increased, on average, within HE (95% CI: 41.39, 393.44), but exhibited no significant change within MBI, and there was a significant between-group difference (Figure 3c; Cohen's d = .74, p = .04). Accounting for baseline fasting glucose, fasting glucose exhibited no change from baseline to 18-months within either condition and there was no statistically significant between-group difference (Cohen's d = .29).

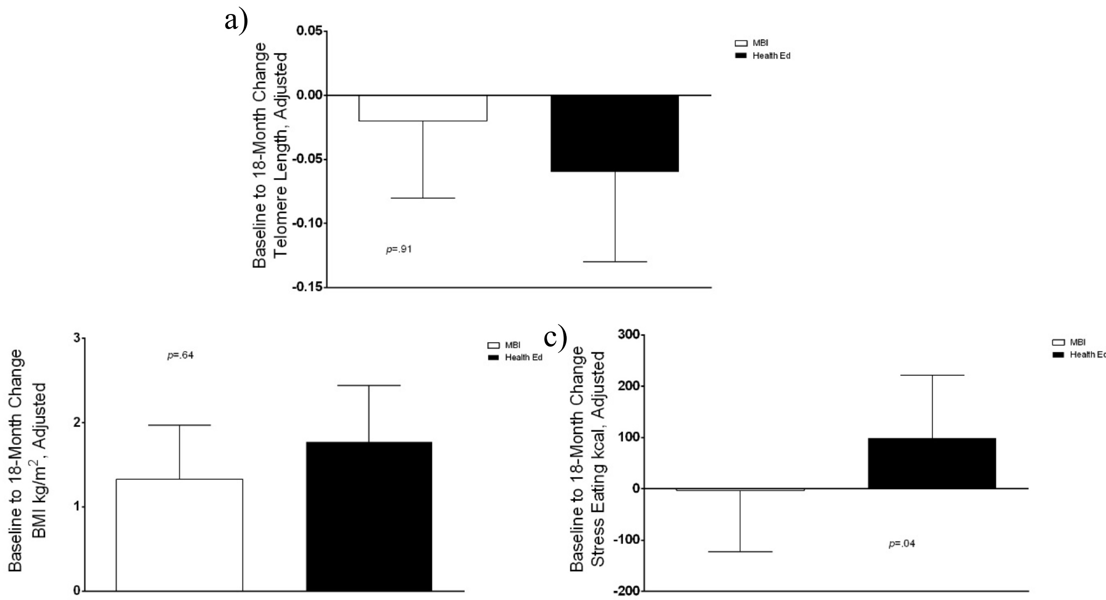

Figure 3. Baseline to 18-month change in (a) telomere length, (b) BMI, and (c) stress eating

Correlations among Changes in Key Variables

Exploratory correlational analyses among changes in key variables, stratified by group assignment, are presented in **Table 3**. In the HE group, correlational analyses revealed significant, expected positive correlations between changes in perceived stress and depression symptoms ($p < .05$). There was an unexpected positive correlation between change in telomere length and change in depression ($p = .02$).

Within the MBI group, correlational analyses indicated a significant, expected positive correlation between change in depression and change in perceived stress ($p < .05$) and a negative trend-level correlation between changes in general mindfulness and perceived stress ($p = .09$).

Table 3. Correlations among changes scores from baseline to 18-months in key variables by condition

	1. MAAS	2. PSS	3. CESD	4. Stress-eating	5. BMI	6. BMIz	7. TL	8. Blood Glucose
1. MAAS	--	-.39	-.14	.15	-.11	.17	-.01	-.42
2. PSS	$-.49^{+}$	--	.71*	-.07	-.04	-.47	.10	-.38
3. CESD	-.45	.58*	--	-.12	-.01	-.24	.67*	-.40
4. Stress-eating, kcal	-.29	-.12	-.46	--	-.01	.31	-.37	.22
5. BMI	.24	-.13	.15	-.08	--	.78*	-.02	.26
6. BMIz	.33	-.12	.17	-.29	.95*	--	-.18	.12
7. Telomere Length	-.29	.21	.23	-.29	-.07	.05	--	-.22
8. Blood Glucose	.08	-.26	$-.58^{+}$	.49	-.41	$-.54^{+}$	-.06	--

Note: Correlations on either side of the diagonal display correlations among the mindfulness-based intervention (MBI) group (n = 13) versus the health education (HE) group (n =12). Correlations within MBI are unshaded. Correlations within HE are shaded. MAAS= Mindful Attention Awareness Scale to assess dispositional mindfulness; PSS = Perceived Stress Scale to measure perceived stress; CESD = Center for Epidemiologic Studies-Depression Scale to assess depression symptoms; BMI = Body Mass Index; BMIz = Body Mass Index z score; TL = Telomere Length; * $p < .05$; $^{+}$ $p < .10$.

DISCUSSION

Key Findings

Although these secondary pilot study analyses lacked the number of participants to establish adequate power, patterns and effect sizes observed in the data provide some support for aspects of the guiding, conceptual model on stress, depression, allostastic load, and cardiometabolic risk in adolescents at-risk for adult obesity. In particular, findings suggested that MBI decreased adolescents' stress-eating 18-months following participation to a greater extent than a HE control condition, with a large effect size. Both change scores in depressive symptoms and perceived stress trended downward in the MBI group as compared to trends upward in the HE group, and were non-significant but reflected moderate between-condition effect sizes. There was a small effect on dispositional mindfulness in the MBI group as compared to the HE group. These patterns were collectively consistent with the hypothesized model, however the expected results for allostatic load measurements were not supported.

Effects of MBI as compared to HE on perceived stress and depression symptoms changes over 18-months did not reach significance, but represented moderate effects in the direction that those randomized to the MBI condition showed lower stress and depression a year and a half later. These findings are consistent with a previous mindfulness pilot study with adolescents at-risk for social-emotional/behavioral concerns using the same MBI program, Learning to BREATHE, and which also found moderate effect sizes for lowering stress and depression symptoms at post-intervention (Bluth, Campo, Pruteanu-Malinici, Reams, Mullarkey, & Broderick., 2015). Further research needs to be done on a larger sample to further test the robustness of these effects.

A key finding was that participation in MBI resulted in stable, as opposed to increased, stress-eating 18-months later compared to HE, as measured objectively with a laboratory test meal. This between-condition standardized effect was significant and moderate-to-large. Adolescents who participated in MBI consumed approximately the same calories in response to a stressor at baseline and 18-month follow-up. In contrast, adolescents who participated in the HE group consumed significantly, on average, 217 kcals more at 18-months following baseline. This finding supports the notion that learning mindfulness-based strategies and tools to cope with stress are effective in preventing continued escalation in stress-eating as a coping mechanism, which is observed as children and adolescents (Francis, Ventura, Marini, & Birch, 2007). Provided this laboratory measure offers some window into routine eating patterns in adolescents' daily lives, over time, this effect could be anticipated to ameliorate energy balance, weight, and cardiometabolic health in meaningful ways.

Nonetheless, significant results were not observed for BMI nor for fasting glucose, and the observed between-condition effects for these variables were small. One possibility may be that although there was a differential effect by condition on changes in stress eating, it may not have been enough to have exerted an impact on BMI or glucose. Perhaps changing stress eating alone does not sufficiently impact energy balance or glucose homeostasis, resulting in the observed non-significant, small effects on changes in BMI and fasting glucose. Alternatively, 18 months may not be a sufficiently long enough follow-up period to detect changes in BMI or glucose trajectories. For instance, some prior literature suggests that differential changes in BMI trajectories resulting from psychosocial/behavioral interventions are not observed in adolescents until 3 years following the intervention (Tanofsky-Kraff et al., 2017). Thus, even longer-term follow-up may be required to detect meaningful differences in adolescent growth trajectories.

Additionally, we only included one marker of cardiometabolic health – fasting glucose. Alternative measures of cardiometabolic health, such as insulin resistance or lipids, would be valuable to include in future work, particularly because these metrics show earlier degradation in the course to cardiometabolic disease than fasting glucose. For instance, our previous studies have found that changes in adolescents' fasting insulin or insulin resistance can be detected at post-treatment or six months after an MBI intervention (Shomaker et al., 2017).

Telomere length was stable in both conditions, with no difference between MBI and HE groups. This null finding could be explained by the relative stability expected in adolescents transitioning into early adulthood (Epel, 2009; Zeichner et al., 1999). The relative stability during this time period would make any change in telomere length resulting from increased stress, depressive symptoms, and cardiometablic risk factors difficult to adequately detect with such a small sample size and short follow-up time. One important future direction would be the measurement of telomerase activity, the enzyme present in stem cells that restores telomeres. Telomerase activity perhaps may be more sensitive to changes in perceived stress, depressive symptoms, and cardiometabolic risk factors for the length of follow-up performed in this study (Daubenmier et al., 2012; Epel et al., 2006; Schutte & Malouff, 2014). Furthermore, telomeres represent only one biomarker of allostatic load. Cortisol, for instance, is an alternative marker of abnormal allostatic load that warrants consideration.

Potential correlations among the key factors explored in this study were evaluated to explore association among baseline to 18-month changes in trait mindfulness, perceived stress, depression, stress-eating, BMI, telomere length, and fasting glucose. Changes in perceived stress were positively related to changes in depressive symptoms in both conditions, meaning that adolescents who perceived decreases in stress also showed decreases in depression symptoms over the 18-months. The link between perceived stress and depression in adolescents is consistent with prior literature in adolescents and underscores the potential value of stress-reduction and MBI training to address depression in this population (Hampel & Petermann., 2006; Liu, Wei, Forsell, & Lavebratt., 2017; Martin, Kazarian, & Breiter., 1995). Unexpectedly, in the MBI group only, increases in dispositional mindfulness trended toward an association with increases in perceived stress and in the HE group only, decreases in telomere length were correlated with decreases in depressive symptoms. These unexpected findings should be treated with extreme caution due to the small sample size, made smaller by the stratification by condition. Furthermore, the negligible changes in telomere length among adolescents in this study render it very difficult to derive meaning from these patterns. Further, because the associations are correlational, any directionality in these correlations cannot be determined.

Study Strengths

This was the first study, to our knowledge, to explore the effects of MBI on psychological characteristics, stress-eating, telomere length, BMI, and glucose in adolescents at-risk for adult obesity. Validated measures of all key constructs, including a laboratory paradigm to objectively assess stress-eating, were utilized. Further, adolescents are a particularly critical population to study from a prevention point of view. Adolescents are in a formative time period in terms of health and health-related habits and findings could shed light on preventive efforts for cardiometabolic health (Jessor, Turbin, Costa., 1998; Maggs, Schulenberg, & Hurrelman, 1997; Stang & Stotmeister., 2017). This study's integration of both behavioral and medical health further adds potential value for future integrated public health preventative efforts. Additionally, this study was unique in terms of its length of 18-months follow-up. Most MBI studies commonly examine effects only to 3-months post-intervention (Matousek, Dobkin, & Pruesner, 2010).

Study Limitations

The sample size was very small and, therefore, was not powered to detect small-to-moderate effects in this pilot study. Caution must be exercised in interpreting effect sizes in pilot studies due to their potential lack of reliability and replication (Kraemer, Mintz, Noda, Tinklenberg, & Yesavage., 2006). Additionally, for the purposes of analyzing effects on allostatic load and biological outcomes, only one biomarker of allostatic load, telomere length, was measured, and future studies should consider additional and/or alternative markers such as cortisol levels, as well as measurement of telomerase activity. Generalizability of findings are limited to adolescents at-risk for excess weight gain and there was limited representation of racial/ethnic minorities. It is not clear to what extent measurements of stress eating generalize to eating patterns in real life in response to sources of external stress. Ambulatory measures, such as ecological momentary assessments, may offer additional insights in future studies. Finally, it is important to point out that the current study was derived from a model in which psychological factors were assumed to have a downstream effect on stress-eating, allostastic load, BMI, and cardiometabolic risk. However, additional consideration should be given to what extent high BMI or increased stress-eating contributes to higher levels of depressive symptoms and perceived stress, thereby impacting telomere length. Literature supports a complex interplay among mental health, allostatic load, and cardiometabolic factors (Epel et al., 2006; Filho et al., 2018; Logan & Barksdale., 2018; Tomiyama et al., 2011).

Future Directions

We are currently completing the remaining 18-month follow-up assessments for the current study, and repeating the analyses and aims of the current thesis with the complete available data, including exploring imputation to handle missing data in the intent-to-treat sample and accounting for covariates, will be important immediate next steps. We also continue to follow the current cohort out to a 36-month follow-up, and evaluating outcomes at this final endpoint for the study may be more telling, particularly in regard to testing changes in telomere length as a result of an MBI program.

With regards to the intervention itself, a stated goal of MBI was not to lower calorie intake or cause weight loss. Studies regarding MBIs in adults have shown that outcomes relating to weight loss are only observed if it is a stated goal and objective of the intervention itself (Forman, Butryn, Hoffman, & Herbert., 2009; Forman, Butryn, Juarascia, Bradley, Lowe, & Herbert, 2013; Katterman, Kleinman, Hood, Nackers, & Corsica., 2014). Therefore, a potential further direction to take this work is to integrate general MBI with designated weight loss/stabilization efforts in adolescents with overweight/obesity. Additionally, adolescents are not developing in isolation. Cardiometabolic diseases relating to excess weight gain are seldom representative of the health choices of an individual adolescent (Hammons & Fiese., 2011), and while interventions are not particularly effective for weight loss in adolescents, behavioral, family-based approaches offer the most promise (Wilfley, Vannucci, & White., 2010; Wilfley, Tibbs, Van Buren, Reach, Walker, & Epstein., 2007). Therefore, a family-centric MBI program or the addition of external supports might be anticipated to have larger effects on health habit changes that could stabilize BMI and improve cardiometabolic health.

The unique nature of the rapidly changing adolescent brain and body, coupled with increasing depression and rates of cardiovascular disease in adolescents, makes development of integrated health interventions capable of addressing both conditions a high public health priority. Studies examining development of pathologies and diseases indicate that many begin to develop during adolescence, and therefore suggest that interventions timed during this age span offer potential for lasting benefits to health extending far into emerging adulthood (Juster, McEwen, & Lupien, 2010). Future research that build on the trends observed in the current pilot study could ultimately lead to the development of more effective MBI programs for adolescents for improvement of long term mental and physical health. However, much more work is needed in examining MBI, particularly in terms of what populations they best serve, what specific conditions they are most well-suited to address, and the precise mechanisms by which increasing mindfulness and decreasing stress/depression can affect both mental and physical health outcomes.

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