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The effect of a mindfulness-based stress intervention on neurobiological and symptom measures in adolescents with early life stress: A feasibility randomized controlled trial

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Abstract

Background

Early life stress (ELS) has been linked to poor mental and physical health outcomes in adolescence and adulthood. Mindfulness reduces symptoms of depression and anxiety and improves cognitive and social outcomes in both youth and adults. However, little is known whether mindfulness can mitigate against the adverse neurobiological and psychological effects of ELS. This study aimed to examine the feasibility of conducting a group mindfulness intervention in adolescents with ELS and provide preliminary indication of potential effects on stress-related biomarkers and mental health symptoms.

Methods

Forty adolescents were randomized to receive either eight sessions of Mindfulness-Based Stress Reduction for Teens in group format (MBSR-T; $n = 21$) or Control (CTRL; $n = 17$). Outcomes were assessed at baseline and follow-up and included measures associated with neurobiological functioning (immune and endocrine biomarkers) and self-reported mental health symptoms. Linear mixed effects models were used to assess the effects of group and time on these outcome measures.

Results

Sixteen of the 21 adolescents completed the intervention, attending an average of 6.5 sessions. The model examining depressive symptoms revealed a medium effect for symptom reduction [Cohen's $d = .69$] in the MBSR-T relative to CTRL groups.

Conclusions

This study demonstrated feasibility of conducting a group-based MBSR intervention for adolescents with ELS. There was some evidence for efficacy on a symptom level with potential subtle changes on a biological level. Future larger studies are needed to determine the efficacy of group-based mindfulness interventions in this population.

Keywords

adolescents, early life stress, inflammation, cortisol, epigenetic, mindfulness, prevention, resilience

Introduction

Early life stress (ELS) is characterized by chronic emotional and physical abuse and neglect, sexual abuse, parental psychopathology and substance abuse, and household dysfunction (e.g., parental incarceration, interpersonal violence). An estimated 678,000 American youth (birth through age 18) are victims of abuse and neglect annually in the United States, with Child Protective Services referrals involving 7.8 million children in 2018¹. Over the last half-decade, the estimated lifetime direct and indirect costs (e.g., medical, productivity loss, criminal justice) of child abuse and neglect per non-fatal victim has increased from \$210,000 to \$831,000^{2,3}, further highlighting ELS as a public health crisis.

ELS has been linked to poorer mental and physical health outcomes in adolescence and adulthood. It accounts for nearly half of all childhood-onset mental health disorders and one third of adult-onset disorders^{4,5}. ELS significantly elevates the risk for mood and anxiety disorders⁶⁻⁹, externalizing and substance use disorders¹⁰⁻¹², personality disorders¹³⁻¹⁵, as well as suicide ideation and attempts^{16,17}. ELS-exposed individuals evidence poorer psychotherapy and pharmacotherapy outcomes relative to their non-exposed treatment-receiving counterparts¹⁸. As a large portion of extant literature focuses on adults, indicating the long-term effects of ELS, there is a need to develop interventions optimized for youth with ELS that can help mitigate their potential for negative mental and physical health outcomes.

The consequences of ELS are complex and are believed to stem from alterations in a number of neurobiological processes involved in generation and regulation of emotional responses, including endocrine, immune, epigenetic, and brain circuits¹⁹⁻²³. ELS has been shown to disrupt the function of the hypothalamic-pituitary-adrenal (HPA) axis, which plays a prominent role in stress response and regulation²⁴⁻³⁰, as well as downstream inflammatory³¹⁻³⁷ and epigenetic changes³⁸⁻⁴². While childhood and adolescence are stages of particular vulnerability to psychopathology⁴³, proximity to ELS exposure, increased plasticity, and ongoing development provide an opportunity for normalization in systems subservient to stress responses and emotion regulation as a result of intervention, as well as increased resilience^{44,45}. A number of psychological interventions have been efficacious in reducing symptoms of depression, anxiety, or posttraumatic stress disorder (PTSD) in ELS-exposed youth⁴⁶. However, it remains unclear whether, and to what extent, interventions exert influence on the disrupted underlying neurobiological mechanisms involved in response to and regulation of stress.

Psychological techniques that promote emotional awareness and regulation are well-suited to target mechanisms involved in responses to psychological stressors and thus may be particularly beneficial for ELS-exposed youth in reducing current symptoms and increasing resilience⁴⁷⁻⁴⁹. Mindfulness practice offers one such approach by encouraging the development of awareness of one's thoughts,

emotions, and behaviors by increasing the ability to observe and direct internal experiences⁵⁰. Research involving both adults and youth shows that mindfulness reduces symptoms of depression and anxiety and improves cognitive and social outcomes⁴⁷⁻⁵¹. Moreover, recent data indicate that mindfulness practice may positively influence processes involved in regulation of stress responses in adults, including gene expression (e.g., decreased expression of pro-inflammatory genes)⁵², immune and endocrine system markers (e.g., reduction in C-reactive protein and increased cortisol reactivity, respectively)^{53,54}, and activation in a distributed network of brain regions involved in interoception, self-referential processing, threat detection, and emotion regulation^{46,55-57}. Therefore, mindfulness represents a potential regulatory intervention that may inhibit or reverse some of the deleterious long-term effects of ELS exposure. However, the efficacy of a mindfulness-based intervention for youth exposed to ELS has not been investigated.

The present study aimed to address this gap in the literature by determining the feasibility of a group mindfulness intervention, Mindfulness-Based Stress Reduction for Teens (MBSR-T), for adolescents exposed to ELS. We examined treatment completion rates and average number of sessions attended to assess feasibility. To provide preliminary data concerning the impact of MBSR-T on biological and clinical outcomes, we assessed changes from pre to post-treatment in cortisol reactivity in response to a psychosocial stressor and immune system function (primary outcomes), symptoms of depression (secondary outcome), and expression of HPA axis regulatory gene FKBP5, incidence of substance use, and self-reported mindfulness and resilience traits (exploratory outcomes).

Methods

Participants

The present pilot study used a parallel randomized controlled trial design. A total of 141 adolescents were assessed for eligibility via a phone screening in which caregivers reported the number of Adverse Childhood Experiences (ACEs)⁵⁸ the adolescent had experienced. Those with three or more parent-reported ACEs were included in the study (≥ 3 ACEs has been associated with greater impairments⁵⁹). Exclusion criteria were kept to a minimum in order to increase generalizability; however, neurological and psychotic disorders and active suicidal ideation were deemed exclusionary. Psychotropic medications were permitted so long as participants had been on a stable (i.e., unchanged) dose for six weeks or longer. A total of 40 adolescents (age: 14.3 [.76]; 59% male) were randomized to either Mindfulness-Based Stress Reduction for Teens (MBSR-T) or Control (CTRL). The Consolidated Standards of Reporting Trials (CONSORT) diagram is provided in Figure 1. Parents and adolescents provided written

consent and assent, respectively. Adolescents were compensated for baseline and follow-up assessment visits, as well as for completing surveys at each time point, but were not compensated for completing the mindfulness intervention. Research was approved by the Western Institutional Review Board and conducted in accordance with the Declaration of Helsinki. The study was registered at the US National Institutes of Health (ClinicalTrials.gov identifier #NCT03633903).

Procedures

Baseline and follow-up assessments included collection of biological samples, a stress-induction task, and a range of self-report measures. At baseline, adolescents completed a number of self-report measures assessing mental health symptoms and traits, as well as a stress-induction task. Adolescents also provided blood samples on a separate day. In the weeks preceding allocation, selected symptom measures were completed electronically to better capture baseline mental health symptoms and traits. Adolescents were then randomly assigned to one of the two conditions, Mindfulness-Based Stress Reduction for Teens (MBSR-T) intervention or control (CTRL). MBSR-T commenced within two weeks of baseline assessment and consisted of eight sessions over four weeks. Prior to each session, MBSR-T participants completed brief symptom and treatment compliance assessments. The CTRL group completed the symptom assessments online. Following the conclusion of four weeks, follow-up assessments (i.e., repeated baseline measures) were completed by both groups.

Mindfulness-Based Stress Reduction for Teens. The active intervention, MBSR-T, was provided in a group format^{51,60}. Relative to MBSR, MBSR-T has been slightly modified for use with adolescents aged 13-18 and takes into account the attentional capabilities of youth and the impact of technology on interpersonal interactions. Adaptations include shortened formal mindfulness practice (10-20 minutes, rather than 40 for adults), On-Your-Own-Practices (rather than homework), and no day-long retreat^{51,60}. Topics of focus included intention (direction of effort toward mindfulness practice), attention (experiencing what is taking place in the present moment), and attitude (nonjudgmental attributions of cognitive, emotional, and somatic experiences). A total of three groups completed the MBSR-T program, ranging between five and nine adolescents per group. Adolescents assigned to MBSR-T were given a workbook to use for On-Your-Own-Practice assignments. The study investigator (a licensed health service psychologist) and a doctoral student in clinical psychology supervised by the study investigator delivered the intervention. Sessions were video recorded. A board-certified child and adolescent psychiatrist (S.C.) provided weekly supervision to promote a developmentally appropriate intervention. Randomization or data collection procedures were undertaken by the study coordinator.

Control condition. Adolescents in the CTRL group were followed for the duration of the study with self-report measures administered at the same time intervals as the MBSR-T groups. Participants were not asked to stop any treatments or activities they were already undergoing, including psychotherapy, pharmacotherapy, or other services during the duration of the study.

Primary outcomes included changes in cortisol and inflammatory markers, while secondary outcomes focused on symptoms depression. Exploratory outcomes assessed changes in HPA axis gene expression, mindfulness, resilience, and substance abuse.

Self-Report Measures

Additional information on all of the measures, as well as an administration schedule (Table S1), is available in the supplemental information. All measures, with the exception of the caregiver reports of ACEs, were reported by adolescents. The ACEs scale⁵⁸ assessed instances of physical, sexual, and emotional abuse; physical and emotional neglect; and household dysfunction (divorce, parental mental illness, domestic violence, parent incarceration). A composite ACEs score was calculated by totaling all instances of an affirmative answer across caretaker (screening) and adolescent reports (baseline and follow-up). Additionally, the Childhood Trauma Questionnaire (CTQ)⁶¹ provided a measure of severity of exposure to childhood trauma.

Adolescent depressive symptoms were measured using the Mood and Feelings Questionnaire-Short Form (MFQ-SF)⁶², while the Adolescent Alcohol and Drug Involvement Scale (AADIS)⁶³ measured adolescents' history of and/or current substance use, potential interference with life, and stigma. The Connor-Davidson Resilience Scale, 10 item (CD-RISC 10)⁶⁴ assessed stress coping abilities, whereas the Mindful Attention Awareness Scale – Adolescent (MAAS-A)⁶⁵ measured intrapersonal awareness. Notably, the MAAS-A has been found to be sensitive to change in mindfulness as a result of topics covered in mindfulness interventions⁶⁶. Finally, the MBSR-T group alone completed the Homework Rating Scale (HRS)⁶⁷ and the Working Alliance Inventory for Children and Adolescents (WAI-CA)⁶⁸ to assess between-session compliance with intervention materials and therapeutic alliance across three subscales: goals, tasks, and bond, respectively.

Stress Induction Task

We used the Trier Social Stress Test-Children (TSST-C)^{69,70} to assess biological responses to stressful situations. The TSST-C consisted of public speaking and mental arithmetic serial subtraction components, with different prompts for the two timepoints. Research confederates not otherwise

involved with the study and data collection delivered the TSST-C. Baseline and follow-up TSST-C administration involved a different pair of associates. Prior to beginning and upon completion of the TSST-C, participants rated how they currently felt on a five-point Likert scale (very calm to very anxious). For the public speaking component, adolescents were given the stem of a story and asked to complete the story in an interesting and exciting way. Further, they were told that the story ending should be better than those provided by other participants. The participant then had a five-minute preparation period, followed by a five-minute presentation to two associates. If finished prior to the five-minute story period, adolescents were prompted to continue until the time elapsed. Directly following this, a serial subtraction task (e.g., subtracting by 13 from 1,023 [baseline]; subtracting by 17 from 1,027 [follow-up]) was completed. This task was also completed over a five-minute period in front of the associates. Adolescents were encouraged to work as quickly and accurately as possible and were asked to restart if errors were made. Salivary cortisol was collected immediately prior to and 10-20 minutes following the completion of the TSST-C.

Biological Samples

Saliva was collected using passive drool SalivaBio collection tubes (Salimetrics) and stored at -30°C. Saliva was then centrifuged, aliquoted, and stored at -80°C. Cortisol concentrations in saliva samples was determined using Salimetrics High Sensitivity Salivary Cortisol enzyme-linked immunosorbent assay (ELISA) kits. Blood was collected using standard venipuncture procedures with BD vacutainer tubes, cell preparation tubes with sodium citrate for Peripheral Blood Mononuclear Cell (PBMC) isolation, and serum vacutainer tubes with clot activator. A total of 25 mL of blood was drawn during the entire study by a trained phlebotomist. PBMCs were aliquoted and stored in liquid nitrogen and serum was isolated and stored at -80°C. Interleukin 6 (IL-6) and C-reactive protein (CRP) levels in the serum samples were assayed using MesoScale Discovery V-PLEX assay kits using the MESO QuickPlex SQ 120. Ribonucleic acid (RNA) was isolated from PBMCs using Qiagen RNeasy Micro kits and a complimentary deoxyribonucleic acid (cDNA) bank was created using Omniscript kits. Gene expression analyses were completed by quantitative real-time polymerase chain reaction (qRT-PCR) using the QuantStudio 12K Flex Real-Time PCR System for a specific gene of interest (i.e., FKBP5) and one control gene (i.e., GAPDH). Saliva samples were collected between 9:30-18:00, whereas blood samples were collected prior to 15:00.

Data Analysis

The primary analysis approach was between-group differences from baseline to follow-up. The report of effects in this study focuses on effect sizes (Cohen's d) due to the feasibility nature of the study. Several measures were normalized to account for outliers. All statistical analyses were performed using R programming environment⁷¹. Descriptive statistics were obtained using the R package 'psych'⁷² and independent samples t-tests examined group differences on demographic variables. Linear regressions were used to evaluate relationships between baseline biological variables and ELS severity. Gender was used as a covariate in all regression analyses. For analyses involving biomarkers and genes, body mass index (BMI) was added as a covariate. Finally, for cortisol regression analyses, wake-up time and time of cortisol collection were included as covariates.

To examine changes in biological variables and self-reported mental health symptoms as a function of treatment, linear mixed effects models (LMEs) were conducted using the 'lmer' function in R package 'lme4'⁷³ and plots were generated with 'emmeans'⁷⁴. Fixed effects included group and time. Random effects included subject. Follow-up pairwise comparisons were conducted using estimated marginal means to further describe the effects of group and time on the outcome variables. Baseline MFQ scores for analysis were calculated by averaging responses across three timepoints (e.g., baseline, online assessments 1 and 2).

Results

Descriptive analyses

Demographic and clinical characteristics across groups are reported in Table 1. The regression model including ACEs, gender, and BMI explained 34% of the variance in CRP levels [$F_{(3,27)} = 6.97, p < .005, f^2 = .46$], with BMI ($\beta = .64$) as the only significant predictor. Similarly, the regression model including ACEs, gender, and BMI explained 36% of the variance in IL-6 levels [$F_{(3,27)} = 6.49, p < .005, f^2 = .55$], with BMI ($\beta = .65$) as the only significant predictor. Full results for regression models are available in Table S2.

MBSR-T Feasibility

Sixteen of the 21 participants allocated to MBSR-T completed the intervention, with an average attendance of 6.5 sessions. One subject never started the intervention, one dropped out after attending one session, and two dropped out after attending two sessions. On average, MBSR-T participants ($N = 21$) were moderately compliant with On-Your-Own-Practices (i.e., homework assignments; Table S3). With respect to working alliance, MBSR-T participants reported that they very

often agreed with goals and tasks of therapy, as well as developed an affective bond with therapists (Table S4). Working Alliance saw minimal increases across each subscale over time, including a small effect increase across training for total scores [$F_{(6,84)} = 1.20, p = .31, f = .12$; Figure S1].

Outcome analyses

Biological variables. Full statistical results for LMEs are provided in Table 3. Our primary interest was in the Group by Time interaction analyses. LMEs revealed a small effect for Group by Time interaction for CRP ($F_{(1,26)} = .77, p = .39, d = -.34$), while no effect was observed for IL-6 ($F_{(1, 22)} = .004, p = .98, d = -.03$). Conversely, LME analysis examining cortisol response to stress induction evidenced a medium effect for the Group by Time interaction [$F_{(3,86)} = 2.36, p = .077, d = .60$; Figure 2a]. Pairwise comparisons revealed a medium effect size differences in anticipatory cortisol levels preceding the social stress task at follow-up for MBSR-T relative to CTRL participants [$t_{(111)} = 1.92, p = .058, d = -.056$]. Similarly, LME analysis examining self-reported anxious arousal to stress induction revealed a large effect for the Group by Time Interaction [$F_{(3,86)} = 4.49, p = .006, d = .83$; Figure 2b]. Follow-up pairwise comparisons revealed a medium effect size reduction in self-reported anxiety following the TSST-C at follow-up for MBSR-T relative to CTRL participants [$t_{(108)} = 2.19, p = .031, d = -.74$].

Depression. LMEs for depression symptoms revealed a medium to large effect for the Group by Time interaction [$F_{(1,28)} = 3.31, p = .079, d = .69$; Figure 3a]. Follow-up pairwise comparisons revealed a large effect size reduction in symptoms of depression from baseline to follow-up for MBSR-T [$t_{(28.2)} = -2.972, p < .01, d = 1.40$], while no effect was observed in the CTRL group [$t_{(29)} = -.016, p = .988, d = .01$]. For the MBSR-T group, a medium effect size was evidence for continuous decrease in symptoms of depression over the course of treatment [$F_{(9,139)} = 5.27, p < .001, d = .51$; Figure 3b].

Exploratory analyses

A large effect was identified for the Group by Time interaction for marijuana use [$F_{(1,29)} = 5.47, p = .03, d = .86$]. Follow-up pairwise comparisons revealed a large effect size increase in marijuana use in the CTRL group from baseline to follow-up [$t_{(29)} = 2.414, p = .02, d = 1.40$], whereas a small effect size decrease in marijuana use was observed within the MBSR-T group [$t_{(29)} = -.74, p = .47, d = .24$]. Small and medium Time by Group effects were found for the AADIS total score [$F_{(1,36)} = 0.26, p = .61, d = .17$] and the alcohol subscale [$F_{(1,31)} = 1.98, p = .17, d = .51$], respectively. Small Group by Time interaction effects were found for mindfulness [$F_{(1,32)} = 0.37, p = .55, d = .21$] and HPA axis regulating gene FKBP5 [$F_{(1,25)} = 0.42, p = .52, d = .08$].

= .26]. Negligible Group by Time interaction effect sizes were found for the measure of resilience [$F_{(1,32)} = 0.01, p = .55, d = .04$].

Discussion

This study aimed to examine the feasibility of a group mindfulness intervention for adolescents with ELS, and to provide preliminary indication of effects on stress-related biomarkers and mental health symptoms. Results yielded two main results. First, the mindfulness training appeared to be an acceptable, safe, and feasible intervention for the population of interest. Second, MBSR-T showed promise for leading to reductions in symptoms of depression and marijuana use, as well as stress reactivity as measured via self-report and cortisol response. However, MBSR-T did not seem to substantially impact self-reported mindfulness or resilience, nor the expression of pro-inflammatory cytokines (IL-6 and CRP) or HPA axis regulatory genes (FKBP5). Take together, the results show some evidence for efficacy on a symptom level but not on a biological level.

A number of cognitive interventions have successfully reduced symptoms of depression, anxiety, and PTSD in youth exposed to ELS⁴⁶. However, many of these interventions are focused on specific diagnoses and/or symptom profiles. MBSR-T offers a transdiagnostic treatment approach that can be more easily disseminated in group-based settings within schools or community programs. Meta-analyses cite mindfulness-based therapies as promising interventions for treating mood and anxiety disorders in clinical adult populations⁷⁵ and adolescents and young adults⁷⁶. Our study extends that research by providing evidence that MBSR is a feasible and acceptable transdiagnostic intervention for ELS-exposed youth. The completion rate (76%) and homework compliance ratings (50%) were similar to that reported in other studies utilizing psychological intervention approaches for adolescents or young adults^{77,78} and working alliance was similar to that reported in validation literature⁶⁸.

Our findings further replicated previous research utilizing MBSR-T in other adolescent populations^{79,80} by demonstrating that MBSR-T may also be effective in reducing symptoms of depression for ELS-exposed youth. This is particularly promising given that the youth in this study were not identified based on elevated depression symptoms, suggesting that it may be beneficial even when delivered to youth without diagnosable mental health disorders. MBSR-T may be particularly helpful for reducing depression and related outcomes for adolescents with ELS, as mindfulness promotes noticing and regulating maladaptive thoughts, emotional responses, and behaviors often precipitating and perpetuating mental health conditions⁸¹. However, further research is needed to delineate the essential mechanisms and long-term impact.

Our study replicates previous research that links mindfulness and decreased stress reactivity⁵⁴. Indeed, participants in the MBSR-T group evidenced changes in stress reactivity both subjectively (e.g., self-report) and objectively (e.g., salivary cortisol). Relative to CTRL, MBSR-T participants evidenced lower levels of cortisol in anticipation of the TSST-C, as well as increased cortisol reactivity following the TSST-C at follow-up. This may indicate a more adaptive physiological stress response⁸². Further, MBSR-T participants reported lower levels of anxiety after completing the TSST-C, which has been demonstrated in previous research⁸³. We posit that MBSR-T participants were able to recruit adaptive stress-reduction techniques discussed in the intervention in response to stress induction. Taken together, the stress reactivity mechanism may be a pathway through which mindfulness techniques exert benefits for trauma-exposed youth and sub-clinical populations.

Although there is preliminary data to suggest that mindfulness practice in adults may positively influence processes involved in regulation of stress responses, including immune and endocrine system markers^{53,54} and gene expression⁵², we were unable to detect these differences in neurobiological markers of interest in our adolescent sample. Nevertheless, it is well known that ELS exposure during critical periods of development alters the functioning of the brain, endocrine, and immune systems involved in regulation of stress response⁸⁴⁻⁸⁷, in turn accounting for the observed short- and long-term negative mental and physical outcomes. Therefore, interventions that can reverse or compensate for these neurobiological disruptions are needed in order to optimize functioning and outcomes in these populations. To see more of an impact on these neurobiological systems, MBSR-T may be enhanced with other psychological (e.g., cognitive restructuring), neuromodulatory (e.g., real time neurofeedback) techniques, and the use of smart-phone technology (e.g., ecological momentary assessments). These enhancements are poised to supplement the dosing of mindfulness and other cognitive techniques, more effectively engage in and self-regulate brain activity, and increase between-session compliance through self-monitoring, respectively. Future studies with larger samples and greater variability in trauma exposure and symptomatology will be needed to further establish potential changes in these and more definitively determine whether mindfulness interventions can exert changes at the neurobiological level for adolescents with ELS exposure.

Limitations and future research

This study possesses many strengths, including the use of a control condition, randomization, and multi-level assessment of a mindfulness-based intervention in adolescents exposed to ELS. However, it is not without limitations. Primarily, we are limited by a small sample size in this pilot study. Large sample

sizes are often required to detect differences in biomarkers, particularly of genes. Further, we examined very few biological markers, severely limiting the conclusions we may draw on the potential effect mindfulness interventions may have on immune and endocrine systems. Additionally, the lack of a standardized blood and saliva collection time introduced natural variability. Next, in an effort to increase generalizability, we included adolescents impacted by ELS, regardless of the presence of mental health symptoms. Larger studies would be able to maintain this approach while allowing for sampling of participants with greater symptom severity and examine the extent MBSR-T may exert over symptom reduction in a clinical population. Finally, longitudinal studies will be able to examine whether these interventions increases resilience in the long-term among youth affected by ELS exposure.

Conclusions

The current study presented results from a randomized controlled trial of a brief mindfulness intervention program (MBSR-T) for adolescents exposed to ELS. This intervention had a positive impact on self-reported symptoms of depression as compared with adolescents in the control group. Therefore, the results demonstrate that mindfulness-based interventions for adolescents exposed to ELS are safe, feasible, and aid in reducing depressive symptoms. MBSR-T also demonstrated changes in stress perception and regulation, indicating that stress reactivity may be one key mechanism underlying the positive effects of MBSR-T. Future larger studies are needed to determine the efficacy of group-based mindfulness interventions in this population.

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Author Contributions

Z. C. contributed to data analysis and interpretation, literature search, writing of the manuscript, and creation of tables and figures. K. C. contributed to intervention delivery, data analysis and interpretation, and writing of the manuscript. E. A. contributed to study design, data collection, and revisions to the manuscript. S.C. contributed to supervision of intervention delivery and revisions to the manuscript. J. H. G. contributed to study design and revisions to the manuscript. K. T. contributed to study design, data analysis, and revisions to the manuscript. M. P. contributed to study design and revisions to the manuscript. R. A. contributed to study design, supervision of intervention delivery, data analysis and interpretation, and revisions to the manuscript. N. K. contributed to study design, data collection, intervention delivery, supervision of intervention delivery, data analysis and interpretation, literature search, writing of the manuscript, and creation of tables and figures.

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Table 1. Baseline demographics and clinical characteristics of the mindfulness-based stress reduction for teens and control groups.

Characteristics	MBSR-T (n=21)		CTRL (n=17)		Group Differences	
	Mean	SD	Mean	SD	t	p
Age	14.33	0.73	14.29	0.77	0.16	0.87
ACEs	5.90	1.70	6.11	2.03	-0.35	0.73
CTQ	46.24	12.45	49.41	11.00	-0.82	0.42
Emotional Abuse	9.81	4.49	11.06	4.88	-0.82	0.42
Emotional Neglect	10.24	4.76	10.53	4.21	-0.20	0.84
Physical Abuse	7.71	3.07	7.18	2.19	0.61	0.55
Physical Neglect	8.24	3.10	8.59	3.71	-0.32	0.75
Sexual Abuse	5.33	0.86	6.94	4.48	-1.61	0.12
	N	%	N	%	χ^2	p
Sex					0.79	0.38
Male	14	67	8	47		
Female	7	33	9	53		
Ethnicity					1.26E-30	1.0
Hispanic	2	10	1	6		
Non-Hispanic	19	90	16	94		
Race					6.99	0.22
White	10	48	9	53		
American Indian or Alaska native	2	10	2	12		
Black or African-American	4	19	5	29		
Asian or Pacific Islander	0	0	0	0		
More than one race	5	24	0	0		
"Other," unspecified	0	0	1	6		
Mental health diagnoses	7	33	4	24	0.90	0.76
Psychotropic medication use	6	29	6	35	0.01	0.93
Psychotherapy	7	33	4	24	0.05	0.94

Parental mental health diagnoses	9	43	9	53	0.09	0.77
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Note. Percentages are rounded to the nearest whole percent.

Abbreviations: ACEs, Adverse Childhood Experiences; CTQ, Childhood Trauma Questionnaire; CTRL, Control; MBSR-T, Mindfulness Based-Stress Reduction for Teens.

Table 2. Unadjusted means, standard deviations, effect sizes, and main analyses of change from baseline to follow-up in mindfulness-based stress reduction for teens and control groups.

[illegible]

All					Interaction	0.17	0.13	0.25	0.51	.61
Baseline	1.48	1.91	3.12	5.17						
Follow-up	1.52	2.69	3.59	7.62						
Alcohol					Interaction	0.51	0.4	0.28	1.41	.17
Baseline	0.71	0.85	0.59	1.06						
Follow-up	0.78	1.00	1.00	1.28						
Marijuana					Interaction	0.86	0.53	0.23	2.34	<.05
Baseline	0.57	1.29	0.59	1.06						
Follow-up	0.50	1.34	1.08	1.68						
Mindfulness					Interaction	0.21	2.41	3.95	0.61	.55
Baseline	53.83	9.92	49.47	7.25						
Follow-up	58.12	12.39	55.75	15.73						
Resilience					Interaction	0.04	0.19	1.94	0.1	.92
Baseline	25.1	6.67	25.18	6.87						
Follow-up	25.82	7.58	27.75	8.30						
FKBP5					Interaction	0.26	0.29	0.44	0.65	.52
Baseline	5.26	0.85	5.35	0.78						
Follow-up	5.25	1.22	5.58	0.52						

Note. Stress is the self-reported anxious arousal prior to and after the stress induction task. Cortisol is measured in $\mu\text{g/dL}$. IL-6 is are measured in pg/mL . CRP is measured in mg/L .

Abbreviations: CRP, C-reactive protein; CTRL, Control; IL-6, interleukin-6; MBSR-T, Mindfulness Based-Stress Reduction for Teens.

Figure 1. CONSORT diagram. Figure shows the flow of adolescents through the phases of the study and the number that withdrew at each time point.

Abbreviations: CTRL, Control; MBSR-T, Mindfulness Based-Stress Reduction for Teens.

Figure 2. a) The trajectory of the self-reported mood scores before and after the Trier Social Stress Task for Children (TSST-C). Participants were asked to rate their mood on a 5-point Likert scale (1 = very calm, 5 = very anxious). Participants completing the mindfulness intervention evidenced reduced anxious arousal before and after the TSST-C when compared with participants assigned to treatment as usual. b) The trajectory of cortisol response before and after the Trier Social Stress Task for Children (TSST-C). Participants completing the mindfulness intervention evidenced reduced cortisol levels prior to the TSST-C commencing when compared with participants assigned to control group. Abbreviations: CTRL, Control; MBSR-T, Mindfulness Based-Stress Reduction for Teens.

Figure 3. Change in depression by group over time. Shown here are interaction plots of a) estimated marginal means based on the fitted linear mixed-effects model for depression from baseline to follow-up between groups and b) means and standard deviations based on the fitted linear mixed-effects model for depression across treatment within the MBSR-T group. The MBSR-T group showed a significant decrease in depressive symptoms from baseline to followup, whereas the TAU group did not. Further, a decreasing trend was observed over the course of treatment. Abbreviations: CTRL, Control group; MBSR-T, Mindfulness Based-Stress Reduction for Teens; MFQ, Mood and Feelings Questionnaire; S, Session.