Acceptance lowers stress reactivity: Dismantling mindfulness training in a randomized controlled trial

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A R T I C L E   I N F O

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A B S T R A C T

Objective: Mindfulness interventions, which train practitioners to monitor their present-moment experience with a lens of acceptance, are known to buffer stress reactivity. Little is known about the active mechanisms driving these effects. We theorize that acceptance is a critical emotion regulation mechanism underlying mindfulness stress reduction effects.

Method: In this three-arm parallel trial, mindfulness components were dismantled into three structurally equivalent 15-lesson smartphone-based interventions: (1) training in both monitoring and acceptance (Monitor + Accept), (2) training in monitoring only (Monitor Only), or (3) active control training (Coping control). 153 stressed adults (mean age = 32 years; 67% female; 53% white, 21.5% black, 21.5% Asian, 4% other race) were randomly assigned to complete one of three interventions. After the intervention, cortisol, blood pressure, and subjective stress reactivity were assessed using a modified Trier Social Stress Test.

Results: As predicted, Monitor + Accept training reduced cortisol and systolic blood pressure reactivity compared to Monitor Only and control trainings. Participants in all three conditions reported moderate levels of subjective stress.

Conclusions: This study provides the first experimental evidence that brief smartphone mindfulness training can impact stress biology, and that acceptance training drives these effects. We discuss implications for basic and applied research in contemplative science, emotion regulation, stress and coping, health, and clinical interventions.

1. Introduction

Mindfulness meditation training has emerged as a leading stress reduction approach in recent years (Creswell and Lindsay, 2014). For example, eight-week mindfulness interventions have been shown to reduce physiological and subjective reactivity to acute stress challenge tasks (Britton et al., 2012; Hoge et al., 2013; Nyklíček et al., 2013). Still, little is known about the active mechanisms of mindfulness interventions that drive these stress reduction effects. Mindfulness training commonly involves using attention to monitor present-moment experiences while fostering acceptance of one’s current state (Bishop et al., 2004). One possibility is that acceptance – defined as an orientation of noninterference and openness toward momentary sensory experience (i.e., thoughts, emotions, body sensations, sights, and sounds) – is a critical emotion regulation mechanism (Hölzel et al., 2011) underlying mindfulness training stress reduction effects (Lindsay and Creswell, 2017). In contrast to avoiding, altering, or focusing narrowly on salient negative stimuli, acceptance is an attitude of receptivity and equanimity toward all momentary experiences that allows even stressful stimuli to arise and pass without reactivity. Self-reported acceptance skills are associated with lower physiological and neural stress reactivity (Paul et al., 2013; Shallcross et al., 2013), and emotional acceptance is an effective strategy for regulating negative affect (Kohl et al., 2012) that may dampen physiological reactivity to emotional stimuli (Dan-Glauser and Gross, 2015). To evaluate the importance of acceptance training as a stress reduction mechanism in mindfulness interventions, we report the results of the first three-arm randomized controlled dismantling trial that compares a full mindfulness training program (Monitor + Accept) to a mindfulness training program without acceptance instructions (Monitor Only) and an active placebo controlled program (Coping control).

Although there are now multiple evidence-based in-person...
mindfulness training interventions demonstrating stress buffering effects (e.g., Mindfulness-Based Stress Reduction (MBSR); Creswell and Lindsay, 2014), a range of ‘remote’ (e.g., online; smartphone-based) mindfulness interventions are now widely used (Creswell, 2017; Wabbeh et al., 2014). These remote interventions are more accessible, inexpensive, and scalable compared to in-person interventions. Several studies have demonstrated benefits of two- to three-week remote mindfulness interventions for increasing compassion (Lim et al., 2015) and reducing general stress perceptions (Cavanagh et al., 2013; Glück and Maercker, 2011), but no studies have tested whether brief remote mindfulness training reduces acute physiological stress reactivity. The present study employed a 15-lesson smartphone intervention to test its efficacy for reducing stress reactivity (Monitor + Accept vs. Coping control) and to clarify the underlying components of mindfulness training that drive these effects (Monitor + Accept vs. Monitor Only). By offering a high degree of experimental control (e.g., one instructor teaches all treatment programs, content is standardized, social contact and discussion is controlled), this smartphone intervention approach allowed for an experimental dismantling of the components unique to mindfulness training.

This study tests the primary hypothesis that acceptance training is a necessary component for mindfulness intervention stress reduction effects. Stressed adults were randomly assigned to receive one of three structurally equivalent programs: (1) Monitor + Accept (MA), standard mindfulness training with instruction in both monitoring and acceptance techniques, (2) Monitor Only (MO), instructing monitoring techniques only, or (3) Coping control, providing guidance in free reflection, analytic thinking, and problem solving. After the two-week at-home intervention period and a pre-stress booster session, stress reactivity was assessed using a modified Trier Social Stress Test (mTSST; Kirschbaum et al., 1993); exaggerated cortisol and blood pressure responses to acute laboratory stressors are important markers of long term health outcomes (e.g., Cohen et al., 2002; Matthews et al., 2004). This pre-registered trial was designed to test the prediction that Monitor + Accept mindfulness training would reduce cortisol, blood pressure, and subjective stress reactivity compared to Monitor Only and control trainings.

2. Methods

2.1. Participants

Enrolled participants were 153 stressed adults (mean age = 32 years, SD = 14; see Table 1A for baseline characteristics) recruited from the Pittsburgh community via participant registries, community advertisements, and mass emails to local organizations for a study testing smartphone training programs for managing stress. Primary study analyses are reported on data available from 144 participants who completed study assessments; N = 4 participants discontinued before the post-intervention assessment, and N = 5 discontinued participation during the mTSST (see Fig. 1 for CONSORT flow chart). No participants withdrew due to adverse effects.

The study design and hypotheses described here are pre-registered with Clinical Trials identifier NCT02433431, and this report describes the stress reactivity outcome data (secondary trial outcomes). Eligible participants were English-speaking smartphone owners (Android or iPhone) between the ages of 18–70 years3 who scored > 5 on the 4-item Perceived Stress Scale (reflecting higher-than-average perceived stress; Cohen et al., 1983; Cohen and Williamson, 1988; Warthig et al., 2013).

To minimize the interference of medical conditions and behaviors on primary stress and biological outcomes (and to ensure the safety of participants and research staff), participant exclusion criteria included: chronic mental or physical disease; hospitalization for mental or physical illness in the past 3 months; medication use that interferes with HPA axis or immune system functioning; current antibiotic, antiviral, or antimicrobial treatment; use of oral contraceptives; and travel to countries on CDC travel alert list in the past 6 months (for potential bloodborne pathogen exposure). Finally, in order to test the effects of developing mindfulness skills in a novice population, those with a regular systematic mind-body practice (greater than 2 times per week) were excluded. Written informed consent was obtained from all participants, and all study procedures were approved by the Carnegie Mellon University IRB. Study data was collected between February 2015 and April 2016. Trial recruitment was stopped when the goal of enrolling 150 participants was reached.

Previous 8-week mindfulness intervention studies have demonstrated a medium effect size for stress reactivity outcomes (Cohen’s $d = 0.63$; Nyklíček et al., 2013) and pilot 2-week online mindfulness training interventions show small-medium effects on general stress perceptions ($d = 0.37–0.46$; Cavanagh et al., 2013; Glück and Maercker, 2011). Thus, estimating an effect size of $d = 0.52$, G*Power calculated a total of $N = 147$ participants needed to detect omnibus differences between three study conditions at 80% power using an ANOVA (Faul et al., 2007). The stress reactivity data reported here were not analyzed until the complete dataset was collected.

2.2. Procedure

Briefly, as part of the larger three-arm parallel trial, interested participants were pre-screened for eligibility by telephone, then further screened at an in-person baseline assessment (which began between 2:00pm and 6:00pm). Subject IDs were assigned sequentially, and the study PI used a random number generator to pre-assign one of three condition codes to each ID in blocks of 8, 16, or 24 using a 3-3-2 randomization sequence (so that for every 8 participants enrolled, 3 were assigned to MA, 3 to MO, and 2 to control). Trained study staff enrolled eligible participants and instructed participants to download their assigned intervention by code (all participants were blind to study condition, and study staff were blind to condition in 76% of baseline sessions). Enrolled participants provided a dried blood spot (DBS) sample, completed a questionnaire and task battery, and were oriented to the at-home study assessments and intervention. During three weeks of at-home study activities, participants completed three consecutive days of pre-intervention experience sampling, a 14-day intervention period (see Materials), and three consecutive days of post-intervention experience sampling. Participants received study reminder texts and phone calls throughout the at-home period, and were able to call or text our study hotline to ask questions or resolve technical issues. DBS and experience sampling outcomes will be reported in other manuscripts.

The mTSST stress reactivity findings described in this report were assessed at post-intervention. Participants returned for this assessment between 2:00pm and 6:00pm to control for diurnal variation in cortisol (mean $= 3:51pm$; no differences between conditions: F(2,145) = 0.30, $p > 0.250$). The appointment was an average of 4.66 days (SD = 1.88) after the at-home intervention (range: 3–12 days, with 86% of appointments occurring within 5 days; see Table 2). In 89% of post-intervention sessions, experimenters were blind to study condition.

Participants first provided a DBS sample and then were seated, fitted with a blood pressure cuff, and administered a post-intervention questionnaire and task battery (not reported here). During this time, the
pre-stress blood pressure (BP) reading (starting ~10 min after arrival) and a pre-stress saliva sample (~25 min after arrival) for cortisol assessment were taken (see Measures). A modified version of the Trier Social Stress Test (mTSSST; Kirschbaum et al., 1993) was used to manipulate social-evaluative stress reactivity in a controlled laboratory setting. Participants heard pre-recorded instructions (2.5 min in length) for the speech performance ("defend yourself against a false shoplifting charge"; Cohen et al., 2002; Franzen et al., 2011) and were given three versions of the Trier mTSSST speech portions of the task (see Measures). If a participant expressed any desire to quit during the mTSSST, an evaluator confirmed by asking, "Would you like to discontinue the task?" and, if affirmed, the experimenter returned to the room for debriefing. Otherwise, participants remained seated for a 5-min recovery period (BP Recovery period), after which the experimenter returned and removed the blood pressure cuff. Participants then completed several post-mTSSST questionnaires and tasks. Saliva samples were taken exactly 25 and 35 min after the start of the mTSSST to measure peak cortisol reactivity. An average of four to five days after the 14-day intervention period, participants received a 20-min booster training (lesson 15) during the post-intervention assessment (before the mTSSST). Each booster lesson began by addressing the upcoming performance task, encouraging participants to apply the skills learned throughout the course during this challenge; the lesson then presented guided content from the training course that best represented the targeted skills. Guided practice, and self-guided practice. An unblinded study manager contacted all participants by phone on Days 3 and 9 of the intervention program to answer training-specific questions, address difficulties, and encourage program adherence. After the 14-day intervention period, the training program was deactivated (although a training program of choice was provided upon study completion).

An average of four to five days after the 14-day intervention period, participants received a 20-min booster training (lesson 15) during the post-intervention assessment (before the mTSSST). Each booster lesson began by addressing the upcoming performance task, encouraging participants to apply the skills learned throughout the course during this challenge; the lesson then presented guided content from the training course that best represented the targeted skills. Guidance was interspersed with silent practice in 30- to 120-s blocks, totaling an average of 13 min of silence (13.5 min in MA, 12.5 min in MO, 12.5 min in control).

The intervention programs were developed in collaboration with leading mindfulness teacher Shinzen Young and were based on his Unified Mindfulness system (Young, 2016b). MA and MO were designed to systematically parse mindfulness instruction in (1) monitoring...
and (2) acceptance. See Supplementary Table 1 in Appendix A for an outline of lesson content in each training condition. Full intervention scripts are available for research purposes by request.

2.3.1.1. Monitor + Accept (MA). MA participants first learned foundational concentration skills, which enabled them to (1) monitor their present-moment body experience (in the lessons, this skill was referred to as ‘sensory clarity’) while (2) welcoming and accepting each experience (referred to as ‘equanimity’). Specifically, concentration was described as an intrinsically rewarding state of stable attention (cf. Csikszentmihalyi, 2000) on the intended target (in this intervention, the focus was physical and emotional body experiences; e.g., physical sensations on the skin, muscle sensations, ongoing physiology, temperature changes, sleepiness, etc., as well as body sensations related to emotions, such as anger, fear, sadness, impatience, interest, joy, enthusiasm, anxiety, etc.). Monitoring (‘sensory clarity’) was explained in terms of two dimensions: resolution (discriminating types of experiences; e.g., pleasant, unpleasant, neutral; physical vs. emotional; level of intensity; locations and movement patterns of sensations) and sensitivity (detecting subtle sensations; e.g., faint sensations related to pleasant activities and emotions; fleeting waves of unpleasant emotions). Acceptance (‘equanimity’) was trained through three tangible strategies that embody the attitude of acceptance: participants were encouraged to (a) maintain a state of global body relaxation,4 (b) mentally welcome all physical and emotional body experiences, and (c) use a gentle, matter-of-fact tone of voice (an ‘equanimity tone’) while labeling these experiences.

2.3.1.2. Monitor Only (MO). The MO program trained participants only to concentrate on and (1) monitor physical and emotional body experience (as described above), with no instruction on acceptance.

2.3.1.3. Coping control. The Coping control training program (referred

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4 In contrast to systematically relaxing each part of the body, the encouragement to maintain a sense of relaxation throughout the body – while simultaneously allowing and accepting physical tension and uncomfortable experiences – is a strategy that creates openness to sensory experiences and cultivates nonreactivity and noninterference.
to in the lessons as ‘MyTime’) was developed to parallel the structure of MA and MO without encouraging focus on or acceptance of present experience. Instead, participants were instructed to freely reflect and let their minds drift (in contrast to concentration developed in MA and MO) without encouraging focus on or acceptance of present experience. Instead, participants were instructed to freely reframe or reappraise past and anticipated events (with past and future emphasis contrasting present-focused monitoring, and change strategies contrasting acceptance strategies), and analyze and solve personal problems (again encouraging active change rather than acceptance of momentary experiences). Although positive reappraisal may be a downstream consequence of practicing mindfulness (cf. Garland et al., 2015), reappraisal is a change-based strategy that is not trained in mindfulness or acceptance-based interventions (cf. Hayes, 2004) and is therefore suitable as a comparison technique. The Coping control program was designed to be useful for managing stress (reinforcing common reappraisal and coping strategies; cf. Carver et al., 1989; Ochsner and Gross, 2005) without training mindfulness and was included to control for nonspecific effects of undergoing a training program (e.g., treatment expectations, daily time and effort toward the goal of reducing stress). Overall, this active Coping control program was expected to modestly reduce subjective stress reactivity and minimally reduce biological stress reactivity.

### 2.3.2. Measures

#### 2.3.2.1. Treatment adherence

The smartphone training application automatically timestamped the initiation and completion of each lesson in the 14-day at-home training period. This electronic timestamp was used to calculate the total number of at-home lessons completed for each individual.

#### 2.3.2.2. Treatment expectancies

To evaluate whether all three training programs produced equivalent perceived treatment benefits, participants completed an adapted 6-item Credibility/Expectancy Questionnaire (Devilly and Borkovec, 2000) to assess their beliefs about the efficacy of the training program at post-intervention (but before beginning the mTSST procedures). Logical (e.g., “how successful do you think this program was in reducing your stress symptoms?”) and emotional (e.g., “how much improvement in your symptoms do you think this program was in reducing your stress symptoms?”) subscales were averaged to create an overall measure of positive treatment expectancies (Cronbach’s α = 0.95).

#### 2.3.2.3. Salivary cortisol

Four saliva samples were collected using Salivettes (Rommelsdorf, Germany): (1) at the beginning of the final study appointment (an average of 26 min after arrival), (2) 25 min after the mTSST start (an average of 81 min after the pre-stress sample was collected), (3) 35 min after mTSST start, and (4) 60 min after mTSST start. Participants held Salivettes in their mouths for two minutes during each collection period, and did not touch the samples with their hands. Bottled water was provided during the session to increase hydration and help avoid sample loss due to lack of saliva, but water was removed 10 min before each sample collection. Salivettes were stored at −20 °C in a secure laboratory freezer. Samples were shipped in one batch to Dresden, Germany for cortisol measurement. Cortisol was measured using a high sensitivity chemoluminescence-immunoassay (IBL International, Hamburg, Germany). Intra- and inter-assay coefficients of variability in this laboratory are typically below 10%. Of the 576 samples collected from mTSST completers, 5.73% of Salivettes did not contain enough saliva to assay.

#### 2.3.2.4. Blood pressure

Oscillometric blood pressure was collected using an automatic sphygmomanometer (Dinamap Carenscope V100, General Electric Company, Finland). Systolic (SBP) and diastolic (DBP) blood pressure were recorded at 2-min intervals during five experimental epochs. Averages of these 2-min readings were calculated during a 5-min Pre-Stress epoch (an average of 12 min after arrival), the 3-min mTSST blood pressure Preparation epoch (an average of 41 min after the Pre-Stress recording), the 20-min booster Training epoch, the 12-min mTSST Performance epoch, and a 5-min Recovery epoch directly after the mTSST. Participants were seated throughout the blood pressure measurement. Due to equipment malfunction, data for one epoch was missing for N = 4 participants (preparation or recovery), data from two epochs was missing for N = 1 participant (performance and recovery), and data from four epochs was missing for N = 1 participant (preparation through recovery).

#### 2.3.2.5. Subjective stress reactivity

During the mTSST procedure, participants used visual analog scales to rate their perceptions of stress immediately after the 5-min speech task and again immediately after the 5-min math task (Creswell et al., 2014; Hellhammer and Schubert, 2012). Specifically, after each task, participants indicated how stressed, anxious, and insecure they felt by drawing a slash mark on a 140 mm line from 0 (not at all) to 100 (highly) (with intermediate anchors at 25, 50, and 75). Distance from 0 was measured in centimeters, divided by 14, and multiplied by 100 to create a stress percentage score for each item. One composite subjective stress reactivity score was created by averaging all six ratings (Cronbach’s α = 0.90), with higher values representing greater stress perceptions.

### Table 2

mTSST stress reactivity outcomes in each condition.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>mTSST Sample (N = 144)</th>
<th>Monitor + Accept (N = 55)</th>
<th>Monitor Only (N = 54)</th>
<th>Control (N = 35)</th>
<th>Condition Difference Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Cortisol (AUC-I)</td>
<td>16.20</td>
<td>–2.25</td>
<td>23.23</td>
<td>27.62</td>
<td>F(2,140) = 3.20</td>
</tr>
<tr>
<td>(EM estimation)</td>
<td>[5.62, 26.78]</td>
<td>[–19.06, 14.56]</td>
<td>[6.31, 40.16]</td>
<td>[6.60, 48.64]</td>
<td></td>
</tr>
<tr>
<td>Log Cortisol</td>
<td>1.27</td>
<td>1.04</td>
<td>1.31</td>
<td>1.54</td>
<td>χ²(2) = 9.09*</td>
</tr>
<tr>
<td>(25 min post-mTSST; N = 136)</td>
<td>[1.14, 1.39]</td>
<td>[0.83, 1.25]</td>
<td>[1.10, 1.51]</td>
<td>[1.28, 1.80]</td>
<td></td>
</tr>
<tr>
<td>Log Cortisol</td>
<td>1.15</td>
<td>0.91</td>
<td>1.21</td>
<td>1.40</td>
<td>χ²(2) = 8.18*</td>
</tr>
<tr>
<td>(35 min post-mTSST; N = 135)</td>
<td>[1.01, 1.28]</td>
<td>[0.69, 1.13]</td>
<td>[0.99, 1.43]</td>
<td>[1.13, 1.68]</td>
<td></td>
</tr>
<tr>
<td>Log Cortisol</td>
<td>0.80</td>
<td>0.62</td>
<td>0.85</td>
<td>1.02</td>
<td>χ²(2) = 4.01</td>
</tr>
<tr>
<td>(60 min post-mTSST; N = 135)</td>
<td>[0.65, 0.96]</td>
<td>[0.37, 0.87]</td>
<td>[0.60, 1.10]</td>
<td>[0.71, 1.33]</td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>139.89</td>
<td>134.51</td>
<td>140.93</td>
<td>146.64</td>
<td>χ²(2) = 11.71*</td>
</tr>
<tr>
<td>(mTSST Performance; N = 142)</td>
<td>[137.18, 142.60]</td>
<td>[130.12, 138.91]</td>
<td>[136.51, 145.35]</td>
<td>[141.12, 152.15]</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>81.36</td>
<td>78.57</td>
<td>82.76</td>
<td>83.56</td>
<td>χ²(2) = 7.67*</td>
</tr>
<tr>
<td>(mTSST Performance; N = 142)</td>
<td>[79.80, 82.93]</td>
<td>[76.04, 81.10]</td>
<td>[80.21, 85.30]</td>
<td>[80.38, 86.73]</td>
<td></td>
</tr>
<tr>
<td>Subjective Stress Reactivity</td>
<td>49.54</td>
<td>48.53</td>
<td>48.52</td>
<td>51.55</td>
<td>F(2,141) = 0.22</td>
</tr>
<tr>
<td>(mTSST Performance)</td>
<td>[45.55, 53.52]</td>
<td>[42.23, 54.84]</td>
<td>[42.16, 54.88]</td>
<td>[43.65, 59.46]</td>
<td></td>
</tr>
</tbody>
</table>

Note: Data are reported as means [95% Confidence Interval]. AUC-I = Area Under the Curve with respect to Increase; EM = Expectation Maximization; mTSST = modified Trier Social Stress Test; BP = Blood Pressure.

* Data adjusted for follicular phase (menstrual cycle days 4-12 vs. all else).

* Average of subjective stress ratings ranging Speech & Math tasks.

* p < 0.05.
2.4. Analyses

Analyses were conducted with SPSS Statistics 23.0 software (IBM, Armonk, New York) and Stata/SE 14.0 (StataCorp, College Station, Texas). Preliminary analyses (conducted in SPSS) evaluated baseline success of randomization using chi-square (for categorical variables) and ANOVA tests (for continuous variables). The measure of treatment expectancies was evaluated as a covariate using ANOVA to test for significant differences between conditions. ANOVAs were also used to test for condition differences in treatment adherence, post-intervention procedures, and pre-stress cortisol and blood pressure. Finally, preliminary analyses checked the success of the mTSST in inducing physiological stress; specifically, paired-samples t tests tested for differences between pre-stress and peak mTSST cortisol and BP reactivity across the entire sample.

To test primary study predictions, ANOVAs (in SPSS) and Mixed Linear Models (MLMs; in Stata) tested for condition differences on stress reactivity outcomes. MLMs are robust to missing data because they model all available data, and were used for analyses that included time as a within-subject variable. Variables of interest (time, study condition) were modeled as fixed effects using maximum likelihood estimation. The repeated measures variable (time) was modeled with an unstructured covariance structure, with pre-stress values used as the first repeated measure to test for time interactions with the predictor variable (study condition). If included, covariates were modeled as fixed effects. Within each MLM, omnibus tests of condition differences at each mTSST reactivity time point were conducted, and pairwise comparisons contrasted MA vs. MO and control at each time point (accounting for pre-stress levels).

2.4.1. Cortisol reactivity analyses

First, because they were not normally distributed, raw cortisol values were natural-log-transformed at each of four time points. Then, intervention condition differences in cortisol reactivity were tested in two steps. Area under the curve with respect to increase (AUC-I) was calculated with a trapezoid formula (Pruessner et al., 2003) that subtractions the pre-stress cortisol level in order to measure reactivity (i.e., increase in cortisol from pre-stress levels): (cortisol 1 + cortisol 2*81 mins/2 + (cortisol 2 + cortisol 3)*10 mins/2 + (cortisol 3 + cortisol 4)*25 mins/2−cortisol 1*(81 + 10 + 25). As this formula requires data at all four time points, and one or more values was missing from N = 14 (9.72%) participants, the Expectation Maximization (EM) algorithm (based on all available cortisol data) was used to replace missing values before calculating a total AUC-I for each participant. An ANCOVA then tested for condition differences in cortisol AUC-I and pairwise comparisons contrasted MA with MO and control training. Then, an MLM (which requires no missing data imputation) tested for condition differences in cortisol reactivity over time (pre-stress, 25-, 35-, and 60-min post-mTSST), as well as omnibus and pairwise differences at each post-mTSST time point (accounting for pre-stress levels). As menstrual cycle phase is known to impact cortisol reactivity (Kirschbaum et al., 1999), all cortisol analyses controlled for follicular stage on the day of the post-intervention session (women on menstrual cycle days 4–12 vs. all others, including men and post-menopausal women).

2.4.2. BP reactivity analyses

Intervention condition differences in SBP and DBP reactivity were tested in MLMs focusing on the interaction between study condition and time (pre-stress, preparation, training, performance, and recovery epochs), using all available data. Follow-up analyses within each MLM tested for omnibus and pairwise condition differences in peak BP reactivity during the mTSST performance epoch (accounting for pre-stress levels), the main contrast of interest.

2.4.3. Subjective stress reactivity analyses

ANOVA were used to test for condition differences in subjective stress reactivity.

3. Results

3.1. Preliminary analyses

First, success of randomization on major demographic characteristics in the full randomized sample (N = 153) was evaluated. There were no pre-existing condition differences on age, sex, race, ethnicity, education, or body mass index (BMI) (see Table 1A for details).

Second, condition differences in the intervention and post-intervention assessment protocol were tested among participants who returned at post-intervention (N = 149; see Fig. 1 and Table 1B for details). Participants in all conditions were highly adherent to the training programs, with no condition differences in treatment adherence (F(2,146) = 0.40, p > 0.250). On average, participants completed 13.49 of the 14 at-home lessons, and 75% of participants completed all 14 lessons (1.3% of participants completed fewer than 10 lessons). All participants who returned for the post-intervention assessment received booster lesson 15. There were no condition differences in treatment expectancies (F(2,146) = 1.55, p = 0.216), indicating similar perceptions of treatment benefits across all three training conditions, and additional analyses that included treatment expectancies as a covariate did not appreciably impact any of the primary outcomes (data not shown). At the post-intervention assessment, there were no condition differences in pre-stress raw or log-transformed cortisol levels (see Table 1B), time of first cortisol sample (M = 4:18pm, SD = 1:37; F(2,145) = 0.28, p > 0.250), or time of peak cortisol sample (M = 5:40pm, SD = 1:37; F(2,144) = 0.22, p > 0.250). Similarly, there were no condition differences in pre-stress systolic or diastolic blood pressure at the post-intervention assessment (see Table 1B).
In a final set of preliminary analyses, paired-samples t tests demonstrated the efficacy of the mTSST manipulation in producing a physiological stress response. Across all participants with pre-stress and peak (25 min post-mTSST onset) saliva samples (N = 135), there was a significant increase in log cortisol from pre-stress to peak reactivity (t(134) = -4.06, p < 0.0005, d = 0.61), confirming that the mTSST produced a significant neuroendocrine stress response. Similarly, there were significant increases in SBP (t(141) = -23.32, p < 0.0005, d = 1.59) and DBP (t(141) = -23.56, p < 0.0005, d = 1.54) from pre-stress to mTSST performance, confirming that the mTSST produced a significant cardiovascular stress response.

### 3.2. Primary analyses

#### 3.2.1. Cortisol reactivity

First, to evaluate the hypothesis that MA training would reduce cortisol reactivity in response to the mTSST to a greater degree than MO and control trainings, an ANOVA tested for condition differences in log cortisol AUC-I (replacing missing data with EM estimated values) and an MLM tested for time × condition interactions in log cortisol (using all available data). All cortisol analyses included follicular phase as a covariate. There was a significant effect of study condition on log cortisol AUC-I (F(2,140) = 3.20, p = 0.044; see Table 2 for descriptive statistics). Specifically, MA-trained participants had significantly lower log cortisol AUC-I than MO- and control-trained participants (MA vs. MO: F(1,140) = 4.44, p = 0.037, d = 0.40; MA vs. control: F(1,140) = 4.79, p = 0.030, d = 0.47). Second, using all available data, an MLM revealed a significant main effect of time across study conditions (χ²(3) = 176.65, p < 0.0005), a significant main effect of study condition across all four time points (χ²(2) = 6.25, p = 0.044), and, consistent with our primary predictions, a significant time × condition effect on log cortisol (χ²(6) = 12.80, p = 0.046). Fig. 2 depicts this time × condition interaction. Within this MLM (which accounts for pre-stress cortisol levels), planned comparisons showed that MA-trained participants had significantly lower log cortisol at 25- and 35-min post-mTSST compared to MO-trained participants (25-min: χ²(1) = 6.05, p = 0.014, d = 0.50; 35-min: χ²(1) = 6.26, p = 0.012, d = 0.51) and control-trained participants (25-min: χ²(1) = 7.26, p = 0.007, d = 0.62; 35-min: χ²(1) = 5.98, p = 0.015, d = 0.55) (see Table 2). There were no significant differences in cortisol reactivity between MO and control interventions at any measurement point (all ps > 0.250).

#### 3.2.2. BP reactivity

MA training was also hypothesized to significantly reduce BP stress reactivity compared to MO and control trainings. To test for condition differences in SBP, an MLM using all available data revealed a significant main effect of time (χ²(4) = 1066.22, p < 0.0005), a significant main effect of study condition (χ²(2) = 6.45, p = 0.040), and a marginal time × condition interaction (χ²(8) = 14.91, p = 0.061). Fig. 3A depicts the time × condition interaction on SBP. Consistent with predictions, there were significant condition differences in SBP during the mTSST Performance period (see Table 2). Planned comparisons (accounting for pre-stress SBP) showed that MA-trained participants had significantly lower SBP during the mTSST Performance compared to MO- and control-trained participants (MA vs. MO: χ²(1) = 4.34, p = 0.037, d = 0.41; MA vs. control: χ²(1) = 10.16, p = 0.001, d = 0.72). MA-trained participants also had significantly lower SBP during the mTSST recovery period compared to control participants (χ²(1) = 4.77, p = 0.029, d = 0.48).

An MLM using all available data did not support our hypothesis that MA training would significantly reduce DBP reactivity; there was a significant main effect of time (χ²(4) = 660.48, p < 0.0005), no main effect of study condition (χ²(2) = 4.18, p = 0.124), and no time × condition interaction on DBP (χ²(8) = 10.52, p = 0.230) across the post-intervention assessment (see Fig. 3B). Although there were significant condition differences in DBP during the mTSST Performance period in isolation (with significant contrasts between MA vs. MO: χ²(1) = 5.23, p = 0.022, d = 0.45, and MA vs. control: χ²(1) = 5.80, p = 0.016, d = 0.53; see Table 2), planned comparisons that account for pre-stress DBP showed no differences between MA-trained participants compared to MO- and control-trained participants (MA vs. MO: χ²(1) = 1.68, p = 0.195, d = 0.25; MA vs. control: χ²(1) = 2.63, p = 0.105, d = 0.35).

We had no specific hypotheses comparing MO vs. control, and MO-trained participants did not have significantly lower SBP reactivity (χ²(1) = 1.82, p = 0.177, d = 0.26) or DBP reactivity (χ²(1) = 0.23, p > 0.250, d = 0.09) during the mTSST Performance period compared to control-trained participants.

#### 3.2.3. Subjective stress reactivity

Finally, an ANOVA tested the hypothesis that MA training would reduce subjective stress reactivity compared to MO and control training. Contrary to this prediction, there were no conditions...
differences in average subjective stress reactivity (see Table 2).

4. Discussion

Acceptance training has been theorized as an essential component of mindfulness interventions for improving affective reactivity, stress, and health outcomes (Lindsay and Creswell, 2017), but no mechanistic dismantling studies have tested this hypothesis. This study provides the first experimental evidence that acceptance is a critical component of mindfulness training for reducing biological stress reactivity; without acceptance training (i.e., in the Monitor Only training condition), mindfulness stress buffering effects are diminished or eliminated. Specifically, Monitor + Accept training reduced both neuroendocrine (salivary cortisol) and sympathetic nervous system (systolic blood pressure only) stress reactivity biomarkers compared to Monitor Only and control training. Acceptance may help to regulate stress reactivity by facilitating the acknowledgement of (Teper and Inzlicht, 2013) and subsequent disengagement from (i.e., letting go; Vago and Nakamura, 2011) all momentary sensory experiences, even difficult or stressful ones.

This study has a number of notable features. It is the first study to show that brief smartphone-based mindfulness training can impact objective biological stress outcomes. This smartphone format also provided a platform for dismantling the active components of mindfulness training, which allowed us to address mechanistic questions. By tightly controlling the intervention content, we were able to observe the unique contributions of attention monitoring and acceptance training beyond non-mindfulness-specific treatment elements (i.e., stress management and reappraisal skills in the placebo comparison program). Additionally, study attrition using this brief smartphone approach was much lower than the typical rates observed in longer group-based mindfulness programs (3% in this study) and program adherence was...
high (96%). The generalizability of this approach is somewhat limited by disparities in smartphone ownership (among lower SES and older adults; Poushter, 2016), although smartphone ownership continues to rise in these populations (e.g., increasing 12 percentage points among both lower-income and older Americans from 2015 to 2016; Smith, 2017). Moreover, program adherence would likely be lower outside the context of a structured study intervention (Rahmati et al., 2012). Still, these findings demonstrate value in implementing smartphone-based mindfulness interventions for a large proportion of stressed adults who lack resources for more expensive, intensive, and potentially inaccessible in-person mindfulness programs.

The present findings have important basic and applied implications. Among mindfulness intervention researchers and contemplative scientists, this study contributes evidence to an ongoing debate about the importance of acceptance in contemporary mindfulness training interventions (e.g., Grossman and Van Dam, 2011). On one hand, mindfulness is translated simply as a state of clear awareness (Boehnigh, 2011; Desbordes et al., 2015; Quaglia et al., 2014); on the other hand, acceptance training is considered a skillful means for learning mindfulness (Dreyfus, 2011) and is an active treatment element in mindfulness and other “third-wave” interventions (Mennin et al., 2013). By comparing mindfulness interventions that include or exclude an acceptance training component, this study shows that learning to accept one’s experiences produces measurable biological stress reduction effects. These results are consistent with Buddhist monastic training, the culture of origin for secular mindfulness training. In the Buddhist paradigm, monitoring (vipaśyāna) leads to sensory clarity and insight (prajñā), whereas acceptance (i.e., equanimity, the ability to experience pleasure and pain without interference) reduces craving (rāga) and aversion (dveśa), the necessary causes (samuccaya) for suffering (dukkha) (Young, 2016b, 2016a). For basic researchers, these findings contribute to a growing understanding of acceptance as an emotion regulation mechanism (Kohl et al., 2012), an approach that has received less attention than other response-focused strategies (e.g., cognitive reappraisal). Likewise, among stress and coping researchers, this study sheds new light on the construct of acceptance; this intentional form of experiential acceptance stands in contrast to the form of acceptance that resembles passive resignation and is generally associated with poor outcomes in the health psychology literature (e.g., Reed et al., 1994). These findings suggest the value of including (or emphasizing) acceptance training in existing stress management interventions. While some psychotherapeutic programs offer extensive acceptance skills modules (e.g., ACT; Hayes et al., 2011), most stress management programs offer little formal instruction in acceptance. Exploring the conditions under which acceptance training is beneficial (e.g., training dosage, individual differences in adopting acceptance strategies) is an important research direction.

Although MA training reduced biological markers of stress reactivity (cortisol, systolic blood pressure), contrary to initial predictions there were no condition differences in self-reported stress during the mTSST. Several possibilities could explain this effect. It may be that all three active training programs compared in this study were effective for decreasing perceptions of stress; participants in all programs reported equivalent treatment benefits, and each program focused on stress management (e.g., the control program reinforced reappraisal and coping strategies). It’s also possible that the self-report stress instrument was prone to well-known response-set biases (Nisbett and Wilson, 1977), or was not sensitive to unique ways that mindfulness trained participants perceive stress. For example, our stress scale did not distinguish between intensity of experience and perceived suffering (similar to intensity and unpleasantness dimensions commonly measured in the pain literature; cf., Price et al., 1987). Monitoring may make the experience of discomfort sensorially richer, while acceptance may lessen the associated suffering (i.e., intensity is not problematic or viewed as unpleasant), dimensions not captured in this stress instrument. Alternatively, although acute psychological and biological stress responses are commonly dissociated, differences in emotion regulation strategy use (e.g., avoidance vs. monitoring; reappraisal vs. acceptance) may moderate psychophysiological correspondence (for a review, see Campbell and Ehlert, 2012). It’s possible that, by increasing awareness of subtle body cues, the Monitor + Accept intervention increased coherence between stress biology (e.g., cortisol) and self-reported stress. Indeed, previous work indicates that meditation experience increases the accuracy of self-reporting on physical sensations (Fox et al., 2012) and mindfulness improves access to implicit emotional states (Brown and Ryan, 2003). Exploratory analyses showed that indeed there was a marginally stronger association between self-reported stress and cortisol reactivity (AUC-I) in the MA condition (r(55) = 0.27, p = 0.043) compared to the MO (r(54) = 0.18, p = 0.201) and control conditions (r(35) = −0.08, p > 0.250) (MA vs. control z = 1.59, p = 0.056). Though consistent with the theory that monitoring one’s body experiences with acceptance facilitates greater openness and access to subtle body cues, this finding requires replication.

While this study supports the Monitor and Acceptance Theory (MAT; Lindsay and Creswell, 2017) prediction that explicit training in both monitoring and acceptance are necessary for reducing biological stress reactivity, it raises additional questions. Contrary to MAT, which presents evidence that the self-reported tendency to monitor one’s experiences may intensify reactivity (e.g., Desrosiers et al., 2014; Pearson et al., 2015), there was no evidence that Monitor Only training exacerbated subjective or biological stress responses compared to control training (which was expected to slightly reduce reactivity). Instead, these findings are more consistent with MAT’s alternative prediction that structured monitoring practice, in contrast to the dispositional tendency to monitor in the absence of meditation training, may promote adaptive outcomes. It’s possible that, by simply acknowledging unpleasant stimuli without psychological resistance, systematically monitoring one’s experiences may begin to engender an implicit orientation of acceptance. Or, strengthening one’s attentional resources may by itself promote mental clarity and help to regulate emotions (Wadlinger and Isacowitz, 2011).

Given the evidence that acceptance training facilitates reductions in biological stress reactivity, one open question is whether acceptance alone is sufficient for driving these effects. Although this study aimed to test the active mechanisms of mindfulness training where acceptance is taught in conjunction with monitoring practice, some may see value in testing acceptance-only interventions (e.g., using a psychoeducational rather than experiential acceptance training approach). A major challenge in developing acceptance interventions devoid of attention monitoring training is how to instruct the orientation of acceptance toward experiences without first bringing attention to those experiences. In this Monitor + Accept intervention and in standardized mindfulness interventions, acceptance is trained in relation to monitored experience; thoughts, sensations, and emotions monitored in the present moment are acknowledged with acceptance and equanimity. Moreover, recent theorizing posits synergistic roles for monitoring and acceptance in reducing stress: monitoring draws attention to emotional stimuli, and orienting toward negative states with acceptance transforms one’s relationship to these experiences in ways that attenuate negative reactivity (Lindsay and Creswell, 2017). Nonetheless, the present results identify an opportunity to investigate whether training in acceptance skills only might be a more efficient way to improve stress-related health outcomes.

It is important to acknowledge that our conclusions about mindfulness components and stress reactivity are based on a 14-lesson mindfulness program plus a booster session. More research is needed to evaluate whether the booster session is a necessary condition for reducing biological stress reactivity (i.e., it was essential for activating the skills developed through the training program) or whether the effects of 14 days of mindfulness training persist without this skills reminder session prior to stress exposure. Although some acute interventions can shift one’s perspective in ways that promote a more adaptive
physiological response to stress (e.g., shifting from self-promotion to compassionate goals; appraising stress as functional; Abelson et al., 2014; Jamieson et al., 2012), these single session inductions are quite different from the intervention approach tested here. Given that previous evidence shows no benefits of mindfulness training for reducing biological stress reactivity after 3 training sessions (with the 3rd session similarly acting as a booster session immediately before mTSST performance; Creswell et al., 2014), the effects observed here likely hinge upon the development of mindfulness skills over the course of 14 lessons. Still, these findings raise broad empirical questions about the comparative efficacy, efficiency, and longevity of stress reduction interventions that induce acute mindset shifts vs. those that develop new, more ingrained skills for responding to stress.

Relatedly, this study lends evidence to a developmental trajectory of mindfulness stress buffering effects. Whereas previous research shows that 8 weeks (but not 3 sessions) of mindfulness training reduces biological stress reactivity (Creswell et al., 2014; Nykliček et al., 2013), we now show that an intermediate dose — two weeks of daily mindfulness training plus a booster session — is effective for reducing biological reactivity. Similarly, these findings contribute to research on the skill development of monitoring and acceptance. Although acceptance inductions have been shown to attenuate physiological responding to mild emotional stimuli (e.g., Campbell-Sills et al., 2006; Dan-Glauser and Gross, 2015; Hofmann et al., 2009), these brief inductions are not effective for those inexperienced with acceptance strategies (e.g., Blacker et al., 2012; Evans et al., 2014); for many, acceptance is a skill that takes time to develop (Baer et al., 2012). Our results imply that two weeks of training is sufficient to develop acceptance skills that effectively reduce the biological impact of stress. These findings prompt questions for further research in establishing the long-term growth, maintenance, and stability of attention monitoring and acceptance skills and their effects on stress reactivity (e.g., whether more extensive training in monitoring alone becomes equally effective as monitoring with acceptance training; the importance of continued formal practice for maintaining benefits).

Finally, one important open question concerns the value of these acute stress reactivity effects for long-term health and disease outcomes. Since greater cortisol and blood pressure reactivity to laboratory stress predict certain health risks (e.g., respiratory infections, cardiovascular disease; Cohen et al., 2002; Matthews et al., 2004), it’s possible that reduced stress reactivity effects like those observed here may confer some protection against stress-related symptoms and disease risk among stressed adults (cf. Loucks et al., 2015).

4.1. Conclusions

This study provides the first experimental evidence that brief remote mindfulness training is effective for reducing cortisol and systolic blood pressure reactivity to stress, and learning to accept one’s experiences is critical for driving these effects. By changing the way individuals relate to and respond to stressors, acceptance may reduce their biological stress responses to threatening events.

Author contributions

EL and JC developed the study concept. All authors contributed to the study design. EL prepared study materials. SY and EL developed interventions. Testing and data collection were performed by trained research assistants. EL performed the data analysis and interpretation under the supervision of JC, JS, and KB. EL drafted the manuscript, and all authors provided critical revisions. All authors approved the final version of the manuscript for submission.

Conflict of interest statement

The authors declare one potential conflict of interest, which has not influenced the authorship of this article or its content, including the research outcomes reported within it: author Shinzen Young owns a portion of 01 Expert Systems, which will be releasing a modified and extended version of the Monitor + Accept mindfulness intervention as a commercial app.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.psyneuen.2017.09.015.

References

Moving beyond mindfulness: defining equanimity as an outcome measure in medi-
tation and contemplative research. Mindfulness 6 (2), 356–372.


Garland, E.L., Farb, N.A., Goldin, P.R., Fredrickson, B.L., 2015. The mindfulness-to-meaning theory: extensions, applications, and challenges at the attention-apprais-


Meditation experience predicts introspective accuracy. PLoS One 7 (9), e45370.

Markovitz, J.H., 2004. Blood pressure reactivity to psychological stress predicts hy-


Pruessner, J.C., Kirschbaum, C., Meinlschmidt, G., Hellhammer, D.H., 2003. Two formulas for computation of the area under the curve that represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28 (8), 916–931.


