Substance Abuse, 30:306–317, 2009

ISSN: 0889-7077 print / 1547-0164 online
DOI: 10.1080/08897070903250241

Routledge
Taylor & Francis Group

Mindfulness Training and Stress Reactivity in Substance Abuse: Results from a Randomized, Controlled Stage I Pilot Study

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ABSTRACT. Stress is important in substance use disorders (SUDs). Mindfulness training (MT) has shown promise for stress-related maladies. No studies have compared MT to empirically validated treatments for SUDs. The goals of this study were to assess MT compared to cognitive behavioral

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The authors would like to thank the participants and the staff of the Substance Abuse Treatment Unit, without whom this research would not be possible. The authors would like to thank Ginny Morgan, Sarah Bowen, and Jon Kabat-Zinn for helpful discussions regarding adaptations for the MT presented in this paper, and Hedy Kober and Megan McGinn for their help with data input and analysis. The authors would also like to thank the staff of the Yale University Clinical Neuroscience Research Unit, and Psychotherapy Development Center, notably, Zubin Bhagwagar, Robert Malison, Jonas Hannestad, Samuel Ball, and Steve Martino, among others, for helpful discussions. This study was funded by the following grants: NIDA K12-DA00167 (J.A.B.), P50-DA09241 (B.J.R.), R37-DA15969 (K.M.C.), T32-DA007238 (J.A.B.), K05-DA00457 (K.M.C.), K05-DA00089 (B.J.R.), P50-DA16556 (R.S.), K02-DA17232 (R.S.), R01 DA020908 (M.N.P.), RL1 AA017539 (M.N.P.), the U.S. Veterans Affairs New England Mental Illness Research, Education, and Clinical Center (MIRECC) (B.J.R.), and a Varela grant from the Mind and Life Institute (J.A.B.).

Disclosures: The authors have no competing interests.

therapy (CBT) in substance use and treatment acceptability, and specificity of MT compared to CBT in targeting stress reactivity. Thirty-six individuals with alcohol and/or cocaine use disorders were randomly assigned to receive group MT or CBT in an outpatient setting. Drug use was assessed weekly. After treatment, responses to personalized stress provocation were measured. Fourteen individuals completed treatment. There were no differences in treatment satisfaction or drug use between groups. The laboratory paradigm suggested reduced psychological and physiological indices of stress during provocation in MT compared to CBT. This pilot study provides evidence of the feasibility of MT in treating SUDs and suggests that MT may be efficacious in targeting stress.

KEYWORDS. Addiction, cognitive behavioral therapy, heart rate variability, mindfulness, stress, substance use

INTRODUCTION

Considerable evidence has accumulated suggesting that stress exposure can produce an increased arousal state similar to that induced by drug cues (1). Acute stress may increase self-administration of drugs (2,3) and alcohol (4). This is consistent with incentive conditioning models stating that exposure to drug-related cues produces conditioned responses, which in turn can cue subsequent drug-seeking behavior and use (5). Stressful events and psychological distress are frequently cited reasons for relapse to drug use among individuals with substance use disorders (SUDs) (6–8). These data support the hypothesis that mechanisms related to stress are critical in the establishment of addictions and their propagation as chronic disorders (9,10).

Mindfulness-based therapies have shown preliminary evidence for efficacy in the treatment of tobacco, alcohol, and drug use disorders (11–17). For example, Zgierska and colleagues found reductions in anxiety, depression, and stress symptom severity in individuals with alcohol dependence who were enrolled in an 8-week mindfulness meditation intervention after completing an intensive outpatient program (12). Bowen and colleagues also found significant reductions in alcohol and drug use after release from prison in individuals who had undergone a 10-day Vipassana meditation course compared to those who had received treatment as usual (16). However, to date, no randomized trials have compared mindfulness training (MT) to empirically validated treatments for SUDs, such as cognitive behavioral therapy (CBT) (18).

Commonly used behavioral strategies in substance abuse treatment include avoidance of associative cues and suppression of "unwanted" thoughts. However, these strategies may be suboptimal. For example, thought suppression has been shown to lead to *stronger* expectancies after cue exposure (e.g., "alcohol makes me. . . ") (19). Mindfulness-based treatment has been shown to decrease alcohol consumption, which is partially mediated in prisoners by *decreases* in thought suppression indices such as avoidance (13). Also, as mindfulness-based treatments teach an attitude of acceptance/nonjudgment, they may help to mediate the avoidance of negative affective states and thoughts, as has been shown with depression (20–22). Accordingly, MT may be efficacious in treating compulsive drug use—characteristic for addiction—through multiple mechanisms related to stress such as tolerating unpleasant thoughts and emotions.

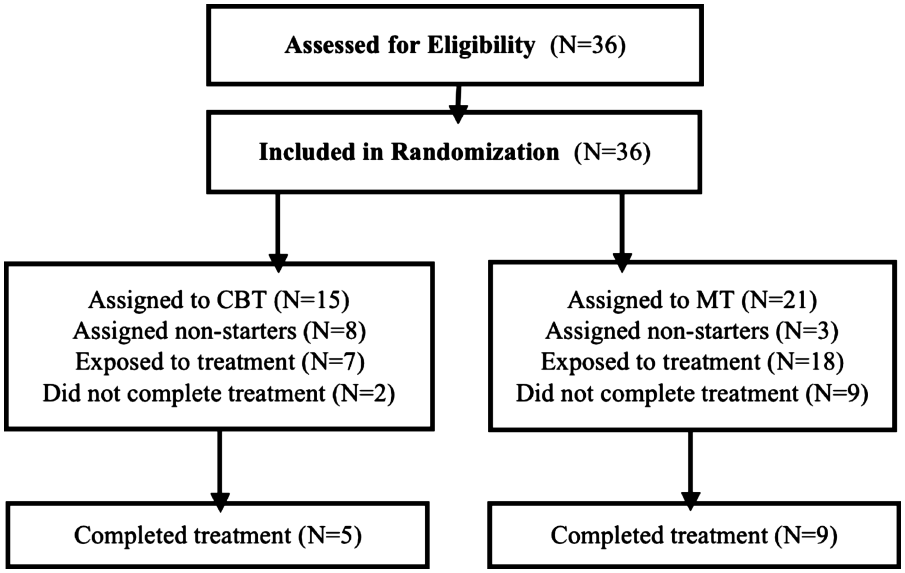
We describe outcomes from a stage I pilot trial in which we modified an existing manualized version of MT for individuals with SUDs. We evaluated (1) its feasibility by comparing it with empirically validated therapy (CBT), and (2) its specificity toward stress, by evaluating reactivity during stress provocation.

METHODS

Participants

Participants were recruited through media advertisements and clinician referrals of individuals seeking treatment at a community-based

FIGURE 1. Flow of participants through the study protocol. CBT = Cognitive Behavioral Therapy; MT = Mindfulness Training. Laboratory session was performed within two weeks of treatment completion.



outpatient treatment facility in New Haven, CT. Eligible participants were English-speaking adults who met DSM-IV criteria for alcohol and/or cocaine abuse or dependence in the past year. Individuals were excluded only if they were under 18 years old, currently at clinically significant risk for suicide or homicide, had a current psychotic disorder (assessed by a psychiatrist), had a cognitive impairment precluding completion of study-related activities, or were on beta-blocker treatment.

All of the 36 screened individuals were found eligible and agreed to participate in the study (Figure 1). They provided written informed consent, and were randomly assigned to treatment condition using a 2-choice random number generator (random.org). Of those, 25 were exposed to and 14 completed treatment. Thus, outcome data were available for the 14 treatment completers. Laboratory data were available for 13 treatment completers (collection error rendered data from the 14th person unusable).

Treatments

All participants received weekly group therapy sessions as their sole primary treatment. All treatments were manualized and delivered by PhD-level therapists experienced in CBT or MT, respectively.

CBT was delivered by one therapist over a 12-week period using the National Institute on Drug Abuse CBT manual (23). Sessions were delivered weekly in a continuous fashion such that individuals could enter treatment based on a weekly rolling admission process. Each session lasted roughly 1 hour. Groups were capped at 8 persons to ensure optimal treatment settings.

MT was delivered weekly, over a 9-week period, in a group session format, by one therapist (12 years of mindfulness practice and several years teaching). Groups were also capped at 8 persons to ensure optimal treatment. The MT manual was based on manualized Mindfulness-Based Relapse Prevention (MBRP) program (12,24). Several adaptations to MBRP were made. First, after the first session (renamed Introduction), the 7 sequential sessions were divided into 2 4-week modules that could be completed in either order (Introduction, then Module 1, then Module 2 or Introduction, then Module 2, then Module 1). This was done to assess "real-world" delivery of the treatment by providing minimal waiting time for individuals to enter

treatment. Module 1 included MBRP sessions 2, 6, and 7, and, in addition, a session that specifically targeted working with anger as a trigger for stress, drug use, or relapse (25), and instruction for using loving-kindness techniques to facilitate working with difficult emotions (26). Module 2 included MBRP sessions 3, 4, 5, and 8. Second, the yoga meditation was removed to decrease confounding, yoga-specific effects; yoga may have beneficial effects as a stand-alone treatment on stress reduction and drug use (27,28). Third, weekly sessions were shortened to approximately 1 hour (mainly by shortening the guided meditation exercises). This was done to assess whether shorter sessions would be sufficient for individuals to attain adequate mindfulness skills for benefits to be seen, and to mimic as closely as possible, group CBT sessions.

Assessments

The *Structural Clinical Interview for DSM-IV* (SCID) alcohol and drug modules were administered at baseline only to establish SUD-related diagnoses (29). Diagnoses were confirmed by a psychiatrist. All other measures were collected at least at baseline, weekly (as noted below) and upon treatment completion, which was roughly 9 weeks after treatment initiation for the MT and 12 weeks after treatment initiation for the CBT group.

The *Substance Use Calendar* was administered at baseline (past month) and weekly during treatment and measured in standardized drinks/day for alcohol (1 oz) and grams/day for cocaine (30). Participant self-reports of drug use were verified by random breathalyzer for alcohol and urine toxicology screens for drug use (approximately every 2 weeks). One hundred percent of the breathalyzer and 98.4% (62/63) of the urine specimens were consistent with self-reports.

The *Five Facet Mindfulness Questionnaire* (FFMQ) was administered at baseline and treatment completion to assess mindfulness skills acquisition (increased scores denote more skill acquisition) (31,32).

The *Treatment Credibility Score* (TCS) questionnaire was administered at treatment completion. It consisted of questions evaluating, using a 5-point Likert scale, how agreeable and practical treatment was both for drug use and symptoms of depression and anxiety.

The *Differential Emotion Scale* (DES) was used during the laboratory session to assess patterns of emotions after stress provocation (33).

Laboratory Paradigm

Within 2 weeks of treatment completion, subjects participated in an 1-hour laboratory session that included 2 imagery conditions: a neutral-relaxing and stress as previously described (34–37). In a separate session several weeks prior to the laboratory session, imagery scripts were developed for each subject for the stress and neutral-relaxing situations as previously described (34–37). Each script was edited by 2 researchers with multiple years of experience recording and editing imagery scripts (K.L.B. and R.S.) to ensure that personalized scripts were standardized in length and content type. These researchers were blinded to treatment group.

Physiological measurements were recorded using a Biopac MP100 system running AcqKnowledge 3.9 software (Biopac Systems, USA), the Biopac electrodermal activity amplifier module (Galvanic Skin Response [GSR] 100c) set at a channel sampling rate of 31 Hz and a gain of 5 μSiemens (μS) per volt (resulting in a resolution of 0.0015 μS), and the electrocardiogram (ECG) amplifier (ECG 100c) set at a channel sampling rate of 1000 Hz for the laboratory session.

The order of the stress and neutral-relaxing imagery scripts was randomized.

Subjective responses after each script were recorded on a laptop computer using ePrime software (Psychology Software Tools, USA). After each imagery script, participants rated how "clearly and vividly" they were able to imagine the scenario on a 10-point Likert scale. Average vividness ratings were 8.1 ± 1.1 and 8.6 ± 0.5 for stress imagery, and average vividness ratings were 8.0 ± 1.1 and 8.2 ± 0.4 for neutral imagery for MT and CBT groups, respectively. Participants then rated their anxiety and drug/alcohol cravings on a 10-point Likert scale, and

completed the DES questionnaire for each imagery condition.

Data Analysis

Analysis of variance (ANOVA) was performed per protocol for between-group comparisons of drug use and scores on the FFMQ and TCS (SPSS 16). Chi-square analysis was used for treatment retention. DES, anxiety, and drug craving Likert scores were compared by 2-tailed t tests. ANOVA was used to evaluate GSR differences by treatment condition (between subjects) and testing condition (within subjects). Within-subject ANOVAs evaluated influences of sympathetic and vagal tone, with treatment condition, testing condition, and the interaction of treatment and testing condition as the predictors using heart rate variability (HRV) power algorithms (38). For the most part, the self-report outcomes did not violate the assumption of normality (11 of 12 items: Shapiro-Wilks $>.05$). Although a few of the physiological variables were non-normally distributed (maximum stress heart rate [HR], neutral sympathetic/vagal ratio), the complexity of the analysis was not one that could be handled with nonparametric tests. Thus, ANOVA was used as noted above.

Data are reported as mean $\pm$ standard deviation. Effect sizes are reported as partial η^2. Level of significance was defined as P value less than .05.

RESULTS

Group Description

As shown in Table 1, most of the randomized participants were male (72%), single or divorced (76%), did not have a college degree (76%), and were not employed full-time (72%). The majority met the DSM-IV criteria for alcohol dependence (68%) and/or cocaine dependence (48%). Analysis of variance and chi-square analysis indicated no significant differences by treatment condition except marital status (57% married in CBT versus 6% married in MT, $P = .02$). No differences in baseline drug or alcohol use were found between treatment completers ($N = 14$) and noncompleters ($N = 22$). Among treatment completers, although substance use in the month prior to treatment initiation was reported by twice as many subjects in the MT (8/9) compared to the CBT group (2/5), it did not differ by group status at baseline (Table 1).

Feasibility: Treatment Retention and Satisfaction

To evaluate the feasibility and acceptability of MT relative to CBT, we compared treatment retention (defined as treatment drop-out) and satisfaction across the two treatment conditions. Of the 36 individuals who entered the study, 9/21 (43%) completed MT, whereas 5/15 (33%) completed CBT ($P = .56$; Figure 1). Participants who initiated treatment ($N = 25$) attended 65% of sessions in MT versus 34% of sessions in CBT group ($F = 4.89$, $P = .04$). Participants who completed treatment ($N = 14$) in both groups rated their treatments as highly satisfactory as assessed by TCS (4.2 ± 0.5 versus $4.4 \pm .5$ of 5, $P = .37$).

Substance Use Outcomes

No differences in alcohol and cocaine use were found during the treatment period but trended toward favoring the CBT group (in MT versus CBT groups, self-reported % days of cocaine use: 5.4 ± 8 versus 0.0 ± 0.0, $P = .17$; and alcohol use: 24.3 ± 28 versus 0.0 ± 0.0, $P = .09$). No side effects or adverse events were noted.

Specificity of MT: Effects of Treatment on Mindfulness Skills Acquisition and Implementation

To determine whether our paradigm adequately fostered mindfulness skills development, we measured the FFMQ scores before and after treatment. At baseline, there were no observed differences in the FFMQ between groups regarding all enrolled participants (MT $= 127 \pm 26$, CBT $= 123 \pm 23$, $P = .64$) as well as treatment completers only (MT $= 122 \pm 26$, CBT $= 119 \pm 29$, $P = .82$).

Treatment completers in both MT and CBT groups showed significantly increased FFMQ scores over time. Although participants in the MT group showed tendency toward greater

TABLE 1. Baseline Demographics and Substance Use

	CBT ($N = 7$)		MT ($N = 18$)		Total ($N = 25$)		P
Sex	N (%)		N (%)		N (%)		
Male	5 (71.4)		13 (72.2)		18 (72)		.968
Female	2 (28.6)		5 (27.8)		7 (28)		
Race							
White	6 (85.7)		10 (55.6)		16 (64)		.213
Black	0		6 (33.3)		6 (24)		
Hispanic	1 (14.3)		2 (11.1)		3 (12)		
Education level							
College or more	4 (57.1)		9 (50)		13 (52)		.748
High school/GED or Partial HS	3 (42.9)		9 (50)		12 (48)		
Marital status							
Never married	2 (28.6)		11 (61.1)		13 (52)		.015
Married	4 (57.1)		1 (5.6)		5 (20)		
Divorced/separated	1 (14.3)		6 (33.3)		7 (28)		
Employment Status							
Employed	4 (57.1)		11 (61.1)		15 (60)		.856
Unemployed	3 (42.9)		7 (38.9)		10 (40)		
Alcohol DSM IV Diagnosis							
Dependence	6 (85.7)		13 (72.2)		19 (76)		.478
Cocaine DSM IV Diagnosis							
Dependence	2 (28.6)		10 (55.6)		12 (48)		.225
MJ positive baseline	0		3 (21.4)		3 (15)		.219
Cocaine positive baseline	0		3 (21.4)		3 (15)		.219
	Mean + SD	N	Mean + SD	N	Mean + SD	N	P
Age (years)	45 + 13.5	7	35.6 + 10.4	18	38.2 + 11.9	25	.075
Years of Education	13.7 + 2.2	7	13.1 + 2.4	18	13.2 + 2.3	25	.541
Days of alcohol use in the past 28 days	0	5	.06 + .24	17	.05 + .21	22	.600
Days of marijuana use in the past 28 days	0	5	.19 + .40	16	.14 + .36	21	.320
Days of cocaine use in the past 28 days	0	5	.06 + .24	17	.05 + .21	22	.600
Days of tobacco use in the past 28 days	.20 + .44	5	.5S + .52	15	.45 + .51	20	.215
Number of lifetime drug treatments	1.6 + 2.5	7	2.2 + 1.9	18	2 + 2.1	25	.492

Note. GED = general educational development diploma; HS = high school; DSM = *Diagnostic and Statistical Manual of Mental Disorders*; MJ = marijuana.

overall increases in FFMQ scores compared to CBT after treatment, these differences did not reach statistical significance (MT = 144 ± 18; CBT = 131 ± 27, $P = .04$ by time, $P = .54$ group by time).

Specificity of MT: Subjective and Objective Responses to Stress Provocation

To determine if MT differentially influenced psychological responses to stress, we compared responses to a personalized stress challenge in treatment completers. Participants who received MT reported significantly attenuated anxiety in both anxiety Likert scales and DES anxious subscale scores (Stress minus Neutral Anxiety: 1.5 ± 2.1 versus 4.6 ± 1.5, $P = .01$, Figure 2a; DES: 1.5 ± 3.9 versus 7.0 ± 3.8, $P = .03$, Figure 3). Though not statistically significant, individuals receiving MT also reported about half the stress-induced drug craving compared to those receiving CBT (1.1 ± 3.7 versus 2.0 ± 3.1, $P = .65$, Figure 2b). These attenuations were echoed in several other negative emotion scores, such as sadness, anger, and fear (Figure 3).

We also sought to determine if MT, compared to CBT, differentially influenced physiological measures of stress. As expected, we found large differences in galvanic skin responses between stress and neutral stories; however, they were not different between groups (MT = 10.0 ± 8.2 versus 4.5 ± 7.4; CBT = 7.0 ± 6.4 versus 0.8 ± 1.1, $F = 12.36$, $P = .01$ for condition). However, no increases in maximum HR were seen in the MT

FIGURE 2. Anxiety and drug craving during stress provocation (MT, $n = 8$; CBT, $n = 5$). Y-axis denotes reported anxiety scores after listening to personalized neutral or stressful stories. (a) Anxiety severity scores: far right indicates normalized scores (stress minus neutral). (b) Normalized drug craving severity scores (stress minus neutral). $^{**}P = .01$ for the difference between treatment groups.

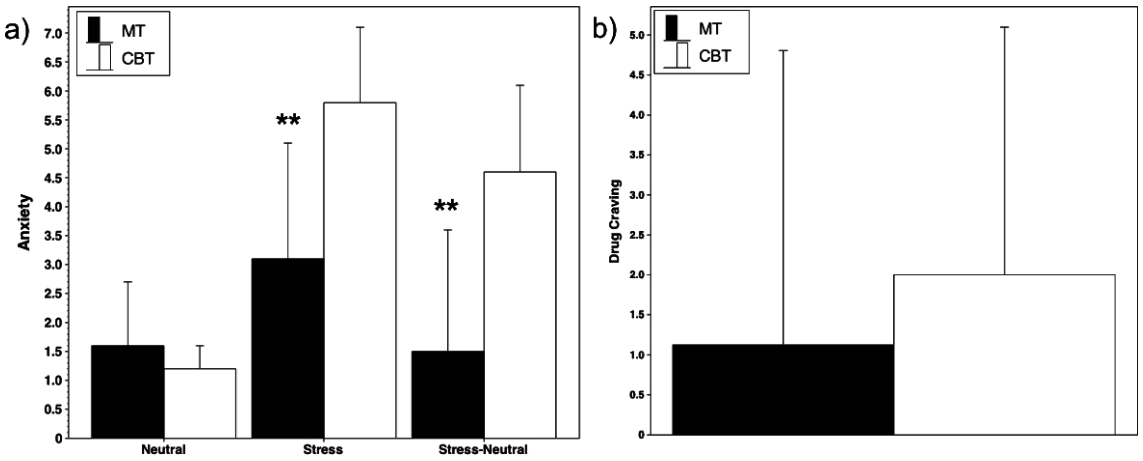


FIGURE 3. Emotional responses during stress provocation (MT, $n = 8$; CBT, $n = 5$). Y-axis denotes normalized Differential Emotion Scale scores after stress provocation (stress minus neutral). $^{*}P \leq .05$ between treatment groups.

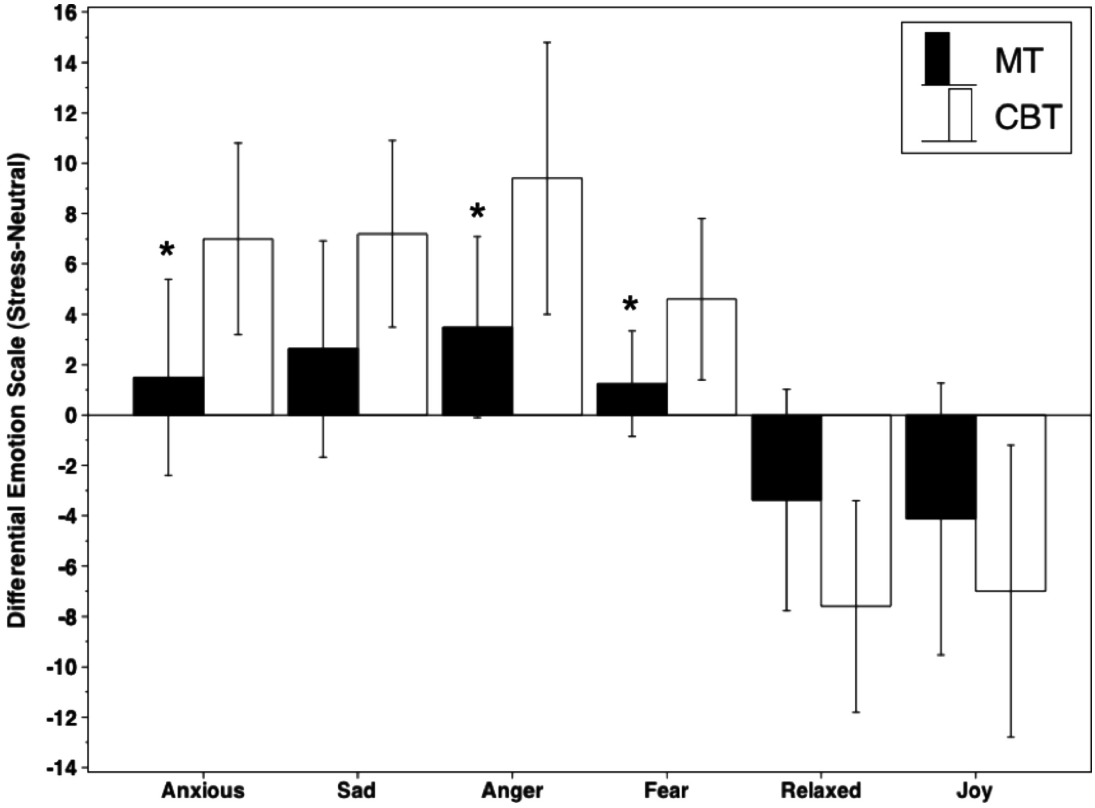
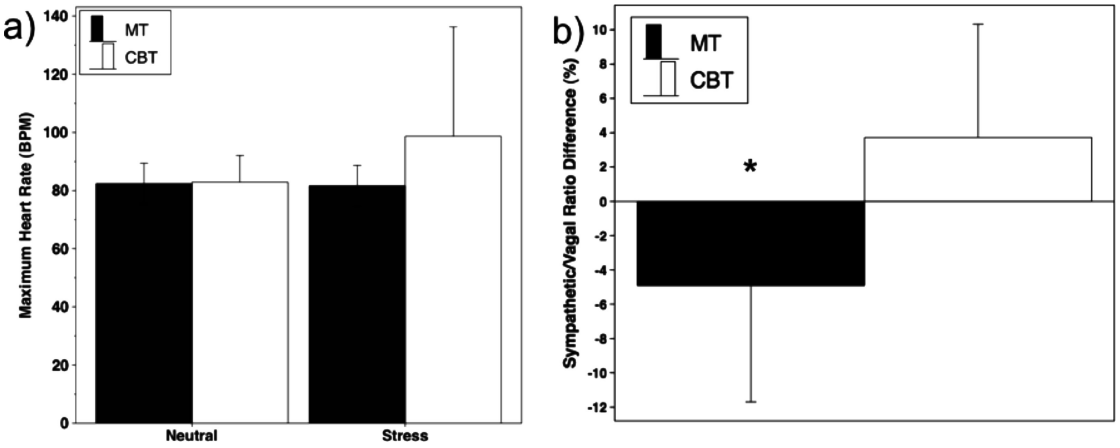


FIGURE 4. Maximum heart rate and autonomic nervous system tone during stress provocation (MT, $n = 8$; CBT, $n = 5$). (a) Maximum heart rate during neutral and stressful stories. (b) Percent change in sympathetic/vagal ratio during stress versus neutral stories. $^{*}F = 7.97$ and $P = .02$ by treatment condition.



group during stress, where these expected increases were observed in the CBT group (MT = 81.4 ± 7.0 versus CBT = 98.7 ± 37.6, $P = 0.19$, Figure 4a). Although these findings were not significant, the partial η^2 indicated this effect size to be large (.15). Corresponding differences were seen in heart rate variability measures: individuals in the MT group showed decreased sympathetic/vagal ratios compared to the CBT group (MT = 4.0 ± .5 versus CBT = 4.2 ± .2, $F = 7.97$, $P = .02$, effect size = .42, Figure 4b).

DISCUSSION

This pilot trial sought to evaluate the feasibility and specificity of 9-week-long MT versus 12-week-long CBT group therapies for individuals with alcohol and/or cocaine dependence. During the treatment period, MT did not significantly differ from CBT in participant retention, treatment satisfaction, or frequency of substance use. However, those who completed MT demonstrated attenuated psychological and physiological responses to stress provocation compared to CBT group. This is, to our knowledge, the first randomized clinical trial comparing MT to an empirically validated treatment for SUDs, such as CBT, and the first to assess responses to stress provocation in laboratory settings in this clinical population.

Treatment Implications

There are several important, clinically relevant implications of this pilot trial. First, the presented data suggest that MT may be a viable, possibly comparable treatment option to CBT regarding treatment feasibility, acceptability, and even outcomes. Of note, MT has not previously been compared head-to-head to CBT in treatment-seeking individuals with SUDs.

Mindfulness training can be conceptualized to target one's relationship with thoughts (i.e., the *process* of events arising), whereas a primary focus of CBT is to change the *content* of thoughts (please see (39) for a full discussion). From this, one might ask if an ability to notice one's thought patterns (i.e., mindfulness) is a prerequisite to changing them, and consequently, whether these techniques might be combined for greater efficacy. Indeed, work with depressed individuals has shown robust effects of treatments that teach mindfulness while incorporating cognitive techniques (Mindfulness-Based Cognitive Therapy) (20,21).

A previous pilot study of individuals from the general population recruited for a "stress-reduction" (Mindfulness-Based Stress Reduction [MBSR]) versus a "stress-management"

(CBT-based stress reduction) class found between-group differences in self-reported health measures such as pain, and energy, but similar effects on perceived stress, depression, and well-being (40). They also found an expected increase in self-reported mindfulness in the MBSR group, but a decrease in this measure in the CBT-based stress reduction group. They suggested that this difference may be due to participants' efforts to "change and control thought and feelings may reduce the awareness of cues . . . " (40). We did not find decreases in self-reported mindfulness in our CBT population, but instead found trends toward increased mindfulness. Though direct comparisons cannot be drawn between these studies due to differences in target populations and treatments, future studies will help to differentiate the effects of CBT on self-reported mindfulness acquisition.

Second, the length of each MT treatment session was significantly shortened compared to standard mindfulness-based programs, and MT was delivered in a modular rather than sequential format. These changes were meant to facilitate subject retention/treatment compliance, and to allow for a more timely and "flexible" subject study entry.

"Standard" mindfulness training programs, such as MBSR, usually utilize 8 sequential sessions of approximately 2-hour duration each, delivered once a week for 8 weeks. Such "standard" training has been shown to result in increased self-reported degree of mindfulness (successful "acquisition"), which, in turn, has recently been documented to correlate with psychological functioning and medical symptom reduction (41). The "dose-response" curve for mindfulness acquisition and MT treatment delivered in a block design—as implemented in the current study—has not been previously evaluated. Our data suggest that shorter-than-standard MT sessions may still provide sufficient training to establish efficacy. They also suggest that a modular format is a viable MT delivery option. Developing treatments that are shorter than typical mindfulness-based approaches may also be more cost-efficient for community clinics and less of a time "burden" for patients. Additionally, modular formats may decrease the number of trained therapists needed to deliver a given intervention as has been shown with dialectical behavioral therapy programs (42).

Stress and Addiction

Our stress paradigm provided robust psychological and physiological responses, as evidenced by increases in emotional and craving ratings and GSR and HR measures. Importantly, the number of GSRs increased in stress stories in both groups, which suggests that all individuals engaged in these stories, and thus, did not employ avoidance or suppression strategies, which have been shown to lead to increased numbers of intrusive drug-related thoughts (43) and have been linked to worse outcomes in SUDs (44,45). Importantly, we found that, compared to CBT group, subjective measures of stress were reduced in MT during stress provocation. This is consistent with the conceptual framework behind mindfulness techniques suggesting that MT fosters an engaged but *nonattached* participation in events (46).

Previously, we and others have found increases in HR indices in individuals with SUDs undergoing stress (1,47,48). In this study, we found an attenuation of HR increases with MT, which provides objective corroboration of individuals' report of attenuated anxiety and negative emotions. These findings are important for individuals with SUDs as self-report measures can be problematic with regard to accuracy due to psychological defense mechanisms (such as denial) coming into play.

The autonomic nervous system (ANS) is important for psychological and physiological allostasis (49–52). In healthy individuals, the heart is under tonic, parasympathetic inhibitory control. This allows for adaptive responses to environmental conditions given the short timecourse of parasympathic effects (milliseconds) compared to sympathetic effects (seconds) (53). ANS imbalance, often characterized by predominance of the sympathetic ANS, has been linked to a range of pathological conditions (54). In this study, we found a decreased sympathetic/vagal ratio in participants in the MT compared to the CBT group. This finding is consistent with the idea that MT promotes a decentered stance toward environmental stimuli: as

individuals are able to engage but are not "caught up" in thoughts or emotions, they are more able to adapt to changing internal and external environmental cues and conditions. As vagal tone has been shown to be a peripheral indicator of prefrontal cortical control of downstream sympathetic responses (e.g., anxiety and/or fear) (55), decreases in the sympathetic/vagal ratio also suggest the possibility of prefrontal cortical circuits playing a mechanistic role in MT's mediation of stress. This is an intriguing possibility as prefrontal cortical activation during a cognitive control task (Stroop) has been shown to be associated with improved treatment outcomes in cocaine-dependent individuals (56). Future studies using functional magnetic resonance imaging may help determine specific brain regions that may be altered by MT and how this may affect individual responses to stress.

Strengths and Limitations

Strengths of this trial include the random assignment of a diverse group of participants from a community clinic, the presence of an active comparison group, and the use of both self-reported and objective, validated outcome measures, including a robust laboratory stress paradigm that utilized discrete psychological and physiological measures.

This study has several limitations as well. In particular, the sample size was small and outcome data were collected from the minority of individuals in both conditions (those who completed treatment). The assessment period was limited to pre-, during, and post-intervention only; it is possible that longer follow-up periods could have yielded different results. Also, it included a heterogeneous population both in regard to SUDs (alcohol and/or cocaine) and drug use status at study entry, though this arguably provided greater ecological validity. This, in the context of a large dropout rate, may have also confounded interpretation of substance use outcomes, as individuals that may have done poorly with treatment, may have also differentially dropped out, leaving a "homogeneous" population of treatment-satisfied abstainers for comparisons. Further, though not statistically different, one may speculate that the higher amount of drug use prior to treatment may suggest a "sicker" cohort at treatment onset in the MT group. Additionally, this study was performed at a single site using single therapists for each condition, and measures of treatment fidelity or discriminability were not conducted. Thus, the amount/quality of treatment was not objectively assessed. Finally, the treatments were of unequal length (9 MT versus 12 CBT weekly sessions), and thus results may have been confounded by natural progression of disease or "dose" of treatment.

In conclusions, results of this pilot study suggest that MT may have promise as a component of addiction treatment and further studies evaluating MT effects on stress reactivity and other substance use related outcomes are warranted.

REFERENCES

1. Sinha R, Talih M, Malison R, Cooney N, Anderson GM, Kreek MJ. Hypothalamic-pituitary-adrenal axis and sympatho-adreno-medullary responses during stress-induced and drug cue-induced cocaine craving states. *Psychopharmacology (Berl).* 2003;170:62–72.

2. Cabib S, Puglisi-Allegra S, Genua C, Simon H, Le Moal M, Piazza PV. Dose-dependent aversive and rewarding effects of amphetamine as revealed by a new place conditioning apparatus. *Psychopharmacology (Berl).* 1996;125:92–96.

3. Kalivas PW, Duffy P. Similar effects of daily cocaine and stress on mesocorticolimbic dopamine neurotransmission in the rat. *Biol Psychiatry.* 1989;25:913–928.

4. Volpicelli JR. Uncontrollable events and alcohol drinking. *Br J Addict.* 1987;82:381–392.

5. O'Brien CP, Childress AR, Ehrman R, Robbins SJ. Conditioning factors in drug abuse: can they explain compulsion? *J Psychopharmacol.* 1998;12:15–22.

6. Marlatt GA, Gordon JR. *Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors.* New York: Guilford Press; 1985.

7. Brownell KD, Marlatt GA, Lichtenstein E, Wilson GT. Understanding and preventing relapse. *Am Psychol.* 1986;41:765–782.

8. Wallace BC. Psychological and environmental determinants of relapse in crack cocaine smokers. *J Subst Abuse Treat.* 1989;6:95–106.

9. Sinha R, Fox HC, Hong KA, Bergquist K, Bhagwagar Z, Siedlarz KM. Enhanced negative emotion and alcohol craving, and altered physiological responses following stress and cue exposure in alcohol dependent individuals. *Neuropsychopharmacology.* 2008;34:1198–1208.

10. Brady KT, Sinha R. Co-occurring mental and substance use disorders: the neurobiological effects of chronic stress. *Am J Psychiatry.* 2005;162:1483–1493.

11. Hoppes K. The application of mindfulness-based cognitive interventions in the treatment of co-occurring addictive and mood disorders. *CNS Spectr.* 2006;11:829–851.

12. Zgierska A, Rabago D, Zuelsdorff M, Coe C, Miller M, Fleming M. Mindfulness meditation for alcohol relapse prevention: a feasibility pilot study. *J Addict Med.* 2008;2:165–73.

13. Bowen S, Witkiewitz K, Dillworth TM, Marlatt GA. The role of thought suppression in the relationship between mindfulness meditation and alcohol use. *Addict Behav.* 2007;32:2324–2328.

14. Davis JM, Fleming MF, Bonus KA, Baker TB. A pilot study on mindfulness based stress reduction for smokers. *BMC Comple Altern Med.* 2007;7:2.

15. Marlatt GA. Buddhist philosophy and the treatment of addictive behavior. *Cogn Behav Pract.* 2002;9:44–50.

16. Bowen S, Witkiewitz K, Dillworth TM, Chawla N, Simpson TL, Ostafin BD, Larimer ME, Blume AW, Parks GA, Marlatt GA. Mindfulness meditation and substance use in an incarcerated population. *Psychol Addict Behav.* 2006;20:343–7.

17. Marlatt G, Witkiewitz K, Dillworth TM, Bowen SW, Parks GA, Macpherson LM, Lonczak HS, Larimer ME, Simpson T, Blume AW, Crutcher R. Vipassana meditation as a treatment for alcohol and drug use disorders. In: Hayes S, Follette VM, Linehan MM, eds. *Mindfulness and Acceptance*. New York: Guilford Press; 2004:261–287.

18. Dutra L, Stathopoulou G, Basden SL, Leyro TM, Powers MB, Otto MW. A meta-analytic review of psychosocial interventions for substance use disorders. *Am J Psychiatry.* 2008;165:179–187.

19. Palfai TP, Monti PM, Colby SM, Rohsenow DJ. Effects of suppressing the urge to drink on the accessibility of alcohol outcome expectancies. *Behav Res Ther.* 1997;35:59–65.

20. Ma SH, Teasdale JD. Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. *J Consult Clin Psychol.* 2004;72:31–40.

21. Teasdale JD, Segal ZV, Williams JM, Ridgeway VA, Soulsby JM, Lau MA. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J Consult Clin Psychol.* 2000;68:615–623.

22. Teasdale JD, Moore RG, Hayhurst H, Pope M, Williams S, Segal ZV. Metacognitive awareness and prevention of relapse in depression: empirical evidence. *J Consult Clin Psychol.* 2002;70:275–287.

23. Carroll KM. A cognitive-behavioral approach: treating cocaine addiction. In: *Therapy Manuals for Drug Abuse.* Vol. 98–4308. Rockville, MD: National Institute on Druge Abuse; 1998.

24. Witkiewitz K, Marlatt GA, Walker D. Mindfulness-based relapse prevention for alcohol and substance use disorders. *J Cogn Psychother.* 2005;19:211–228.

25. Roth B. Incorporating an experiential exploration of anger and forgiveness into the MBSR curriculum. Presented at the Center for Mindfulness Annual Scientific Conference, 2006, Worchester, MA.

26. Gunaratana H. *Mindfulness in Plain English*. Somerville, MA: Wisdom Publications; 2002.

27. Kirkwood G, Rampes H, Tuffrey V, Richardson J, Pilkington K. Yoga for anxiety: a systematic review of the research evidence. *Br J Sports Med.* 2005;39:884–891, discussion 891.

28. Shaffer HJ, LaSalvia TA, Stein JP. Comparing Hatha yoga with dynamic group psychotherapy for enhancing methadone maintenance treatment: a randomized clinical trial. *Altern Ther Health Med.* 1997;3:57–66.

29. Spitzer RL, Williams JB, Gibbon M, First MB. The structured clinical interview for DSM-III-R (SCID). I: History, rationale, and description. *Arch Gen Psychiatry.* 1992;49:624–629.

30. Miller WR, Del Boca FK. Measurement of drinking behavior using the Form 90 family of instruments. *J Stud Alcohol.* [*Special Issue: Alcoholism Treatment Matching Research: Methodological and Clinical Approaches.*] 1994;(Suppl 12):112–118.

31. Baer RA, Smith GT, Hopkins J. Krietemeyer J, Toney L, Using self-report assessment methods to explore facets of mindfulness. *Assessment.* 2006;13:27–45.

32. Baer RA, Smith GT, Lykins E, Button D, Krietemeyer J, Sauer S, Walsh E, Duggan D, Williams JMG. Construct validity of the five facet mindfulness questionnaire in meditating and nonmeditating samples. *Assessment.* 2008;15(3):329–342. 1073191107313003.

33. Izard C. *Patterns of Emotions: A New Analysis of Anxiety and Depression.* New York: Academic Press; 1972.

34. Sinha R, Lacadie C, Skudlarski P, Fulbright RK, Rounsaville BJ, Kosten TR, Wexler BE. Neural activity associated with stress-induced cocaine craving: a functional magnetic resonance imaging study. *Psychopharmacology (Berl).* 2005;183:171–180.

35. Sinha R, Garcia M, Paliwal P, Kreek MJ, Rounsaville BJ. Stress-induced cocaine craving and hypothalamic-pituitary-adrenal responses are predictive of cocaine relapse outcomes. *Arch Gen Psychiatry.* 2006;63:324–331.

36. Sinha R, Fuse T, Aubin LR, O'Malley SS. Psychological stress, drug-related cues and cocaine craving. *Psychopharmacology (Berl).* 2000;152:140–148.

37. Sinha R, Catapano D, O'Malley S. Stress-induced craving and stress response in cocaine dependent individuals. *Psychopharmacology (Berl).* 1999;142:343–351.

38. Kleiger RE, Stein PK, Bigger JT Jr. Heart rate variability: measurement and clinical utility. *Ann Noninvasive Electrocardiol.* 2005;10:88–101.

39. Gilpin R. The use of Theravada Buddhist practices and perspectives in mindfulness-based cognitive therapy. *Contemporary Buddhism.* 2008;9:223–251.

40. Smith BW, Shelley BM, Dalen J, Wiggins K, Tooley E, Bernard J. A pilot study comparing the effects of

mindfulness-based and cognitive-behavioral stress reduction. *J Altern Comple Med.* 2008;14:251–258.

41. Carmody J, Baer RA. Relationships between mindfulness practice and levels of mindfulness, medical and psychological symptoms and well-being in a mindfulness-based stress reduction program. *J Behav Med.* 2008;31:23–33.

42. Linehan MM, Schmidt H, 3rd, Dimeff LA, Craft JC, Kanter J, Comtois KA. Dialectical behavior therapy for patients with borderline personality disorder and drug-dependence. *Am J Addict.* 1999;8:279–292.

43. Salkovskis PM, Reynolds M. Thought suppression and smoking cessation. *Behav Res Ther.* 1994;32:193–201.

44. Leary MR, Adams CE, Tate EB. Hypo-egoic self-regulation: exercising self-control by diminishing the influence of the self. *J Personality.* 2006;74:1803–1832.

45. Wilson KG, Murrell AR. Values work in acceptance and commitment therapy: setting a course for behavioral treatment. In: Hayes S, Follette VM, Linehan MM, eds. *Mindfulness and Acceptance*. New York: Guilford Press; 2004:120–151.

46. Shapiro SL, Bootzin RR, Figueredo AJ, Lopez AM, Schwartz GE. The efficacy of mindfulness-based stress reduction in the treatment of sleep disturbance in women with breast cancer: an exploratory study. *J Psychosomatic Res.* 2003;54:85–91.

47. Back SE, Brady KT, Jackson JL, Salstrom S, Zinzow H. Gender differences in stress reactivity among cocaine-dependent individuals. *Psychopharmacology (Berl).* 2005;180:169–76.

48. Back SE, Waldrop AE, Saladin ME, Yeatts SD, Simpson A, McRae AL, Upadhyaya HP, Contini Sisson R, Spratt EG, Allen J, Kreek MJ, Brady KT. Effects of gender and cigarette smoking on reactivity to psychological and pharmacological stress provocation. *Psychoneuroendocrinology.* 2008;33:560–568.

49. Goldstein DS, McEwen B. Allostasis, homeostats, and the nature of stress. *Stress.* 2002;5:55–58.

50. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. *Ann N Y Acad Sci.* 1998;840:33–44.

51. McEwen BS. Protection and damage from acute and chronic stress: allostasis and allostatic overload and relevance to the pathophysiology of psychiatric disorders. *Ann N Y Acad Sci.* 2004;1032:1–7.

52. McEwen BS, Wingfield JC. The concept of allostasis in biology and biomedicine. *Horm Behav.* 2003;43:2–15.

53. Thayer JF, Brosschot JF. Psychosomatics and psychopathology: looking up and down from the brain. *Psychoneuroendocrinology.* 2005;30:1050–1058.

54. Thayer JF, Sternberg E. Beyond heart rate variability: vagal regulation of allostatic systems. *Ann N Y Acad Sci.* 2006;1088:361–372.

55. Amat J, Baratta MV, Paul E, Bland ST, Watkins LR, Maier SF. Medial prefrontal cortex determines how stressor controllability affects behavior and dorsal raphe nucleus. *Nat Neurosci.* 2005;8:365–371.

56. Brewer JA, Worhunsky PD, Carroll KM, Rounsaville BJ, Potenza MN. Pretreatment brain activation during stroop task is associated with outcomes in cocaine-dependent patients. *Biol Psychiatry.* 2008;64:998–1004.