

Mindfulness-Based Cognitive Therapy Improves Polysomnographic and Subjective Sleep Profiles in Antidepressant Users with Sleep Complaints

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Key Words

Mindfulness-Based Cognitive Therapy • Meditation • Sleep • Depression • Antidepressant medication

Abstract

Background: Many antidepressant medications (ADM) are associated with disruptions in sleep continuity that can compromise medication adherence and impede successful treatment. The present study investigated whether mindfulness meditation (MM) training could improve self-reported and objectively measured polysomnographic (PSG) sleep profiles in depressed individuals who had achieved at least partial remission with ADM, but still had residual sleep complaints. **Methods:** Twenty-three ADM users with sleep complaints were randomized into an 8-week Mindfulness-Based Cognitive Therapy (MBCT) course or a waitlist control condition. Pre-post measurements included PSG sleep studies and subjectively reported sleep, residual depression symptoms. **Results:** Compared to controls, the MBCT participants improved on both PSG and subjective measures of sleep. They showed a pattern of decreased wake time and increased sleep efficiency. Sleep depth, as measured by stage 1 and slow-wave sleep, did not change as a result of mindfulness training. **Conclusions:** MM is associated with increases

in both objectively and subjectively measured sleep continuity in ADM users. MM training may serve as more desirable and cost-effective alternative to discontinuation or supplementation with hypnotics, and may contribute to a more sustainable recovery from depression.

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Introduction

Because monotherapy is unlikely to ameliorate all depression symptoms, the sequential model of depression treatment recommends the use of psychotherapy following remission by pharmacotherapy for sustained wellness and relapse prevention. The choice of treatment depends on the nature of the residual symptoms, which may be a result of non-responsiveness to or a side effect of pharmacotherapy [1–4].

Sleep disturbances are one of the most common residual symptoms after successful treatment with antidepressant medication (ADM), and are associated with perpetuating mood disturbance and increased risk for relapse [5–10]. Many ADMs, including selective serotonin reuptake inhibitors (SSRI) [11, 12], norepinephrine reuptake inhibitors (NRI) [11], dopamine reuptake inhibitors (DRI) [13],

monoamine oxidase inhibitors (MAOI) [14–16], and tricyclics [17] have been found to disrupt sleep continuity and increase awakenings in sleep studies using polysomnography (PSG). Regardless of whether they result from incomplete response to ADM, or whether they are induced by ADM, these ADM-related sleep disturbances often result in non-adherence, require switching medicine or the addition of a hypnotic [12, 18]. Because maintenance ADM treatment is often prolonged (i.e. years), and long-term hypnotic use is discouraged, a behavioral intervention could help to maximize both adherence and treatment response.

Mindfulness meditation (MM) training has been associated with improvements in subjective sleep quality [19–26]. However, few studies have used objective measures (i.e. PSG) to measure sleep and no studies have examined the effect of MM training on ADM-related sleep disturbances.

The present study investigated whether 8 weeks of MM training could improve subjective and objectively measured PSG sleep profiles in depressed individuals who had achieved at least partial remission with ADM, but still had residual sleep complaints. Based on previous reports of improved sleep quality following meditation, we predicted that MM would be associated with: (1) improved sleep continuity, as manifested by an increase in total sleep time, a decrease in time spent awake, and an increase in sleep efficiency (SE) [27]; and (2) deeper sleep, as manifested by increased slow-wave sleep and decreased stage 1 sleep. In order to imbed the findings within the context of clinical utility, we also examined the relationships between objective and subjective sleep and residual depression symptoms.

Patients and Methods

Participants

The current analysis was part of a larger study that investigated the effects of mindfulness training in recurrent depression [28, 29]. The protocol and inclusion criteria were identical to Britton et al. [28], except that participants in the current study were taking ADMs, while the other sample was medication-free. Briefly, the target population was individuals with a recurrent form of unipolar depression who had achieved at least partial remission with ADM but still had residual sleep complaints. Participants met DSM-IV criteria for major depression in the last 60 months and had a lifetime history of at least 3 episodes, but were in full or partial remission during the last 8 weeks. Partial remission was defined by a subjectively reported improvement in symptoms in the last 2 months, BDI score ≤ 20 and the exclusion of individuals with severely depressed mood/anhedonia, or active suicidal ide-

ation. In addition, all eligible participants reported difficulties with either sleep initiation, sleep maintenance/non-restorative sleep, or early awakening (2 times/week), but not hypersomnia in the last 2 months.

Exclusion criteria included: (1) a history of bipolar, psychotic or borderline personality disorder, or organic brain damage; (2) current panic, obsessive-compulsive, eating, or substance-related disorder; (c) inability to read/write in English; (d) current psychotherapy; (e) regular meditation practice; (f) modification of type/dose of ADM in the last 3 months; (g) untreated sleep disorder besides insomnia. The study protocol was approved by the University of Arizona's Institution Review Board, and all participants provided written informed consent. No adverse events occurred during the trial.

Design

After completing 3 weeks of sleep diaries, pre-treatment questionnaires, an adaptation night and baseline assessment in the sleep laboratory, participants were block randomized (block size = 5) to a Mindfulness-Based Cognitive Therapy (MBCT) program or waitlist control condition in a 3:2 ratio without reference (stratification) to baseline characteristics, using identical shuffled opaque sealed envelopes [30]. Treatment allocation was recorded by the first author, who was also the intervention therapist, and therefore not blind to intervention allocation. Research personnel who collected any post-baseline data were blind to treatment conditions. After 8 weeks of treatment or waitlist condition, participants completed a post-treatment questionnaire packet and returned to the laboratory to repeat the 'study night' procedure. The experiments were conducted between May 2004 and December 2005 at the University of Arizona Department of Psychology in Tucson, Ariz., USA.

Measures

Pre- and Post-Treatment Assessments

Participants underwent an adaptation night in the sleep laboratory and returned within 1 week for a 'study night' that was scheduled according to average diary bed/wake times. Participants were asked to avoid: scheduling appointments after an anticipated stressor or time-zone travel, altering regular sleep schedule, and substances that interfere with sleep for 24 h before the study.

PSG and EEG

PSG recordings followed the International 10–20 system, and standard electrooculogram and electromyogram placements, and were recorded into the 32-channel Grass Polysomnograph (Aurora Model, Twin 3.2 Software). Following lights out, subjects were allowed to sleep ad libitum from their usual bedtime (see Britton et al. [28] for details).

Sleep Parameters

Each record was scored in 30-second epochs according to the standard sleep stage scoring guidelines of Rechtschaffen and Kales [31] (C3/C4, O1/O2, electrooculogram, electromyogram) by a registered PSG sleep technician who had an inter-rater reliability of >0.90 with other technicians. Inter-rater reliability for a subset of sleep records in this study was >0.95 . Sleep stages were calculated into minutes of each stage and a number of other sleep parameters. Sleep onset was defined by the first epoch of any

stage of sleep [32, 33]. Sleep onset latency (SOL) and wake after sleep onset (WASO) reflect sleep initiation and sleep maintenance difficulties that were not shared by all participants. Therefore, SOL and WASO were combined into total wake time (TWT) to create an overall sleep disturbance variable that applied to all subjects. SOL and WASO were reported as secondary outcomes. SE is the ratio of total sleep time (TST) to time in bed (TIB). In addition to TWT and TST, TIB includes epochs containing movement, breathing or muscle artifacts, or recording difficulties, which were excluded from analysis. Because of the focus on sleep continuity and the heterogeneous effects of ADM on REM [12, 34, 35], investigations of REM sleep were not included in this paper.

Depression

The Beck Depression Inventory (BDI) [36] is a 21-item self-report measure of depressive symptomatology with excellent psychometric properties [37]. Sleep-related items on the BDI were omitted for correlations with sleep variables, but otherwise were retained in order to convey overall clinical significance ($\alpha = 0.81$ pre-treatment, 0.90 post-treatment).

The Hamilton Rating Scale for Depression (HRSD-24) is a widely used clinician-administered interview assessment of depressive symptomatology [38]. The HRSD and diagnostic interviews were conducted by the first author (>0.90 inter-rater reliability, internal consistency = 0.77). The HRSD was used for pre-treatment screening only; the BDI was used for the post-treatment assessment of depressive symptoms.

Sleep Diaries

Participants kept track of their sleep for a 3-week baseline and for the 9 weeks of the treatment phase. Weekly averages required a minimum of 3 days/week of valid data to be included in analysis. Each morning the participant recorded the TST, TIB, SOL, WASO, and subjective sleep quality rating. The diary data were then used to calculate SE (TST/TIB) and TWT (SOL + WASO). While estimates of sleep parameters from sleep diaries have been found to be reliable and valid in adults with insomnia [39], it should also be noted that both good sleepers and insomniacs are poor estimators of sleep/wake duration. While good sleepers overestimate their time asleep, insomniacs tend to overestimate time awake [40].

Meditation Practice Logs

Participants in the MBCT group kept track of their daily MM practice, including: (1) the type of meditation (body scan, breath awareness, etc.), (2) the number of minutes practiced, and (3) whether they fell asleep during practice. Logs for the preceding week were collected at each class meeting.

Treatment

MBCT is an 8-week group intervention [41] for the treatment and relapse prevention of recurrent depression [28, 42–49]. Participants attended weekly 3-hour sessions and an all-day retreat (9 sessions total). Sessions focused on cultivating non-judgmental present-moment awareness of internal (thoughts, emotions) and external events. Homework assignments consisted of practicing MM exercises with the aid of a guided audio CD (45 min/day). A session-by-session description is available in the MBCT manual [41]. The intervention included 5 groups of 6–10 participants, and

was explicitly aimed at depression symptoms/relapse prevention (i.e. not improvement in sleep). Sessions were conducted by the first author who had more than 10 years (approximately 3,000 h) of MM practice experience and has received extensive training in delivery of the program through the Center for Mindfulness Mindfulness-Based Stress Reduction Instructor Certification Program, and through MBCT training with Dr. Zindel Segal, the first author of the MBCT manual. Sessions were taped and supervised by two licensed clinical psychologists with experience in cognitive-behavioral therapies to ensure patient safety. Although treatment fidelity was not formally assessed, an earlier report demonstrated that this MBCT intervention was efficacious in reducing residual depression symptoms through increases in mindfulness [29].

Statistical Analysis

Preliminary Analyses

Because of the preliminary nature of this investigation, a per protocol analysis was used. Prior to analysis, all variables were examined for normality, and any outlying cases were winsorized such that outliers were replaced with the next highest non-outlying value [50]. Analyses were performed on both the winsorized data and the raw untransformed data, and no differences in outcomes were found. Thus, because transformed data is difficult to interpret, the raw data is displayed in tables and analysis. Preliminary analyses were used to describe baseline characteristics, severity of sleep disturbance, patient flow/adherence, and investigate any baseline group differences that might affect the main analyses.

Main Analyses

The main analyses investigated the effect of treatment on sleep quality according to two different methods of data collection: overnight PSG recordings (objective laboratory measurement) and sleep diaries (subjective reports). We conducted separate 2-way repeated-measures ANOVAs to examine changes in PSG and diary sleep variables from baseline to post-treatment. PSG sleep variables were two-level within-subject variables (pre, post) and consisted of TIB, TST, SE, TWT, stage 1 min, and slow-wave sleep min. Diary sleep variables consisted of self-reported TIB, TST, SE, TWT, and subjective quality rating. Diary- and PSG-based SOL and WASO are reported as secondary outcomes. The between-subjects variable was treatment (MBCT, control). Because of the relationship between depression and sleep, baseline BDI score was entered as a covariate [51]. Using SPSS 17.0 software, statistical significance was set at α levels <0.05 (two-tailed), with effect sizes reported as partial η^2 (η_p^2 ; small = 0.01, medium = 0.06, large = 0.14) [52].

Because of the exploratory nature of the study and small sample size, all trends ($p < 0.10$) that related to main predictions and had effect sizes on par or larger than expected for mindfulness RCTs [53] (i.e. medium effect size) were reported in order to identify patterns that warrant future investigation. Follow-up analyses used Pearson product moment correlation coefficients to examine the relationship changes in PSG and diary sleep and changes in residual depression.

Table 1. Baseline characteristics

	Completers		All	
	MBCT	controls	MBCT	controls
n	14	10	15	11
Female, %	78.5	90.0	80.0	81.8
Age, years	47.7 ± 8.0	45.1 ± 14.2	47.9 ± 7.8	45.7 ± 8.0
BDI score	8.3 ± 5.9	11.8 ± 7.3	8.2 ± 5.7	10.8 ± 7.6
HRSD score	9.9 ± 7.4	11.8 ± 6.7	9.6 ± 7.2	10.7 ± 7.3
Previous depression ¹ , months	57.5 ± 38.0	57.8 ± 36.3	58.6 ± 36.9	64.0 ± 40.1
In remission ² , %	50.0	60.0	46.7	54.5
SSRIs, %	71.0	70.0	73.0	73.0
Completers, %	100	100	93.3	90.9

Data denote means ± SD unless otherwise indicated. No significant differences between treatment groups in age, BDI, previous depression (independent sample t tests) or gender, remission, or completers (Fisher's exact test).

¹ Total duration of previous depression across all episodes. ² BDI score <10.

Results

Preliminary Analyses: Participant Flow

Twenty-six individuals completed baseline assessment and randomization procedures (15 MBCT, 11 controls) and 2 dropped out once enrolled (1 MBCT, 1 control), so a total of 24 participants completed the 8-week protocol (14 MBCT, 10 controls). One participant was excluded from PSG analysis due to technical problems, so complete data from all time points were available from 23 participants (13 MBCT, 10 controls).

Preliminary Analyses: Treatment Attendance and Adherence

Out of the 15 MBCT participants, 1 dropped out after the first class, and the remaining 14 attended at least 6 sessions and the all-day retreat. Outside of class, the 14 completers engaged in formal MM practice an average of 40.4 ± 8 min/day 5.0 ± 1.6 days/week (mean adherence = 75 ± 17%).

Preliminary Analyses: Baseline Characteristics

Participants (n = 26, 21 female) had a mean age of 47.0 ± 10.5 years (range = 24–61 years). Approximately half of the participants in each group were in remission (BDI score <10) [54], with a history of previous depression ranging from 11 to 152 months (mean 60.9 ± 37.6).

Preliminary Analyses: Antidepressant Medications

The majority (92%) of the sample was taking a single compound, 2 (8%) were taking two medications. Based

on dose-related mechanism(s) of action [55], ADM use can be categorized as follows: 73% SSRI, 38% norepinephrine reuptake inhibitors, 15% dopamine reuptake inhibitors, 12% tetracyclics.

There were no significant differences between treatment groups in age, gender, depression severity, duration of previous depression, percent taking SSRIs, or any diary or PSG sleep measure at baseline. See table 1 for summary by treatment group.

Preliminary Analyses: Baseline Sleep Disturbance

All participants reported some level of sleep complaints at the initial screening, including trouble initiating sleep (SOL > 30 min, 42.3%), disturbed/non-restorative (WASO > 30 min, 100%), or early morning awakening (>30 min prior to normal time, 50.0%) at least 2 nights/week during the month prior to the interview. According to sleep diaries, approximately 40% of the sample met formal severity and frequency criteria for insomnia, defined as ≥31 min of WASO or SOL on ≥3 nights/week during the first week of baseline assessment [56]. Seventy percent of the sample had SE <90% according to both diaries and PSG, with an average of 43 ± 36 (diary) and 56 ± 27 (PSG) min spent awake each night. Half of the sample described their average night of sleep as 'restless' or 'very restless'. Reduced slow-wave sleep, as defined by less than 8% of total sleep time [57], was apparent in 80% of the sample.

Main Analyses: PSG Data

A significant group × time interaction indicated a greater reduction in PSG TWT for the MBCT group com-

Table 2. Polysomnographic sleep

	Treatment	Pre-intervention, mean \pm SD	Post-intervention, mean \pm SD	Time, F	Treatment \times time, F	Effect size, η_p^2
TIB, min	MBCT control	458.8 \pm 45.7 465.1 \pm 45.9	440.5 \pm 74.6 474.3 \pm 47.7	0.005	0.66	0.032
TST, min	MBCT control	393.8 \pm 38.5 406.6 \pm 66.6	392.3 \pm 80.0 390.3 \pm 79.5	0.13	0.14	0.007
SE, %	MBCT control	86.0 \pm 5.4 87.1 \pm 9.2	88.7 \pm 5.8 82.1 \pm 14.1	0.54	3.1 [#]	0.13
SOL, min	MBCT control	11.1 \pm 11.6 12.8 \pm 8.6	7.2 \pm 8.4 21.8 \pm 31.9	0.02	1.4	0.07
WASO, min	MBCT control	45.9 \pm 16.5 40.3 \pm 33.3	39.5 \pm 21.7 48.1 \pm 31.5	0.06	1.4	0.07
TWT, min	MBCT control	57.0 \pm 20.6 53.1 \pm 36.9	46.7 \pm 23.8 69.9 \pm 50.6	0.14	5.1 [*]	0.20
Stage 1, min	MBCT control	40.2 \pm 11.4 34.3 \pm 21.8	32.8 \pm 16.0 37.6 \pm 23.4	0.30	2.1	0.10
SWS, min	MBCT control	22.0 \pm 24.5 24.2 \pm 26.0	24.5 \pm 35.9 30.8 \pm 27.4	0.37	0.40	0.02

SWS = Slow-wave sleep. MBCT: n = 13; control: n = 10. * p < 0.05; [#] p < 0.10.

Table 3. Sleep diaries

	Condition	Pre-intervention, mean \pm SD	Post-intervention, mean \pm SD	Time, F	Treatment \times time, F	Effect size, η_p^2
TIB, min	MBCT control	517.1 \pm 60.1 529.2 \pm 61.5	492.1 \pm 58.4 510.4 \pm 53.5	1.9	0.02	0.001
TST, min	MBCT control	419.6 \pm 82.7 451.4 \pm 71.3	436.3 \pm 62.3 440.3 \pm 61.9	3.9	2.6	0.12
SE, %	MBCT control	81.3 \pm 13.0 85.1 \pm 6.5	88.8 \pm 8.8 86.1 \pm 6.9	1.9	9.3 ^{**}	0.33
SOL, min	MBCT control	19.3 \pm 19.6 19.8 \pm 10.5	11.8 \pm 9.4 18.3 \pm 8.4	0.006	1.5	0.07
WASO, min	MBCT control	27.5 \pm 39.5 14.3 \pm 14.2	15.9 \pm 25.8 16.7 \pm 24.6	0.05	4.2 [#]	0.18
TWT, min	MBCT control	46.8 \pm 52.4 34.2 \pm 20.7	27.7 \pm 28.4 35.0 \pm 30.0	0.04	4.5 [*]	0.19
Quality ¹	MBCT control	2.9 \pm 0.5 3.1 \pm 1.0	3.3 \pm 0.6 2.9 \pm 0.5	0.08	0.74	0.04

¹ Subjective sleep quality rating. MBCT: n = 13; control: n = 10. * p < 0.05; ** p < 0.01; [#] p < 0.10.

pared to controls [$F(1, 20) = 5.1, p = 0.035, \eta_p^2 = 0.20$]. A similar pattern of increased SE in the MBCT group appeared at the trend level [$F(1, 20) = 3.1, p = 0.09, \eta_p^2 = 0.13$].

When TWT was decomposed into SOL and WASO, group \times time interactions were not significant (table 2) [SOL = $F(1, 20) = 1.44, p = 0.24, \eta_p^2 = 0.067$; WASO = $F(1, 20) = 1.39, p = 0.25, \eta_p^2 = 0.065$].

Main Analyses: Sleep Diaries

Significant group \times time interactions indicated a greater decrease in TWT [$F(1, 20) = 4.54, p = 0.046, \eta_p^2 = 0.19$] and greater improvement in SE [$F(1, 20) = 9.3, p = 0.007, \eta_p^2 = 0.33$] for the MBCT group compared to controls. When TWT was decomposed into SOL and WASO, group \times time interaction was close to significance for WASO [$F(1, 20) = 4.24, p = 0.053, \eta_p^2 = 0.18$] but not for SOL [$F(1, 20) = 1.51, p = 0.24, \eta_p^2 = 0.07$] (table 3).

Residual Depression and Relationship to Sleep

A trend-level group \times time interaction indicated a greater reduction in residual depression symptoms for the MBCT group versus controls [$F(1, 22) = 3.6, p = 0.07, \eta_p^2 = 0.14$]. Mean BDI scores for the MBCT group decreased 2.6 points from 8.3 ± 5.9 to 5.1 ± 3.5 , while control group BDI scores increased 3.2 points from 11.8 ± 7.2 to 14.4 ± 10.2 .

For all completers and the MBCT group alone, improvements in BDI scores (with sleep items removed) were associated with decreases in self-reported wake time ($r = 0.45, p = 0.04$), WASO ($r = 0.48, p = 0.02$), and increases in total sleep time ($r = -0.58, p = 0.005$) and SE ($r = -0.70, p < 0.001$), but were not associated with changes in self-reported SOL, or any objectively measured sleep variable.

Discussion

This study investigated the effects of MBCT on PSG and subjective sleep profiles in depressed individuals who had achieved at least partial remission on ADM, but still had sleep complaints. After 8 weeks of MM training, the MBCT group spent less time awake at night and had higher sleep efficiencies than controls according to both objective and subjective measures. Improvements in self-reported sleep continuity were associated with improvement in residual depression symptoms. Together these data suggest that MM training may improve ADM-related sleep discontinuity, one of the most common complaints and reasons for discontinuation of ADMs [15].

It is important to note that these meditation-related benefits were specific to sleep continuity and not sleep depth or architecture. While the MBCT group showed a decrease in wake time and improved SE, there was no change in the total amount of sleep, or the amount of slow-wave 'deep' or stage 1 'light' sleep as a result of MM training. Sleep continuity improved even though pre-treatment sleep disruption was not severe. Slow-wave sleep remained pathologically truncated between 5 and 8% following treatment. Two cross-sectional studies have reported increased slow-wave sleep in advanced meditators [58, 59], but we did not replicate this finding in the context of a longitudinal RCT of meditation-naïve ADM users. While there was no change in slow-wave sleep or stage 1 in this sample, several other studies suggest that meditation may decrease sleep depth and increase wakefulness or cortical arousal [28, 60–65]. Future studies should be careful to dissociate the effects meditation on sleep depth and sleep continuity.

Our primary measure of sleep continuity, TWT, was an aggregate of sleep initiation and sleep maintenance difficulties. When TWT was decomposed into WASO and SOL and analyzed separately, only subjective WASO was close to significance. This finding has several implications: The sample size may be too small to show the effect from SOL and WASO separately and TWT may be a more sensitive measure for mixed forms of insomnia that include both sleep initiation and maintenance difficulties. Similarly, Morin et al. [66] found that TWT (but not SOL and WASO separately) in both sleep diaries and PSG benefited from a behavioral intervention for insomnia compared to controls. While it is true that SOL and WASO reflect different types of sleep disturbance, it is also true that total wake time is associated with cognitive and affective functioning. For example, Van Dongen et al. [67] found that total amount of wakefulness was associated with neurobehavioral impairment in a linear dose-response manner. Similarly, in this paper, improvements in total wake time were associated with improved mood ($r = 0.45, p < 0.05$).

The observation that that subjective WASO improved, but not SOL, may suggest that sleep maintenance difficulties are more influenced by MM, but the opposite pattern has been found in other trials [68] and is most likely related to type of sleep complaints at baseline. This finding is probably better explained by the tendency of subjective reported sleep to be more amenable to change by MM training than objectively measured sleep [28, 68].

The dissociation between subjective and objective measures of sleep is a well-known phenomena in sleep re-

search [69–71] and is beginning to appear in meditation-based sleep studies as well. Subjective measures have produced more favorable [19–22, 26, 68] or equivocal [28, 72–74] sleep-promoting effects of meditation while objective or EEG-based measures tend to suggest more wake-promoting or arousing effects [28, 60–65]. In the current study, the subjective and objective measurements of sleep showed differential patterns that reinforce MM's stronger benefits for subjectively reported sleep. By subjective accounts, MBCT showed clear improvement over relatively stable controls, where by PSG measurement, deterioration of control sleep may have contributed to the group \times time interaction. Given that BDI scores increased slightly for the controls, it is possible that deterioration of PSG sleep in controls is related to depressive relapse.

The present study has several limitations, most notably the lack of statistical power due to the small sample size, and a per protocol rather than intent-to-treat analysis. The use of an 8-week MM course limits the ability to speculate on the effects of other forms of meditation or the effects of longer durations of training. Because MBCT uses a variety of meditative techniques, it is difficult to sort out which techniques relate to which outcomes. While the MBCT group's previously reported increase in mindfulness and improvement in depression is consistent with other studies where high-quality MBCT was administered, checks on competency [75] and adherence [76] should be included in future research to ensure treatment fidelity.

In addition, varying levels of mood and sleep disturbance at baseline and heterogeneous ADM types may have confounded or diluted the effects. The current study cannot clearly delineate to what extent mindfulness training improved sleep versus prevented deterioration associated with depressive relapse. The current study also does not distinguish between residual depression-related sleep disturbances that fail to respond to ADM and sleep

disturbances that are induced by ADM. Future studies with larger and more targeted samples should investigate these distinctions. Future studies should also assess whether the improvements in ADM-related sleep disturbance affect medication adherence and long-term remission rates.

In conclusion, this study suggests that individuals who experience sleep disturbances as a side effect from ADM may benefit from training in MM. MM training may represent a treatment choice within the sequential model of depression treatment. By serving as more desirable and cost-effective alternative to discontinuation or supplementation with hypnotics, MM training may contribute to a more sustainable recovery from depression.

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References

- 1 Fava GA, Tomba E: New modalities of assessment and treatment planning in depression: the sequential approach. *CNS Drugs* 2010; 24:453–465.
- 2 Guidi J, Fava GA, Fava M, Papakostas GI: Efficacy of the sequential integration of psychotherapy and pharmacotherapy in major depressive disorder: a preliminary meta-analysis. *Psychol Med* 2011;41:321–331.
- 3 Lichtenberg P, Belmaker RH: Subtyping major depressive disorder. *Psychother Psychosom* 2010;79:131–135.
- 4 Bech P: Struggle for subtypes in primary and secondary depression and their mode-specific treatment or healing. *Psychother Psychosom* 2010;79:331–338.
- 5 Pigeon WR, Hegel M, Unutzer J, Fan MY, Sateia MJ, Lyness JM, Phillips C, Perlis ML: Is insomnia a perpetuating factor for late-life depression in the IMPACT cohort? *Sleep* 2008;31:481–488.
- 6 Buysse DJ, Frank E, Lowe KK, Cherry CR, Kupfer DJ: Electroencephalographic sleep correlates of episode and vulnerability to recurrence in depression. *Biol Psychiatry* 1997; 41:406–418.
- 7 Perlis ML, Smith LJ, Lyness JM, Matteson SR, Pigeon WR, Jungquist CR, Tu X: Insomnia as a risk factor for onset of depression in the elderly. *Behav Sleep Med* 2006;4:104–113.

- 8 Dew MA, Reynolds CF 3rd, Houck PR, Hall M, Buysse DJ, Frank E, Kupfer DJ: Temporal profiles of the course of depression during treatment: predictors of pathways toward recovery in the elderly. *Arch Gen Psychiatry* 1997;54:1016–1024.
- 9 Thase ME, Buysse DJ, Frank E, Cherry CR, Cornes CL, Mallinger AG, Kupfer DJ: Which depressed patients will respond to interpersonal psychotherapy? The role of abnormal EEG sleep profiles. *Am J Psychiatry* 1997; 154:502–509.
- 10 Dombrovski AY, Cyranowski JM, Mulsant BH, Houck PR, Buysse DJ, Andreescu C, Thase ME, Mallinger AG, Frank E: Which symptoms predict recurrence of depression in women treated with maintenance interpersonal psychotherapy? *Depress Anxiety* 2008;25:1060–1066.
- 11 Thase ME: Antidepressant treatment of the depressed patient with insomnia. *J Clin Psychiatry* 1999;60 suppl 17:28–31, discussion 46–48.
- 12 Rush AJ, Armitage R, Gillin JC, Yonkers KA, Winokur A, Moldofsky H, Vogel GW, Kaplita SB, Fleming JB, Montplaisir J, Erman MK, Albala BJ, McQuade RD: Comparative effects of nefazodone and fluoxetine on sleep in outpatients with major depressive disorder. *Biol Psychiatry* 1998;44:3–14.
- 13 Kupfer DJ: Pathophysiology and management of insomnia during depression. *Ann Clin Psychiatry* 1999;11:267–276.
- 14 Nierenberg AA, Keck PE Jr: Management of monoamine oxidase inhibitor-associated insomnia with trazodone. *J Clin Psychopharmacol* 1989;9:42–45.
- 15 Nierenberg AA, Adler LA, Peselow E, Zornberg G, Rosenthal M: Trazodone for antidepressant-associated insomnia. *Am J Psychiatry* 1994;151:1069–1072.
- 16 Neylan TC: Treatment of sleep disturbances in depressed patients. *J Clin Psychiatry* 1995; 56(suppl 2):56–61.
- 17 Ancoli-Israel S: Insomnia in the elderly: a review for the primary care practitioner. *Sleep* 2000;23 suppl 1:S23–S30, discussion S36–S38.
- 18 Dording CM, Mischoulon D, Petersen TJ, Kornbluh R, Gordon J, Nierenberg AA, Rosenbaum JE, Fava M: The pharmacologic management of SSRI-induced side effects: a survey of psychiatrists. *Ann Clin Psychiatry* 2002;14:143–147.
- 19 Heidenreich T, Tuin I, Pflug B, Michal M, Michalak J: Mindfulness-based cognitive therapy for persistent insomnia: a pilot study. *Psychother Psychosom* 2006;75:188–189.
- 20 Carlson LE, Speca M, Patel KD, Goodey E: Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. *Psychoneuroendocrinology* 2004;29: 448–474.
- 21 Carlson LE, Garland SN: Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. *Int J Behav Med* 2005;12: 278–285.
- 22 Kreitzer MJ, Gross CR, Ye X, Russas V, Treesak C: Longitudinal impact of mindfulness meditation on illness burden in solid-organ transplant recipients. *Prog Transplant* 2005; 15:166–172.
- 23 Gross CR, Kreitzer MJ, Thomas W, Reilly-Spong M, Cramer-Bornemann M, Nyman JA, Frazier P, Ibrahim HN: Mindfulness-based stress reduction for solid organ transplant recipients: a randomized controlled trial. *Altern Ther Health Med* 2010;16:30–38.
- 24 Kvillemo P, Branstrom R: Experiences of a Mindfulness-Based Stress-Reduction intervention among patients with cancer. *Cancer Nurs* 2011;34:24–31.
- 25 Ong JC, Shapiro SL, Manber R: Mindfulness meditation and cognitive behavioral therapy for insomnia: a naturalistic 12-month follow-up. *Explore* 2009;5:30–36.
- 26 Britton WB, Bootzin RR, Cousins JC, Hasler B, Peck T, Shapiro S: The contribution of mindfulness practice to a multicomponent behavioral sleep intervention following substance abuse treatment in adolescents: a treatment-development study. *Subst Abuse* 2010;31:86–97.
- 27 Perlis M, Jungquist C, Smith M, Posner D: *Cognitive Behavioral Treatment of Insomnia: A Session-by-Session Guide*. New York, Springer, 2005.
- 28 Britton WB, Haynes PL, Fridel KW, Bootzin RR: Polysomnographic and subjective measures of sleep continuity before and after mindfulness-based cognitive therapy in partially remitted depression. *Psychosom Med* 2010;72:539–548.
- 29 Shahar B, Britton W, Sbarra D, Figueredo A, Bootzin R: Mechanisms of change in mindfulness-based cognitive therapy for depression: preliminary evidence from a randomized controlled trial. *Int J Cog Ther* 2010;3: 402–418.
- 30 Doig G, Simpson F: Randomization and allocation concealment: a practical guide for researchers. *J Crit Care* 2005;20:187–191.
- 31 Rechtschaffen A, Kales A: *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*. Los Angeles, Brain Information Service/Brain Research Institute, University of California, 1968.
- 32 Carskadon MA, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S: Guidelines for the Multiple Sleep Latency Test (MSLT): a standard measure of sleepiness. *Sleep* 1986; 9:519–524.
- 33 Hori T, Sugita Y, Koga E, Shirakawa S, Inoue K, Uchida S, Kuwahara H, Kousaka M, Kobayashi T, Tsuji Y, Terashima M, Fukuda K, Fukuda N: Proposed supplements and amendments to 'A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects', the Rechtschaffen & Kales (1968) standard. *Psychiatry Clin Neurosci* 2001;55:305–310.
- 34 Nofzinger EA, Reynolds CF, 3rd, Thase ME, Frank E, Jennings JR, Fasiczka AL, Sullivan LR, Kupfer DJ: REM sleep enhancement by bupropion in depressed men. *Am J Psychiatry* 1995;152:274–276.
- 35 Schittecatte M, Dumont F, Machowski R, Cornil C, Lavergne F, Wilmotte J: Effects of mirtazapine on sleep polygraphic variables in major depression. *Neuropsychobiol* 2002; 46:197–201.
- 36 Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J: An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–571.
- 37 Beck A, Steer R, Carbin M: Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. *Clin Psychol Rev* 1988;8:77–100.
- 38 Gelenberg AJ, Wojcik JD, Falk WE, Baldessarini RJ, Zeisel SH, Schoenfeld D, Mok GS: Tyrosine for depression: a double-blind trial. *J Affect Disord* 1990;19:125–132.
- 39 Bootzin RR, Engle-Friedman M: The assessment of insomnia. *Behav Assessment* 1981;3: 107–126.
- 40 Mercer JD, Bootzin RR, Lack LC: Insomniacs' perception of wake instead of sleep. *Sleep* 2002;25:564–571.
- 41 Segal ZV, Williams JM, Teasdale JD: *Mindfulness-Based Cognitive Therapy for Depression: A New Approach to Preventing Relapse*. London, Guilford, 2002.
- 42 Williams JM, Alatiq Y, Crane C, Barnhofer T, Fennell MJ, Duggan DS, Hepburn S, Goodwin GM: Mindfulness-based cognitive therapy (MBCT) in bipolar disorder: preliminary evaluation of immediate effects on between-episode functioning. *J Affect Disord* 2008;107:275–279.
- 43 Barnhofer T, Crane C, Hargus E, Amarasinghe M, Winder R, Williams JM: Mindfulness-based cognitive therapy as a treatment for chronic depression: a preliminary study. *Behav Res Ther* 2009;47:366–373.
- 44 Eisendrath SJ, Delucchi K, Bitner R, Fenimore P, Smit M, McLane M: Mindfulness-based cognitive therapy for treatment-resistant depression: a pilot study. *Psychother Psychosom* 2008;77:319–320.
- 45 Finucane A, Mercer SW: An exploratory mixed methods study of the acceptability and effectiveness of mindfulness-based cognitive therapy for patients with active depression and anxiety in primary care. *BMC Psychiatry* 2006;6:14.
- 46 Kingston T, Dooley B, Bates A, Lawlor E, Malone K: Mindfulness-based cognitive therapy for residual depressive symptoms. *Psychol Psychother* 2007;80:193–203.

- 47 Kuyken W, Byford S, Taylor RS, Watkins E, Holden E, White K, Barrett B, Byng R, Evans A, Mullan E, Teasdale JD: Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *J Consult Clin Psychol* 2008;76:966–978.
- 48 Kenny MA, Williams JM: Treatment-resistant depressed patients show a good response to mindfulness-based cognitive therapy. *Behav Res Ther* 2007;45:617–625.
- 49 Schroevers MJ, Brandsma R: Is learning mindfulness associated with improved affect after mindfulness-based cognitive therapy? *Br J Psychol* 2009;101:95–107.
- 50 Cohen B: *Explaining Psychological Statistics*. New York, John Wiley & Sons, 2001.
- 51 Hamilton KE, Dobson KS: Cognitive therapy of depression: pretreatment patient predictors of outcome. *Clin Psychol Rev* 2002;22:875–893.
- 52 Green S, Salkind N: *Using SPSS for Windows and Macintosh: Analyzing and understanding data*, ed 4. Upper Saddle River, Pearson Education, 2005.
- 53 Grossman P, Niemann L, Schmidt S, Walach H: Mindfulness-Based Stress Reduction and health benefits: a meta-analysis. *J Psychosom Res* 2004;57:35–43.
- 54 Teasdale JD, Segal ZV, Williams JM, Ridgeway V, Soulsby J, Lau M: Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J Consult Clin Psychol* 2000;68:615–623.
- 55 Walsh P: *Physicians' Desk Reference*, ed 57. Montvale, Thomson, 2003.
- 56 Lichstein KL, Durrence HH, Taylor DJ, Bush AJ, Riedel BW: Quantitative criteria for insomnia. *Behav Res Ther* 2003;41:427–445.
- 57 Thase ME, Fasiczka AL, Berman SR, Simons AD, Reynolds CF 3rd: Electroencephalographic sleep profiles before and after cognitive behavior therapy of depression. *Arch Gen Psychiatry* 1998;55:138–144.
- 58 Patra S, Telles S: Positive impact of cyclic meditation on subsequent sleep. *Med Sci Monit* 2009;15:CR375–CR381.
- 59 Sulekha S, Thennarasu K, Vadamurthachar A, Raju T, Kutty B: Evaluation of sleep architecture in practitioners of Sudarshan Kriya yoga and Vipassana meditation. *Sleep Biol Rhythms* 2006;4:207–214.
- 60 Mason L, Alexander C, Travis F, Marsh G, Orme-Johnson D, Gackenbach J, Mason DC, Rainforth M, Walton K: Electrophysiological correlates of higher states of consciousness during sleep in long term practitioners of the TM program. *Sleep* 1997;20:102–110.
- 61 Banquet JP, Saitan M: EEG analysis of spontaneous and induced states of consciousness. *Rev Electroencephalogr Neurophysiol Clin* 1974;4:445–453.
- 62 Cahn BR, Polich J: Meditation (Vipassana) and the P3a event-related brain potential. *Int J Psychophysiol* 2009;72:51–60.
- 63 Elson B, Hauri P, Cunis D: Physiological changes in Yoga meditation. *Psychophysiology* 1977;14:52–57.
- 64 Kaul P, Passafiume J, Sargent C, O'Hara B: Meditation acutely improves psychomotor vigilance, and may decrease sleep need. *Behav Brain Functions* 2010;6:47–56.
- 65 Lutz A, Slagter HA, Dunne JD, Davidson RJ: Attention regulation and monitoring in meditation. *Trends Cogn Sci* 2008;12:163–169.
- 66 Morin CM, Colecchi C, Stone J, Sood R, Brink D: Behavioral and pharmacological therapies for late-life insomnia: a randomized controlled trial. *JAMA* 1999;281:991–999.
- 67 Van Dongen HP, Maislin G, Mullington JM, Dinges DF: The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep* 2003;26:117–126.
- 68 Gross CR, Kreitzer MJ, Reilly-Spong M, Wall M, Winbush NY, Patterson R, Mahowald M, Cramer-Bornemann M: Mindfulness-based stress reduction versus pharmacotherapy for chronic primary insomnia: a randomized controlled clinical trial. *Explore* 2011;7:76–87.
- 69 Zhang L, Zhao ZX: Objective and subjective measures for sleep disorders. *Neurosci Bull* 2007;23:236–240.
- 70 Silva GE, Goodwin JL, Sherrill DL, Arnold JL, Bootzin RR, Smith T, Walsleben JA, Baldwin CM, Quan SF: Relationship between reported and measured sleep times: the sleep heart health study (SHHS). *J Clin Sleep Med* 2007;3:622–630.
- 71 Edinger JD, Fins AI, Glenn DM, Sullivan RJ Jr, Bastian LA, Marsh GR, Dailey D, Hope TV, Young M, Shaw E, Vasilas D: Insomnia and the eye of the beholder: are there clinical markers of objective sleep disturbances among adults with and without insomnia complaints? *J Consult Clin Psychol* 2000;68:586–593.
- 72 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 Psychosom Res* 2003;54:85–91.
- 73 Goldenberg D, Kaplan K, Nadeau M, Brodeur C, Smith S, Schmid C: A controlled trial of a stress-reduction, cognitive behavioral treatment program in fibromyalgia. *J Musculoskel Pain* 1994;2:53–56.
- 74 Roth B, Robbins D: Mindfulness-based stress reduction and health-related quality of life: findings from a bilingual inner-city patient population. *Psychosom Med* 2004;66:113–123.
- 75 Crane R, Kuyken W, Hastings RP, Rothwell N, Williams JMG: Training teachers to deliver mindfulness-based interventions: learning from the UK experience. *Mindfulness* 2010;1:74–86.
- 76 Segal ZV, Teasdale JD, Williams JM, Gemar M: The Mindfulness-Based Cognitive Therapy Adherence Scale: inter-rater reliability, adherence to and treatment distinctiveness. *Clin Psychol Psychother* 2002;9:131–138.