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Mindfulness-Based Cognitive Therapy for Depression: Replication and Exploration of Differential Relapse Prevention Effects

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Recovered recurrently depressed patients were randomized to treatment as usual (TAU) or TAU plus mindfulness-based cognitive therapy (MBCT). Replicating previous findings, MBCT reduced relapse from 78% to 36% in 55 patients with 3 or more previous episodes; but in 18 patients with only 2 (recent) episodes corresponding figures were 20% and 50%. MBCT was most effective in preventing relapses not preceded by life events. Relapses were more often associated with significant life events in the 2-episode group. This group also reported less childhood adversity and later first depression onset than the 3-or-more-episode group, suggesting that these groups represented distinct populations. MBCT is an effective and efficient way to prevent relapse/recurrence in recovered depressed patients with 3 or more previous episodes.

Cognitive–behavioral therapy (CBT) for depression (Beck, Rush, Shaw, & Emery, 1979) administered during depressive episodes is effective in reducing subsequent relapse and recurrence. Patients who recover following treatment of acute depression by CBT subsequently show less relapse or need for further treatment than do patients who recover following treatment with antidepressant medication and are then withdrawn from medication (Blackburn, Eunson, & Bishop, 1986; Evans et al., 1992; Shea et al., 1992; Simons, Murphy, Levine, & Wetzel, 1986). As a result of CBT, patients presumably acquire skills, or changes in thinking, that confer some protection against future onsets.

A recent approach of combining treatment of the acute episode by antidepressant medication with provision of CBT following recovery, while antidepressant medication is gradually withdrawn, has yielded preliminary successful findings in preventing relapse/recurrence (Fava, Grandi, Zielezny, Canestrari, & Morphy, 1994; Fava, Grandi, Zielezny, Rafanelli, & Canestrari, 1996; Fava, Rafanelli, Grandi, Canestrari, & Morphy, 1998). The strategy of combining acute pharmacotherapy with psychological prophylaxis has the advantage of capitalizing on the cost-efficiency of antidepressant medication to reduce acute symptoms while reducing the need for patients to remain indefinitely on maintenance medication to prevent future relapse and recurrence. This strategy has also been evaluated using a novel, theory-driven approach to psychological prophylaxis, mindfulness-based cognitive therapy (MBCT; Segal, Williams, & Teasdale, 2002), formerly called attentional control (mindfulness) training. An initial evaluation of MBCT (Teasdale et al., 2000) demonstrated encouraging prophylactic effects. The present study examined the replicability of those findings and explored a number of related issues.

MBCT was derived from a model of cognitive vulnerability to depressive relapse (Segal, Williams, Teasdale, & Gemar, 1996; Teasdale, 1988; Teasdale, Segal, & Williams, 1995) that assumes that individuals who have previously experienced episodes of major depression differ from those who have not in the patterns of negative thinking that become activated in mildly depressed mood. Specifically, it is assumed that in recovered depressed patients, compared with never-depressed controls, dysphoria is more likely to activate patterns of self-devaluative depressogenic thinking, similar to those that prevailed in preceding episodes. Considerable evidence supports this assumption (Ingram, Miranda, & Segal, 1998; Segal, Gemar, & Williams, 1999). Reactivation of such depressogenic-thinking patterns by dysphoria in recovered depressed patients may progress to relapse to major depression through escalating cycles of ruminative cognitive–affective processing (Teasdale, 1988, 1997). It is assumed that repeated associations between depressed mood and negative thinking patterns during successive episodes of major depression increase the tendency for depressogenic thinking to be reactivated subsequently by depressed mood. This provides an explanation for the findings that risk of further episodes increases with every consecutive episode and that successive episodes of major depression require less and less external provocation by stressful life events (Kendler, Thornton, & Gardner, 2000; Lewinsohn, Allen, Seeley, & Gotlib, 1999; Post, 1992). It appears that the processes mediating relapse/recurrence become more autonomous with repeated experiences of depression.

The previous account suggests that risk of relapse and recurrence in recurrent major depression will be reduced if patients can learn to be aware of negative thinking patterns reactivated during dysphoria and disengage from those ruminative depressive cycles (Nolen-Hoeksema, 1991). MBCT was designed to achieve these aims (Segal et al., 2002). MBCT is an 8-week group program involving up to 12 recovered recurrently depressed patients. It is

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based on an integration of elements of CBT (Beck et al., 1979) with components of the mindfulness-based stress reduction (MBSR) program (Kabat-Zinn, 1990), which provides training in voluntary deployment of attention, based on mindfulness meditation. MBCT aims at developing participants' awareness of, and changing their relationship to, unwanted thoughts, feelings, and body sensations, so that participants no longer avoid them or react to them in an automatic way but rather respond to them in an intentional and skillful manner.

In an initial study that examined the effectiveness of MBCT in relapse prevention in recurrent major depression, Teasdale et al. (2000) obtained promising results. In that multicenter trial, 145 patients, in remission or in recovery from major depression, were randomized to continue with treatment as usual (TAU) or TAU plus MBCT. For patients with three or more previous episodes of depression, who constituted 77% of the sample, relapse rates were 66% for the TAU controls, but they were 37% for the patients also receiving MBCT, a 44% reduction. This study provided the first demonstration that a group-based psychological intervention, initially administered in the recovered state, could significantly reduce risk of future relapse/recurrence in patients with recurrent major depression. Reflecting the cost-efficient group-skills-learning format, the gains were achieved with an average of less than 5 hr therapist contact time per patient.

In contrast to the positive results they found for patients with three or more episodes, Teasdale et al. (2000) found no benefits from MBCT for a group of patients with only two previous episodes, both of which had occurred within the preceding 5 years; the MBCT group experienced a 54% relapse and the TAU group experienced a 31% relapse. Teasdale et al. suggested that this differential effect of MBCT on the group with only two episodes versus the group with more than two episodes might reflect different processes mediating relapse in the two groups. Specifically, as noted above, relapse or recurrence of major depression becomes less likely to be provoked by external stressful life events with every succeeding episode, but it may be more likely to become mediated by autonomous ruminative-thinking cycles reactivated by dysphoric mood. The effectiveness of MBCT in the group with three or more episodes but not in the group with only two (recent) episodes could be explained if MBCT was, as intended (Teasdale et al., 1995), specifically effective in reducing these more autonomous ruminative processes, which make individuals with three or more episodes more vulnerable to depression than individuals with two.

Alternatively, it might be that the differences in response to MBCT of these two groups did not arise solely from their differences in previous experience of depression but from the fact that they came from different base populations with distinct psychopathologies. In this case, in the context of Teasdale et al.'s (2000) investigation, the number of previous episodes might have been a marker of particular psychopathologies rather than (or as well as) the cause of the observed differential response to MBCT. Consistent with this possibility, Teasdale et al. found that their group of individuals with only two previous episodes was significantly older when they experienced their first episode of depression than were the individuals with three or more episodes. Patients with late onset of first depression have also been found not to benefit from continuation CBT, whereas patients with early onset benefited (Jarrett et al., 2001). These findings of differential treatment effect in patients with late onset versus early onset of first depression suggest the importance of understanding the relapse-related psychopathologies in different types of depressed patients.

One aim of the present investigation was to see whether the relapse prevention effects of MBCT observed by Teasdale et al. (2000) for individuals with three or more previous episodes of depression could be replicated. A second aim was to see whether further evidence could be obtained of differential response to MBCT in a group of patients with three or more episodes versus a group with only two (recent) episodes. A third aim was to test the hypothesis that MBCT is specifically effective in preventing relapses mediated by autonomous, internal processes (such as reactivation of patterns of negative ruminative thinking by dysphoria) rather than relapses provoked by stressful life events and that this can account for its ineffectiveness in the group of patients with only two previous episodes.

A fourth aim was to seek evidence that would clarify whether the patients with only two episodes were from the same base population as those with three or more, and simply at an earlier point in their depressive career, or whether these two groups actually represented distinct populations with different psychopathologies. In addition to examining possible differences in age of onset of first episode, the present study also investigated possible differences between groups in reports of early childhood experience. Lack of care, overprotection, and abuse in childhood consistently have been found to be directly associated with vulnerability to depression and poor treatment outcome (Randolph & Dykman, 1998; Sakado, Sato, Uehara, Sakado, & Someya, 1999). Early onset of depression has been found to mediate entirely the relationship between childhood neglect and increased risk of relapse (Bifulco, Brown, Moran, Ball, & Campbell, 1998). If patients with three or more episodes are found to have both an earlier onset of first depression and more adverse childhood experience, then it will lend further support to the hypothesis that, in the context of the selection criteria used in these trials, patients with three or more episodes and patients with two episodes come originally from distinct populations.

Method

Design

The design of the replication trial was similar to that of Teasdale et al. (2000), with the exceptions that one rather than three treatment sites were involved and that patients were stratified on the severity of last episode of depression and number of previous episodes rather than on the recency of last episode and number of previous episodes. Patients currently in remission or in recovery from major depression were randomly allocated to continue with TAU or to receive TAU plus MBCT. Following an 8-week treatment phase, patients were followed for a year at 3-month intervals. At the end of the follow-up, patients initially allocated to TAU were offered the opportunity to participate in MBCT.

Randomization of patients to treatment condition was by a statistician, who was not part of the research team, on receipt of the participant's date of birth, gender, date of assessment, number of previous episodes of depression, and severity of last episode. (Severity of last episode was calculated by summing retrospective severity ratings for the 16 depressive symptoms in the *Diagnostic and Statistical Manual of Mental Disorders* [4th ed.; *DSM–IV*; American Psychiatric Association, 1994] and dichotomizing at a median derived from comparable data in Teasdale et al., 2000.)

Patients were stratified on two baseline binary variables known to be predictive of risk of relapse (severity of last episode [above and below the median] and number of previous episodes of major depressive disorder [2 vs. more than 2]) and randomized by strata.

To determine whether patients with only two previous episodes were from the same base population as those with three or more episodes, we compared these two groups on age of onset at their first episode of major depression and, along with a group of never-depressed controls (matched for age and gender), on measures of childhood experience.

Participants

Recovered Recurrently Depressed Patients

Seventy-five patients currently in remission or recovery from major depression were recruited through general practitioners and advertisements in local newspapers. Inclusion criteria were (a) being 18–65 years of age; (b) meeting enhanced *DSM–IV* criteria for a history of recurrent major depression—these normally require a history of two or more previous episodes of *DSM–IV* major depression in the absence of a history of mania or hypomania; we required, further, that (i) at least two episodes of major depression occurred within the past 5 years and (ii) at least one of those episodes was within the past 2 years; (c) having a history of treatment by a recognized antidepressant medication, but being off antidepressant medication and in recovery/remission at the time of baseline assessment and for at least the preceding 12 weeks; and (d) having, at baseline assessment, a Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1960) score of less than 10. Exclusion criteria were history of schizophrenia or schizoaffective disorder, current substance abuse, borderline personality disorder, organic mental disorder or pervasive developmental delay, current obsessive–compulsive disorder, current eating disorder, dysthymia before age 20, more than four lifetime sessions of CBT, and current psychotherapy or counseling more frequently than once per month.

Never-Depressed Controls

Fifty participants, matched for age ($M = 44.5$, $SD = 8.9$) and gender (37 women; 74%) with the recovered depressed patients, were recruited from a volunteer panel, meeting the criteria: (a) Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) score less than 11; (b) a negative response to both of the following screening questions for *DSM–IV* major depression: "Has there been a time when you were depressed or down most of the day nearly every day for as long as two weeks?" and "Has there been a time when you were a lot less interested in most things or unable to enjoy things you used to enjoy for as long as two weeks?"

Informed Consent

Participants meeting selection criteria gave written informed consent on a form approved by the Cambridge, United Kingdom Local Research Ethics Committee.

Measures

HAM-D

Patients' baseline assessment included the 17-item HAM-D, a widely used interviewer-administered measure of severity of depression. It covers a range of affective, behavioral, and biological symptoms and has acceptable psychometric properties (Rabkin & Klein, 1987). Scores can range from 0 to 52.

BDI

The BDI is a widely used 21-item questionnaire measure of the severity of affective, cognitive, behavioral, and somatic symptoms of depression; scores range from 0 to 63. Internal consistency, validity, and test–retest reliability are high in psychiatric and nonpsychiatric samples (Beck, Steer, & Garbin, 1988). It was completed by patients at baseline assessment and by controls in individual testing sessions.

Measure of Parenting Style (MOPS)

MOPS (Parker et al., 1997) is a 15-item self-report measure of dysfunctional parenting. Participants rate each item as a description of their mother's and, on a separate form, their father's behaviors toward them in their first 16 years, using a 4-point scale (0 = *not true at all*, 1 = *slightly true*, 2 = *moderately true*, 3 = *extremely true*). All items are dysfunctional in content. MOPS includes three scales: Indifference (six items), Overcontrol (four items), and Abuse (five items). The scales have acceptable internal consistency: Parker et al. (1997) reported alpha coefficients of .93 for both maternal and paternal indifference, .82 and .76 for maternal and paternal overcontrol, and .87 and .92 for maternal and paternal abuse. As evidence of concurrent validity, Parker et al. reported that the Indifference and Overcontrol scales correlated highly with, respectively, the Care and Protection subscales of the Parental Bonding Instrument (Parker, Tupling, & Brown, 1979) and had correlations from .39 to .66 between Abuse scores and psychiatrists' ratings of patients' reported abusive experience. Order of presenting the maternal and paternal forms was counterbalanced, and scores were averaged across the two parents. Patients completed the MOPS at baseline assessment and controls completed the MOPS in individual testing sessions.

Relapse/Recurrence

The primary treatment outcome variable was the occurrence of relapse or recurrence meeting *DSM–IV* criteria for major depressive episode (American Psychiatric Association, 1994). Assessments were modeled on the Structured Clinical Interview for *DSM–III–R* (Spitzer, Williams, Gibbon, & First, 1992) and done by a clinical psychologist blind to patients' treatment condition. To examine interrater reliability, we audiotaped interviews, and those in which patients met screening criteria for major depression were evaluated by an independent, blind, experienced research psychiatrist. Any information that might prejudice blindness was erased from the tapes presented to the independent assessor. The kappa for agreement on the presence or absence of major depression ($n = 48$) was 0.78, suggesting good to excellent agreement. In case of disagreement, the two raters discussed it and came to a consensus, if possible, and the agreed rating was used for analysis. If no agreement was reached after discussion, the rating of the independent assessor was used for analysis.

Following baseline assessment, interviews were scheduled at points corresponding to the completion of the initial eight MBCT training sessions, and every 3 months thereafter over the course of the follow-up year.

Life Events

In follow-up interviews, if it was established that relapse/recurrence had occurred, patients were asked whether the onset of depression had been brought on by any events. If they responded in the negative, their answer was scored 0 (*no event*). If they described an event that they believed had triggered the relapse, the clinical psychologist who interviewed them and who was blind to their treatment condition made a judgment about whether the event described could be regarded as "a significant life event that is more than likely to bring about serious depressed feelings in an average person." The answer was scored 1 (*event of borderline significance*) if the event did not fall into such a category and 2 (*significant event*) if it did. A second independent rater categorized all the responses ($n = 37$). Spear-

man's rho between the two sets of ratings was .88, indicating good to excellent agreement. Concurrent validity for these ratings was examined by correlating the interviewer's rating with the Social Readjustment Rating Scale (SRRS; Holmes & Rahe, 1967). The SRRS includes 43 events with values ranging from 11 to 100; the higher the value, the more readjustment is required and the more stressful is the event. Events reported by patients that corresponded to SRRS events with values of 50 to 100 (the 7 most stressful events on the scale) were scored 2, and those that did not were scored 1. Spearman's rho between the study rater and the SRRS ($n = 37$) was .94, indicating excellent agreement.

Treatment

TAU

Patients were told to seek help from their family doctor or other sources as they normally would if they encountered symptomatic deterioration or other difficulties over the course of the study. The treatment patients in the TAU and MBCT groups received was monitored at the 3-month assessment sessions and is described in the Results section.

MBCT

MBCT is a manualized group skills-training program (Segal et al., 2002) based on an integration of aspects of CBT for depression (Beck et al., 1979) with components of the MBSR program developed by Kabat-Zinn (1990). It is designed to teach patients in remission from recurrent major depression to become more aware of, and to relate differently to, their thoughts, feelings, and bodily sensations—for example, relating to thoughts and feelings as passing events in the mind, rather than identifying with them or treating them as necessarily accurate readouts on reality. The program teaches skills that allow individuals to disengage from habitual ("automatic") dysfunctional cognitive routines, in particular depression-related ruminative thought patterns, as a way to reduce future risk of relapse and recurrence of depression.

After an initial individual orientation session, the MBCT program is delivered by an instructor in 8 weekly 2-hr group-training sessions involving up to 12 recovered recurrently depressed patients. During that period, the program includes daily homework exercises. Homework invariably includes some form of guided (taped) or unguided awareness exercises directed at increasing moment-by-moment nonjudgmental awareness of bodily sensations, thoughts, and feelings together with exercises designed to integrate application of awareness skills into daily life. Key themes of MBCT include empowerment of participants and a focus on awareness of experience in the moment. Participants are helped to cultivate an open and acceptant mode of response, in which they intentionally face and move into difficulties and discomfort, and to develop a "decentered" perspective on thoughts and feelings, in which these are viewed as passing events in the mind.

Increased mindfulness is relevant to the prevention of relapse/recurrence of depression, as it allows early detection of relapse-related patterns of negative thinking, feelings, and body sensations and so allows them to be "nipped in the bud" at a stage when that could be much easier than it would be if such warning signs are not noticed or are ignored. Further, entering a mindful mode of processing at such times allows disengagement from the relatively automatic ruminative thought patterns that would otherwise fuel the relapse process. Formulation of specific relapse/recurrence prevention strategies (such as involving family members in an early warning system, keeping written suggestions to engage in activities that are helpful in interrupting relapse-engendering processes, or looking out for habitual negative thoughts) are also included in the later stages of the initial 8-week phase.

Following the initial phase of weekly group meetings, two follow-up meetings were scheduled at intervals of 1 and 6 months. MBCT sessions were video- or audiotaped, with patients' permission, to allow monitoring of treatment integrity.

Instructors

The two instructors were experienced cognitive therapists. One had participated in the Teasdale et al. (2000) trial. Both had previously led at least two groups of recovered depressed patients through the MBCT program.

Results

Treatment Outcome

Strategies of Analyses

Because MBCT has been found to reduce relapse in individuals with three or more episodes of depression but not in a group with only two (recent) episodes (Teasdale et al., 2000), effects of MBCT for those with three or more episodes were assessed separately first, followed by assessment of those with two episodes.

Normally, outcome analyses would be conducted for both a per-protocol sample (which would comprise all patients allocated to TAU, together with those patients allocated to MBCT who received a "minimally adequate dose" of MBCT by attending at least four MBCT sessions) and an intent-to-treat sample (which would comprise all patients included in the random allocation). However, in our study, for individuals with three or more episodes, the per-protocol and intent-to-treat samples differed by only 1 participant. Hence, it was deemed unnecessary to conduct analyses for both samples, and only the intent-to-treat sample was analyzed. For those with only two episodes, analyses for both samples were conducted.

Patient Flow

Seventy-six patients met inclusion criteria at a baseline screening interview and were invited to participate in the study. Of these, 1 declined, leaving 75 patients to be randomized. Six patients allocated to MBCT were not included in the per-protocol sample. Of these, 3 failed to attend any training session, and 3 (8% of all allocated to MBCT) dropped out after attending less than four sessions. Complete data on relapse/recurrence were available for 73 (97%) of the 75 patients in the intent-to-treat sample and for 68 (99%) of the 69 patients in the per-protocol sample, data being incomplete for 1 TAU patient and 1 "insufficient treatment" MBCT patient.

Patient Characteristics

Table 1 shows baseline characteristics of the intent-to-treat sample. TAU and MBCT groups were closely similar on each of the baseline variables. The 31 patients who completed four or more training sessions were compared with the 6 who did not. There were no statistically significant differences between these two groups on baseline characteristics, except for on the number of previous episodes of depression (Mann–Whitney's $U = 29$, $z = -2.714$, $p = .007$). In fact, 5 of the 6 patients who did not complete four sessions had two episodes of depression. The difference in dropout rate between those with two episodes and those with three or more was significant (Fisher's exact test, $p = .002$).

Table 1
Baseline Characteristics of Treatment-as-Usual (TAU) and Mindfulness-Based Cognitive Therapy (MBCT) Samples

Characteristic	TAU (n = 38)	MBCT (n = 37)
Female (%)	79	73
White (%)	100	100
Age, in years, *M* (*SD*)	46.1 (9.3)	42.9 (8.4)
Marital status (%)		
Single	8	14
Married or cohabiting	66	62
Separated, divorced, or widowed	26	24
Years of education, *M* (*SD*)	15.8 (3.5)	16.0 (3.0)
Depression		
HAM-D score, *M* (*SD*)	5.68 (2.97)	5.70 (3.02)
BDI score, *M* (*SD*)	15.13 (9.51)	13.49 (7.16)
Previous episodes, *Mdn* (IQR)	3.0 (2.0)	3.0 (2.0)
Age (in years) at first onset, *M* (*SD*)	32.4 (13.0)	28.8 (11.6)
Duration in weeks of episodes, *Mdn* (IQR)		
Last	16 (21)	12 (10)
Penultimate	20 (24)	24 (24)
Previous treatment for depression (%)		
Antidepressant medication	100	100
Hospitalization	10	3
Psychotherapy/counseling	74	68
Social class (%)[a]		
Class 1 (4%)	3	14
Class 2 (21%)	61	57
Class 3 (46%)	29	19
Class 4 (17%)	5	8
Class 5 (8%)	3	3

Note. HAM-D = Hamilton Rating Scale for Depression; BDI = Beck Depression Inventory; IQR = interquartile range.
[a] Social class data are from the Office of Population Censuses and Surveys, 1991 (Class 1, e.g., general manager; Class 5, e.g., road sweepers). The parenthetical percentages are the breakdown in the general population of England and Wales.

Treatment Received

Nontrial treatment for depression was monitored in the trimonthly interviews. There were no significant differences between the TAU and MBCT groups for any of the measures of nontrial treatment received (all *p*s >.10; see Table 2).

Outcome Analysis: Prevention of Relapse/Recurrence to Major Depression

Time to onset of relapse or recurrence (in weeks) was compared between the treatment condition and TAU groups using Cox's proportional hazards regression models (SPSS, 1994, pp. 291–328) with MBCT as a categorical (indicator) variable and TAU as the reference condition. Wald and hazard ratio statistics as well as 95% confidence intervals (CIs) for hazard ratios are reported.

To examine whether treatment effects were moderated by the number of previous episodes of major depressive disorder, we conducted preliminary Cox's regression analyses that included the number of episodes (2 vs. > 2) and its interaction with treatment condition, as covariates, together with treatment condition (MBCT vs. TAU) for the intent-to-treat sample. The interaction of number of previous episodes and treatment condition was significant, Wald (1, N = 73) = 5.66, p = .017, hazard ratio = .104 (CI = .016–.672). (Inclusion of age as an additional covariate left the results unchanged.) The significant interaction showed that differences in outcome between treatment conditions were not the same in patients with three or more episodes as in patients with only two episodes (see Table 3), mandating the separate analyses for the two groups that had, as indicated previously, already been planned and that are reported later.

Comparable preliminary analyses for the other stratifying variable, severity of last episode, yielded no significant interactions. Consequently, separate analyses were unnecessary for patients with more severe and less severe prior episodes.

Table 2
Other Treatment for Depression From Other Sources Over the 60-Week Study Period for Treatment-as-Usual (TAU) and Mindfulness-Based Cognitive Therapy (MBCT) Groups

	2 episodes		≥ 3 episodes	
Other treatment	TAU	MBCT	TAU	MBCT
One or more depression-related visits to general practitioner (%)	36	25	33	25
Psychiatric treatment (%)				
Outpatient	0	0	4	4
Day patient	0	0	0	4
Inpatient	0	0	0	4
Counseling, psychotherapy, or professional mental health support (%)[a]	30	13	19	21
Other mental health contacts (%)[b]	0	13	15	11
Medication for depression (%)	36	13	33	21
Duration in weeks, *M* (*SD*)[c]	27.5 (14.5)	27.0[e]	34.6 (20.2)	25.4 (8.2)
Reported dosage SSRI, *M* (*SD*)[c,d]	22.5 (5.0)	26.7[e]	23.6 (8.9)	27.0 (5.4)

[a] The category includes the following: psychiatric social worker, community psychiatric nurse, community mental health team worker, counselor, psychotherapist, group therapy/support, and marital/family therapy. [b] The category includes the following: voluntary mental health organizations (e.g., Samaritans) and health visitor. [c] The category includes only those who had medication. [d] Selective serotonin reuptake inhibitors (SSRI) were the most commonly prescribed antidepressants. Reported dosage is expressed in mg fluoxetine daily dose equivalents. [e] There was only 1 participant in this category.

Table 3
Relapse/Recurrence (Rel/Rec) in Treatment-as-Usual (TAU) and Mindfulness-Based Cognitive Therapy (MBCT) Samples

	TAU		MBCT	
Group	%	Rel/Rec	%	Rel/Rec
≥ 3 episodes (intent to treat)	78	21/27	36	10/28
2 episodes (intent to treat)	20	2/10	50	4/8
2 episodes (per protocol)	20	2/10	25	1/4

Patients with three or more previous episodes. Figure 1 shows survival (i.e., nonrelapse/recurrence) curves comparing relapse/recurrence over the 60-week study period for MBCT and TAU in patients with a history of three or more episodes of depression. These patients constituted 75% (55/73) of the total intent-to-treat sample for whom relapse/recurrence data were available. This proportion was comparable to that (77%) in Teasdale et al. (2000). Cox's regression analyses showed significantly less hazard of relapse/recurrence in MBCT participants compared with TAU participants, Wald (1, $N = 55$) = 10.79, $p = .001$, hazard ratio = .278 (CI .130–.597). The treatment effect remained significant when baseline BDI or HAM-D scores were also entered as covariates. Over the total 60-week study period, 36% (10/28) of MBCT participants had a relapse/recurrence compared with 78% (21/27) of the TAU participants, $\chi^2(1, N = 55) = 9.89$, $p = .002$, a 54% reduction in risk of relapse/recurrence in MBCT participants. The difference between 36% relapse and 78% relapse yields an *h* value of .88, indicating a large effect size (Cohen, 1988, p. 185). This effect is larger than the medium effect size reported by Teasdale et al. (2000).

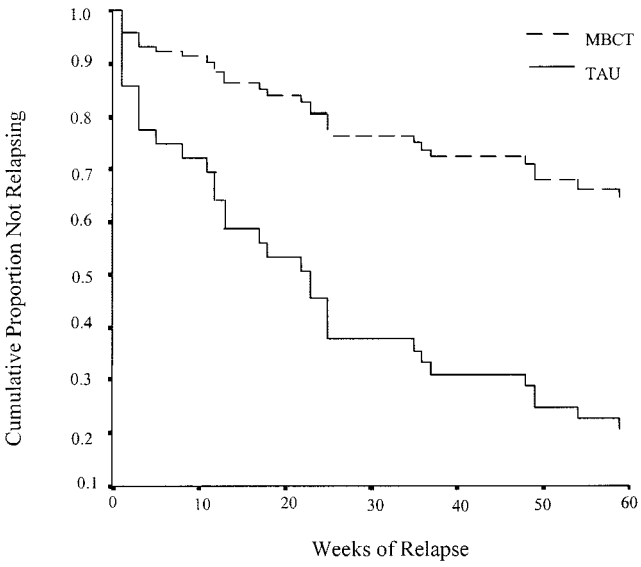

Figure 1. Survival (nonrelapse/nonrecurrence) curves comparing relapse/recurrence to *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.) major depression for treatment-as-usual (TAU) and mindfulness-based cognitive therapy (MBCT) in patients with three or more previous episodes of major depression (intent-to-treat sample).

Patients with two previous episodes of depression. These constituted 25% (18/73) of the intent-to-treat sample for whom relapse/recurrence data were available and 21% (14/68) of the per-protocol sample. These proportions were comparable to those (23% in both cases) in Teasdale et al.'s (2000) previous trial. Cox's regression analyses showed no significant differences in hazard of relapse/recurrence in MBCT participants compared with TAU participants for either the intent-to-treat sample, Wald (1, $N = 18$) = 1.43, $p = .231$, or the per-protocol sample, Wald (1, $N = 14$) = .040, $p = .841$. Over the total 60-week study period, in the intent-to-treat sample, 50% (4/8) of MBCT participants had a relapse/recurrence compared with 20% (2/10) of the TAU participants (Fisher's exact test $p = .321$). In the per-protocol sample, 25% (1/4) of MBCT participants had a relapse/recurrence compared with 20% (2/10) of the TAU participants (Fisher's exact test $p = .837$). In Teasdale et al.'s (2000) study relapse/recurrence rates in the intent-to-treat sample (MBCT: 56%, TAU: 31%) were comparable to our findings, whereas rates in the per-protocol sample (MBCT: 54%, TAU: 31%) were slightly higher.

Number of previous episodes and risk of relapse. To investigate further the relationship of number of previous episodes and differential response to TAU and MBCT, we examined rates of relapse/recurrence for patients with two, three, and four or more episodes separately in the TAU and MBCT groups (see Table 4). A positive linear relationship between number of previous episodes and risk of relapse/recurrence was found in the TAU group (Mantel–Haenszel's test for linear association, $\chi^2[1, N = 37] = 7.83$, $p = .005$) but not in the MBCT group (Mantel–Haenszel test for linear association, $\chi^2[1, N = 36] = 0.09$, $p = .753$). This pattern of results is consistent with MBCT preventing relapse specifically through changes in processes that mediate the increased risk of relapse with increasing numbers of previous episodes.

Life-Event-Related Relapse and Differential Response to MBCT

Patients' responses to the question of whether there were triggers for their relapse and the interviewer's ratings are shown in Table 5. Table 6 shows, for patients with three or more episodes, the numbers of relapses associated with significant events, borderline events, and no events in the MBCT and TAU groups. The effectiveness of MBCT in preventing relapse was greatest for relapses in which there was no reported provocation by events (ratio of percentage of such relapses in the MBCT vs. TAU groups is 1:7.19, Fisher's exact test $p = .025$) but less for relapses where provocation by borderline events was reported (relapse ratio in the

Table 4
Rates of Relapse/Recurrence (Rel/Rec) by Number of Episodes in Mindfulness-Based Cognitive Therapy (MBCT) and Treatment-as-Usual (TAU) Groups

		2 episodes		3 episodes		≥ 4 episodes	
Group	*n*	Rel/Rec	%	Rel/Rec	%	Rel/Rec	%
MBCT	36	4/8	50	4/12	33	6/16	38
TAU	37	2/10	20	9/15	60	12/12	100

Table 5
Events Reported as Preceding Relapse

Event	No. of patients: ≥ 3 episodes	No. of patients: 2 episodes	Rating
No event	8	0	0
Work stress	5	0	1
Loss of job because of company changeover	1	0	1
Minor financial loss	1	0	1
Stressful holiday with family	1	0	1
Arguments with husband	1	0	1
Daughter's overdose	1	0	1
Daughter is pregnant	1	0	1
Son failed exam	1	0	1
Mother going to nursing home	1	0	1
Death anniversary of family member	2	0	1
Pregnancy	0	1	1
Progesterone treatment	1	0	1
Unexpected termination of psychotherapy	1	0	1
Minor lawsuit involvement	1	0	1
Conviction for assault and probation sentence	0	1	1
No presents or party for 40th birthday	1	0	1
Incurable/life threatening illness diagnosed	2	1	2
Marital separation	2	0	2
Sudden death of parent	0	1	2
Daughter seriously injured and disfigured	0	1	2
Pedestrian killed in driving accident	0	1	2

Note. In the ratings, 0 indicates no event, 1 indicates nonsignificant event, and 2 indicates significant event.

MBCT vs. TAU groups is 1:1.78, $\chi^2[1, N = 55] = 2.30$, $p = .130$), and there was no preventive effect of MBCT whatever for relapses where provocation by significant events was reported (Fisher's exact test $p = 1.000$).

Could the lack of effectiveness of MBCT in preventing relapses provoked by significant life events explain the relative lack of effectiveness of MBCT in preventing relapse in the group of patients with only two previous episodes, as Segal et al. (2002, p. 320) have suggested? In other words, was MBCT relatively ineffective in such patients because proportionately more of their relapses were provoked by significant environmental events, consistent with the evidence from Kendler et al. (2000), Lewinsohn et al. (1999), and Post (1992), reviewed in the introduction? Table 7 shows, for TAU patients, the numbers of relapses for which significant, borderline, or no life events were reported as antecedents. All (2/2; 100%) relapses in TAU patients with only two previous episodes were reportedly preceded by significant life events, whereas this was true of only 10% (2/21) of relapses in TAU patients with three or more episodes, a significant difference in proportions (Fisher's exact test, $p = .024$). The preponderance of relapses preceded by significant events in patients with two episodes and the ineffectiveness of MBCT in preventing such relapses (evident in the data for patients with three or more episodes above) can account for the relative lack of effectiveness of MBCT in patients with two episodes.

Are the Three-or-More Episode Group and the Two-Episode Group From the Same Base Population?

Early Experience

MOPS scores (see Table 8) were not available for 5 of the 75 recovered depressed patients (4 two-episode patients, 1 three-or-more-episodes patient). Indifference and Abuse scores were normalized by reciprocal transformations and Overcontrol scores were normalized by logarithmic transformations prior to analysis. One-way analyses of variance comparing MOPS scores for never-depressed, two-episode, and three-or-more episode groups yielded significant between-groups effects for all three MOPS scales, Indifference: $F(2, 117) = 9.16$, $p < .001$; Overcontrol: $F(2, 117) = 3.87$, $p = .023$; Abuse: $F(2, 117) = 12.26$, $p < .001$. Planned comparisons showed that patients with three or more episodes scored significantly higher than never-depressed controls on all three MOPS scales and scored significantly higher than patients with two episodes on Indifference and Abuse but not on Overcontrol. Patients with two episodes did not differ significantly from never-depressed controls on any of the three scales.

These findings support the hypothesis that patients with two episodes and patients with three or more episodes came from different populations. BDI scores were not significantly correlated with Abuse or Indifference scores in either the never-depressed or the recovered depressed groups (largest $r = .07$, $df = 48$, $p > .1$), showing that mood at the time of report did not affect participants' recall of early experience on these two dimensions on which significant differences were found between patients with two and three or more episodes.

Table 6
Numbers of Patients With Three or More Episodes Reporting Relapses by Event in Treatment-as-Usual (TAU) and Mindfulness-Based Cognitive Therapy (MBCT) Groups

		TAU ($n = 27$)		MBCT ($n = 28$)	
Relapse	Life event	*n*	%	*n*	%
Yes	No	7	26	1	4
	Borderline	12	44	7	25
	Significant	2	7	2	7
No		6	22	18	64

Table 7
Reports of Life Events Preceding Relapse in Treatment-as-Usual Patients

		2 episodes ($n = 10$)		≥ 3 episodes ($n = 27$)	
Relapse	Life event	*n*	%	*n*	%
Yes	No	0	0	7	26
	Borderline	0	0	12	44
	Significant	2	20	2	7
No		8	80	6	22

Table 8
Measure of Parenting Style Scores (Parent Average) for Patients and Never-Depressed Controls

	Never depressed		2 episodes		≥ 3 episodes	
Measure	*M*	*SD*	*M*	*SD*	*M*	*SD*
Indifference	1.52	2.68	1.28	1.47	4.43	4.42
Over-control	2.92	2.05	3.38	2.52	4.37	2.77
Abuse	0.66	1.33	1.16	1.92	2.91	3.65

Note. Never depressed $n = 50$, 2 episodes $n = 16$, ≥ 3 episodes $n = 54$.

Cox's regressions predicting time to relapse from treatment condition, and either Indifference or Abuse, and its interaction with treatment condition yielded no significant interaction terms. This suggests that the differential treatment response of the three-or-more-episode group and the two-episode group cannot be accounted for by the differences between these groups on the Indifference and Abuse measures.

Age at First Onset of Depression

Consistent with Teasdale et al.'s (2000) findings, mean age at first onset of major depression in patients with two previous episodes of depression (37.5, $SD = 8.0$, $n = 20$) was significantly later, $t(54.5) = 3.61$, $p < .001$, than it was in patients with three or more episodes (28.4, $SD = 12.9$, $n = 55$). This finding suggests that the patients with two episodes originated from a different population than did the patients with three or more episodes rather than that they were simply at an earlier stage of their depressive career.

Also consistent with Teasdale et al.'s (2000) findings, mean age at entry to the trial was significantly lower, $t(73) = 2.12$, $p < .05$, in patients with two episodes (41.2, $SD = 7.9$, $n = 20$) than in patients with three or more episodes (45.7, $SD = 9.1$, $n = 55$). Cox's regressions predicting time to relapse from treatment condition and either age at first onset or age of entry to the trial, and their interaction with treatment condition, yielded no significant interactions. This suggests that the differential treatment response of the three-or-more episode group and the two-episode group cannot be accounted for by the differences between the groups in age of first onset or age at entry to the trial.

Discussion

Efficacy of MBCT

This study replicated both the positive and negative outcome findings of Teasdale et al.'s (2000) clinical trial. In a group of recovered recurrently depressed patients with three or more previous episodes of major depression, MBCT more than halved relapse/recurrence rates compared with patients who continued with TAU. The effect size was larger than that in Teasdale et al. The protective effects of MBCT were most obvious in patients with four or more episodes: Only 38% of those receiving MBCT relapsed compared with 100% of their TAU counterparts. The beneficial effects of MBCT could not be attributed to MBCT patients receiving more in the way of other forms of treatment.

MBCT patients were still at a risk considerably higher than the expected annual incidence rate of major depression among those with no prior history of major depressive disorder in general population samples. Nonetheless, the observed effect of MBCT reducing relapse/recurrence in a high-risk group is of clinical as well as statistical significance. In the present study, MBCT, as a group-based treatment, required less than 3 therapist-contact hours per patient, on average, making it a highly cost-efficient approach to relapse prevention in recurrent depression. Our findings put MBCT in the category of a "probably efficacious" treatment, as two randomized-controlled trials have shown its effectiveness (American Psychological Association, 1995).

The earlier finding that a group of patients with two previous episodes of depression (both of which had occurred in the preceding 5 years) showed no evidence of benefit from MBCT was also replicated. As in Teasdale et al.'s (2000) study, these patients showed a nonsignificantly greater tendency to relapse following MBCT than did patients who received TAU. These findings suggest that MBCT may be contraindicated for this group of patients. It is important to note that these patients, selected according to the inclusion criteria of this and the previous trial, are not necessarily representative of all patients with two previous episodes of major depression. In particular, as we discuss later, they do not seem to be simply the same population as the three-episode group at an earlier stage in their depressive career. For that reason, the efficacy of MBCT for groups of patients with only two previous episodes meeting alternative selection criteria remains an open question. The finding that MBCT can be relatively unhelpful for a particular group of patients highlights the need to understand the relevance of MBCT to particular relapse-related psychopathologies (Teasdale, Segal, & Williams, 2003).

A limitation of the present study, as of the original Teasdale et al. (2000) trial, is that the lack of another group intervention comparison condition, matched to MBCT for exposure to therapist and group support, means that the effects of the nonspecific factors of MBCT, such as group support and therapeutic alliance, cannot be assessed. It follows that the beneficial effects of MBCT cannot be unambiguously attributed to its specific components rather than to more nonspecific factors. However, the effects of MBCT reported by Teasdale et al. represented the first demonstration that a group psychological intervention, initially administered in the recovered state, could significantly reduce risk of future relapse in patients with recurrent major depression. For that reason, it seemed more important to establish the replicability of those findings before attempting to investigate the specificity of the effects of MBCT, particularly as the latter type of study would require very large sample sizes if it were to have adequate statistical power. A further limitation of the present study is that the small sample size of patients with only two episodes makes it difficult to know whether the nonsignificant treatment effects observed for that group reflect an absolute lack of effectiveness of MBCT, a relative ineffectiveness of MBCT, or actual harmful effects of MBCT compared with TAU.

MBCT and Internally Versus Externally Provoked Relapse/Recurrence

Present findings suggest that MBCT is not equally effective in preventing all forms of relapse/recurrence. The extent to which

patients with three or more previous episodes of depression benefited from MBCT was inversely related to the extent to which relapse/recurrence was associated with significant life events: The reduction in relapse/recurrence in MBCT relative to TAU was greatest for onsets of depression in which no antecedent life events were reported, it was somewhat less for onsets with borderline antecedent events, and there was no difference between MBCT and TAU for onsets preceded by significant life events. In other words, MBCT is very effective in reducing autonomous, presumably internally provoked, relapse/recurrence but quite ineffective in reducing relapse/recurrence associated with severe life events. This pattern of results would be expected if, as intended (Segal et al., 2002, p. 37), MBCT acts specifically by disrupting autonomous relapse processes involving the reactivation of ruminative patterns of negative thinking by dysphoria at times of potential relapse.

If, as the data from patients with three or more previous episodes of depression suggest, MBCT is specifically effective in preventing autonomous relapse/recurrence but ineffective in preventing relapse/recurrence associated with significant life events, this would also account for the relative ineffectiveness of MBCT in the groups of patients with only two (recent) episodes in the present trial and Teasdale et al. (2000). Findings from the TAU condition in the present study indicated that in patients with only two previous episodes, in contrast to those with three or more, relapse/recurrence was overwhelmingly associated with the occurrence of antecedent severe life events. As these are just the types of relapse/recurrence that MBCT is ineffective at preventing, the relative lack of benefit from MBCT in this group would be expected.

The overall pattern of results in the present study is consistent with Teasdale et al.'s (2000, p. 622) suggestions that (a) the greater risk of relapse/recurrence in the group with three or more episodes than in the group with only two episodes (apparent in the TAU group) was attributable to autonomous relapse/recurrence processes involving reactivation of depressogenic thinking patterns by dysphoria and (b) the prophylactic effects of MBCT arose, specifically, from disruption of those processes at times of potential relapse/recurrence.

A limitation of the present methodology was that the occurrence of stressful life events was only probed at times when patients had met criteria for relapse. For this reason, it is not possible to examine directly the protective effects of MBCT in the face of different severities of environmental stress because the occurrence of events in those who did not relapse was not examined.

Are the Three-or-More Episode Group and the Two-Episode Group From the Same Base Population?

In both Teasdale et al. (2000) and the present study, the group of patients with two episodes reported a later onset of their first episode of major depression than did patients with three or more episodes. This suggests that these two groups originated from different base populations and were not simply members of the same base population at different points in their depressive careers. Further support for this hypothesis comes from the finding in the present study that patients with three or more episodes reported more adverse early experience in terms of indifference and abuse than both patients with two episodes and never-depressed controls. Patients with only two episodes did not differ from controls on reported early experience.

Retrospective reports of childhood experience are clearly open to various reporting biases and so cannot necessarily be taken as veridical. On the other hand, after reviewing evidence on reports of childhood experience, Brewin, Andrews, and Gotlib (1993) concluded that claims concerning the general unreliability of retrospective reports were exaggerated. Further, the fact that BDI scores did not correlate with the MOPS scores on which the two patient groups differed from each other suggests that mood at the time of completing the MOPS did not bias the way participants reported their early experience on these dimensions.

The conclusion that, in the contexts of the inclusion criteria of this and the earlier trial, patients with two versus three or more episodes originated from different base populations has important treatment implications. It suggests that these two groups may have distinct treatment needs and that, if the present two-episode group were subsequently to experience a further episode of depression (giving them three in all), they would not necessarily benefit from MBCT in the same way as the present three-or-more episodes group. Patients with late onset of first depression also do not benefit from continuation cognitive therapy, in contrast to patients with early onset (Jarrett et al., 2001). Patients with late onset of first depression appear to need different prevention strategies than patients with early onset, presumably reflecting different pathways to relapse in these two groups (Nezu, Nezu, Trunzo, & McClure, 1998).

Conclusions

The present study provided further evidence that MBCT is a cost-efficient and efficacious intervention to reduce relapse/recurrence in patients with recurrent major depressive disorder who, following a reportedly adverse childhood, have experienced three or more previous episodes of depression, the first of which was relatively early in their lives. MBCT is most effective in preventing relapse/recurrence that is unrelated to environmental provocation. This finding is consistent with MBCT having its effects, as intended, through the disruption of autonomous, relapse-related cognitive-affective ruminative processes reactivated by dysphoria at times of potential relapse. The relative failure of MBCT to prevent relapse in the particular group of patients with only two previous episodes that were studied in this trial and by Teasdale et al. (2000) appears to reflect the fact that these patients originated from a different base population, with normal reported childhood experience, later initial onset of major depression, and relapse/recurrence predominantly associated with major life events.

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