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Comparison of Cognitive Behavioral and Mindfulness Meditation Interventions on Adaptation to Rheumatoid Arthritis for Patients With and Without History of Recurrent Depression

Alex J. Zautra, Mary C. Davis, and John W. Reich
Arizona State University

Perry Nicassio
University of California, Los Angeles

Howard Tennen
University of Connecticut Medical Center

Patrick Finan, Anna Kratz, and Brendt Parrish
Arizona State University

Michael R. Irwin
University of California, Los Angeles

This research examined whether cognitive behavioral therapy and mindfulness interventions that target responses to chronic stress, pain, and depression reduce pain and improve the quality of everyday life for adults with rheumatoid arthritis (RA). The 144 RA participants were clustered into groups of 6–10 participants and randomly assigned to 1 of 3 treatments: cognitive behavioral therapy for pain (P); mindfulness meditation and emotion regulation therapy (M); or education-only group (E), which served as an attention placebo control. The authors took a multimethod approach, employing daily diaries and laboratory assessment of pain and mitogen-stimulated levels of interleukin-6 (IL-6), a proinflammatory cytokine. Participants receiving P showed the greatest Pre to Post improvement in self-reported pain control and reductions in the IL-6; both P and M groups showed more improvement in coping efficacy than did the E group. The relative value of the treatments varied as a function of depression history. RA patients with recurrent depression benefited most from M across several measures, including negative and positive affect and physicians' ratings of joint tenderness, indicating that the emotion regulation aspects of that treatment were most beneficial to those with chronic depressive features.

Keywords: cognitive behavioral, mindfulness, interventions, depression, arthritis

Stresses in life are unavoidable, but most people are well equipped to respond effectively to most of these stressors. Responses to acute threats of harm have evolved to preserve health and functioning (Ursin & Olff, 1993). However, the sustained demands that accompany a chronic pain condition pose the additional challenge of accommodation to a daily life punctuated by pain, functional impairment, and affective disturbance. In the face of such chronic recurrent stressors, new responses need to be acquired. Methods of coping that promote down-regulation of arousal and a reduction in attentional focus are often more adaptive than vigilance in this situation (Dixon, Keefe, Scipio, Perri, & Abernethy, 2007). In fact, the development of reliable methods of preserving rewarding social relationships and other satisfying pursuits in spite of pain and other distressing symptoms may be essential to sustaining psychological well-being and physical functioning (DeVellis, Lewis, & Sterba, 2003). In this study, we examined whether individuals with the autoimmune disease rheumatoid arthritis (RA) exhibit greater resilience in the face of the demands of their disease when they are given the opportunity to learn new responses to their chronic pain and functional limitations.

The "gold standard" of behavioral approaches, cognitive behavioral therapy (CBT), attempts to change maladaptive ways of thinking and feeling in response to the illness. The specific techniques have encompassed an extensive range of strategies, including biofeedback and relaxation training, cognitive restructuring and distraction, and activity pacing. The majority of studies have focused on the management of pain, but some CBT trials have also emphasized the management of stress and the development of more general life-management skills. A recent review of 25 randomized clinical trials that tested psychosocial treatments for RA underscored the effectiveness of CBT in increasing efficacy in coping with pain and in reducing pain, physical disability, and depressive symptoms (Astin, Beckner, Soeken, Hochberg, & Berman, 2002). Yet the findings showed substantial variability across outcome measures. The effects were strongest for active coping outcomes

Alex J. Zautra, Mary C. Davis, John W. Reich, Patrick Finan, Anna Kratz, and Brendt Parrish, Department of Psychology, Arizona State University; Perry Nicassio and Michael R. Irwin, Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles; Howard Tennen, Department of Community Medicine and Health Care, University of Connecticut Medical Center.

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Correspondence concerning this article should be addressed to Alex J. Zautra, P.O. Box 871104, Arizona State University, Tempe, AZ 85287-1104. E-mail: alex.zautra@asu.edu

(effect size $d = 0.46$) and relatively more modest for pain ($d = -0.22$) and affective disturbance ($d = -0.15$), a pattern that was also evident in a review of behavioral treatments for both RA and osteoarthritis (Dixon et al., 2007). The findings invite speculation about the general efficacy of CBT interventions for RA and the role of individual differences in the response to treatment based on patients' history and clinical needs.

In general, existing interventions for RA pain have not explicitly addressed how depression may increase vulnerability to pain and distress, thereby increasing the adaptation challenges of this autoimmune condition (Brown, 1990; Creed & Ash, 1992; Dickens & Creed, 2001; Katz & Yelin, 1993). Stressors, including pain and other RA symptoms, may be thought of as the provoking agents that challenge adaptation, and recent attention has turned toward an evaluation of depressive disorder as a vulnerability factor for adjustment difficulties and disease progression in RA (Fifield, Tennen, Reisine, & McQuillan, 1998; Parker et al., 1992; Smith, Peck, & Ward, 1990). Perhaps the most troubling aspect of major depressive disorder is its chronicity (Judd et al., 2000; Keller et al., 1995). An individual who has experienced a depressive episode has a 50%–85% chance of having another episode at some time in the future (Angst, 1988; Charney & Weissman, 1988), and up to one third of all those with prior depression continue to experience residual symptoms (Tranter, O'Donovan, Chandarana, & Kennedy, 2002). Depression history may incorporate experiences and processes that adversely affect the coping process in RA, exerting an adverse influence on pain and other symptoms even after the depressive episode has remitted (Fifield et al., 1998).

Two studies our team conducted using data from pretests of participants in the current study contribute additional evidence of the wide-ranging vulnerabilities to pain among RA patients with a history of depression. Conner et al. (2006) found that affective disturbance during pain episodes was intensified for RA patients with a history of major depression, even when controlling for current level of depressive symptoms. This disturbance included both higher negative mood and lower positive mood on days of elevated pain for RA patients with a history of depressive disorder. Zautra et al. (2007) further examined pain reports in this sample and found that recurrent depression, in particular, was associated with greater pain overall and with more stress-reactive pain, along with losses in positive affect and increases in negative affect. Together, these findings demonstrate that past depressive episodes are associated with more disturbance in affect regulation, particularly if there have been multiple episodes (Thase et al., 1995).

Depression may be particularly important in autoimmune conditions like RA. It is associated with complex patterns of changes in immune cell number and functioning, immune activation, and proinflammatory activity (Irwin, 2002). Especially relevant for RA is the cellular production of the proinflammatory cytokine interleukin-6 (IL-6; Choy & Panayi, 2001), a signaling molecule produced primarily by immune cells and associated with radiographic evidence of joint destruction in RA patients (Forsblad d'Elia et al., 2003; van Leeuwen, Limburg, van Riel, & van Rijswijk, 1995). Depression is correlated with increased in vivo and ex vivo secretion of IL-6, a finding supported in our prior studies of RA (Zautra, Hamilton, Potter, & Smith, 1999; Zautra et al., 2004). Moreover, data drawn from pretests of RA patients enrolled in the current study revealed that their chronic stress was correlated with greater ex vivo IL-6 production (Davis et al., in press), providing further evidence of an interaction between negative affective conditions and proinflammatory markers for this sample of RA patients.

In this study we designed an intervention for RA that would target affective disturbances explicitly through attention to the better regulation of negative affective responses to stress and more encouragement of positive affective engagement in daily life. Teasdale and colleagues (Segal, Teasdale, & Williams, 2002; Teasdale et al., 2000, 2002) have reported on mindfulness-based cognitive therapy (MBCT), a treatment for those at risk for recurrent depression that may be relevant to RA patients as well. This treatment enhances emotion regulation through mindfulness meditation training (Kabat-Zinn, 1990) by fostering strategies that promote enhanced awareness of and change in the meaning given to dysfunctional thoughts. It has been effective in preventing relapse among individuals with multiple past episodes of depression (Teasdale et al., 2002), in part because it specifically targets the capacity to relate differently to thoughts and feelings during periods of elevated negative affect (Monroe & Simons, 1991). According to Segal et al. (2002), heightened awareness and acceptance of existing experience act to interrupt the maladaptive automatic responding that commonly occurs during negative emotional states.

The enhancement of positive emotion through mindfulness-based awareness of positive states is not a part of standard CBT treatments for pain. Also missing in CBT for pain (and traditional mindfulness interventions) is the promotion of desirable activities. Encouragement to engage in positive activities may provide essential benefits for RA patients. Indeed, prior research points to a separate positive affective dimension that may be influenced by attention to positive cues (Zautra, 2003). Moreover, CBT and behavioral approaches to the treatment of depression have often aimed to increase positive engagement by including pleasant events scheduling (Lewinsohn, Sullivan, & Grosscup, 1980). For chronic pain patients, access to positive affect facilitates more adaptive responses to current circumstances and reduces helplessness in the management of everyday stress and pain (Zautra, Johnson, & Davis, 2005). An emotion regulation intervention that increases positive affective resources should therefore result in enhanced well-being in RA.

In the current investigation, we examined the value of two distinct approaches to the treatment of RA, one based on established cognitive behavioral methods emphasizing pain management (P) and the other based on mindfulness meditation and positive social engagement to target emotion regulation (M). We compared both active treatments with an established arthritis education curriculum (E) to determine whether P and M produced greater benefits than E. Three primary hypotheses guided this research. First, we expected that P would increase efficacy in coping with pain, including greater overall benefits in self-reports of coping efficacy and pain levels, and that P would result in lower in vitro stimulated IL-6 production in comparison to the E intervention. Second, we expected that M would be particularly useful in promoting well-being due to its emphasis on emotion regulation through awareness and acceptance of current experiences, including pain and stress, and positive emotion engagement. Thus, we expected to see larger increases in positive affect, lower negative

affect, and greater decreases in the in vitro production of IL-6 for M in comparison with both the P and E groups. Third, we probed the role of history of depressive disorder as a moderator of P and M effects for RA patients. We anticipated that those RA participants with recurrent depression would benefit in terms of lower pain, better affective health, and diminished IL-6 production from M compared with P and E programs. RA participants without recurrent depression were expected to show more improvement in these outcomes following P relative to M and E.

Method

Overview of Study Plan

The flow of the participants through the study is shown in Figure 1. Participation began with a clinical evaluation of participants' history of major depression. Participants completed 30 days of daily diary assessments of joint pain, negative and positive affect, and depressive symptoms. This was followed by a first laboratory pain assessment with blood draw for a randomly selected half of the participants. These field and laboratory data constituted the preintervention (Pre) assessment portfolio. For each of eight intervention waves, 20–28 participants provided their schedules of available days and were then assigned to one of three possible group meeting days. The project manager, under the supervision of the study's principal investigator (Alex J. Zautra), randomly assigned these clusters to one of three treatment conditions using a random numbers table. A postintervention (Post) diary assessment and a second lab followed for all participants. Data collection began January 2003 and ended June 2005, once a sufficient sample size was obtained to allow for a .8 or greater probability of rejection of the null hypothesis regarding Pre–Post differences between treatment groups for small to medium effect sizes (Cohen, 1988).

Participants

A total of 144 patients (68.1% women, 31.9% men) were screened into the study and agreed to participate in the intervention trials. Participants were recruited from the Phoenix, AZ region via solicitations at health fairs, to Arthritis Foundation members, and at local physicians' offices as well as from rheumatologist referrals at the Carl T. Hayden Veterans Affairs (VA) Medical Center in Phoenix. Accepted into the study were participants who were not taking any cyclical estrogen replacement therapies, did not have Lupus, and described themselves as having RA at screening and could obtain a written confirmation of RA from their rheumatologist.

Intervention Plan

This research compared a mindfulness-based emotion regulation therapeutic program (M) with CBT for pain (P) for RA patients who varied in depression history. Both interventions were contrasted with an education control group (E) in which information about RA and other health-related topics was provided. Participants in the E group were recruited to join an 8-week group that provided information on ways to manage their arthritis, but they were not given descriptions of treatment alternatives. Thus, they were blind to alternative treatment conditions and hypotheses. The E condition controlled for nonspecific treatment elements such as attention, expectation for improvement, and group support that pose rival explanations for the effectiveness of the two treatment conditions. Participants in the E condition did not receive training regarding handling either emotional difficulties or pain.

The treatments followed a parallel format. Each treatment included eight modules dealing with specific themes that defined the content areas of the intervention. The initial session for all treatments presented a rationale for and overview of the specific intervention. Sessions within each module addressed specific objectives that reflected the skills participants were helped to achieve for the two active treatment conditions. Within each session, therapists introduced didactic information, implemented skill-related exercises, reviewed with individual participants their understanding and learning of the specific skills, and assigned weekly homework related to session activities. Therapists reviewed homework at the beginning of each treatment session to reinforce adherence and to problem solve application difficulties.[1]

CBT for pain (P). The following modules focused on increasing pain management skills, following a standard cognitive behavioral format: (a) introduction and review of pain concepts; (b) relaxation training; (c) autogenic training and other methods of relaxation; (d) activity pacing and managing daily activities; (e) cognitive coping; (f) alternative pain management approaches; memory and concentration; (g) managing intense pain episodes; problem-solving; and (h) relapse prevention, generalization, and maintenance.

Mindfulness meditation and emotion regulation therapy (M). The M intervention was developed on the basis of our work examining emotion regulation and adaptation in chronic pain (e.g., Davis, Zautra, & Smith, 2004; Zautra et al., 2005; Zautra, Smith, Affleck, & Tennen, 2001). It was designed to develop two distinct sets of skills, one to reduce the negative impact of stressful life events and illness burdens and the other to enhance the ability to sustain positive social engagements despite pain and stress. The treatment modules included (a) mindfulness and the bidimensional model of emotion; (b) mindfulness and awareness; (c) emotional clarity and well-being; (d) acceptance, negative thoughts, and reframing; (e) positive emotions and pleasant event scheduling; (f) enhancing social relations; (g) intimacy, stress, and mindfulness; and (h) maintenance and generalization. The modules were organized so that early sessions introduced the concept of two distinct dimensions of emotional health, positive and negative, and the role of mindfulness meditation practice in promoting awareness and acceptance of the full range of emotional experiences. Subsequent sessions included didactic activities and experiential exercises to more fully develop understanding of emotional awareness and acceptance and to foster the development of positive emotional and social resources.

The intervention drew on mindfulness meditation aspects of the mindfulness-based stress reduction (MBSR) approach developed by Kabat-Zinn (1990) and on MBCT (Segal et al., 2002). In particular, we included a 10-min sitting meditation component both in sessions and as a home practice, which is considerably shorter than the meditation components for MBSR and MBCT. We

[1] Treatment manuals describing session content, exercises, and objectives are available at www. public.asu.edu/~atajz/

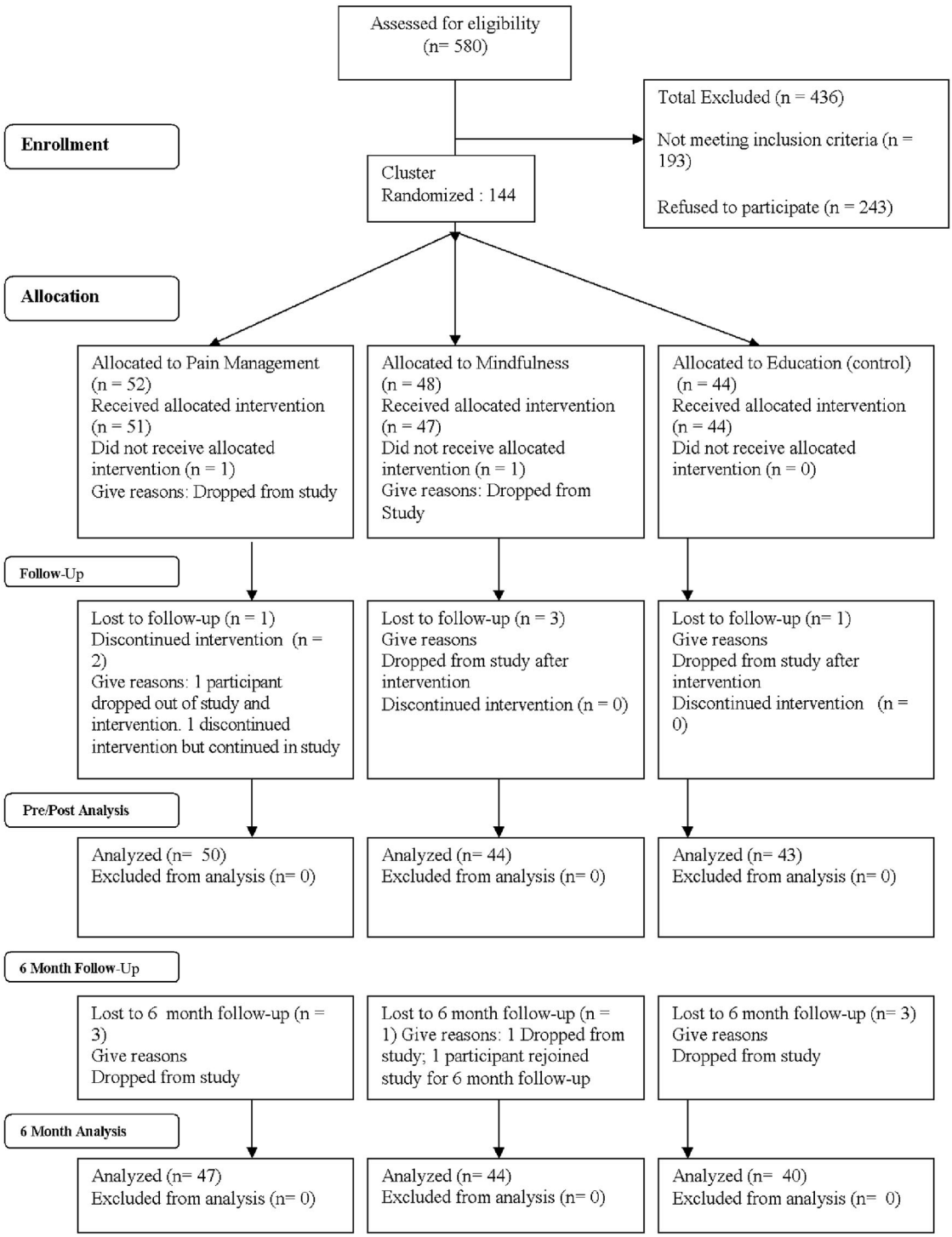

Figure 1. CONSORT flowchart.

did not conduct a day-long workshop, nor did we include yoga as part of the treatment, to assure that the time and physical demands of the M intervention were comparable to those of the P and E interventions. It is important that the current intervention also included a heavy emphasis on building the skills necessary to cultivate and sustain positive emotional experiences, particularly within social relationships (three of eight sessions). Our own and others' work points to positive interpersonal events as central to the emotional well-being of pain patients. Distinct from the P intervention, in the M intervention stress and pain management

were discussed only within the context of understanding how to preserve emotional well-being in difficult times.

Education-only group (E). This condition provided a control for nonspecific therapeutic elements that pose rival explanations for treatment effectiveness in the M and P groups. The education control condition intentionally omitted information on coping practices from its protocol and was organized around a series of didactic presentations in which general information about RA and related themes in health and medicine were presented. E modules included the following: (a) introduction to rheumatoid arthritis: definitions, pathophysiology, and epidemiology; (b) prognosis and treatment, diagnostic tests, and medical specialists; (c) RA medications and medication use; (d) neurophysiology of pain: surgical intervention; (e) natural remedies: nutrition and diet; (f) exercise and sleep; (g) communicating with your doctor and traveling with RA; and (h) review and group closure.

A doctoral-level psychologist and an advanced doctoral student in clinical psychology who received prior training in CBT methods and behavioral medicine cofacilitated treatment sessions for all three conditions at each wave, with two doctoral-level psychologists and three predoctoral students serving as clinicians over the full study. Interventions were administered in groups of 5 to 8 participants (average group size = 6) over an 8-week treatment period in weekly 2-hr sessions. To ensure treatment fidelity and adherence to intervention protocols, clinicians audiotaped the sessions and they were reviewed by an experienced treatment supervisor (Perry Nicassio). In addition, the treatment supervisor conducted weekly review sessions to discuss participant problems, establish logistics for implementation of the protocols, and foster adherence. An examination of attrition, shown in the CONSORT diagram in Figure 1, revealed no differences between groups. Attendance records were available for five of the eight waves of data collection, due to inadequate record keeping by the lead therapist for the first three waves. On average, participants attended 5.98 sessions in the P group, 5.94 in the M group, and 6.59 in the E group, showing no significant difference between intervention groups that would suggest a preference for one of the three treatments. Research assistants, blind to treatment condition, were responsible for data collection.

Assessment of Depression History

History of major depression was measured by the mood disorders modules of the Structured Clinical Interview for *DSM–IV* (SCID-I; First, Spitzer, Gibbon, & Williams, 2002). Telephone interviews were conducted by advanced clinical psychology graduate or postdoctoral students who received extensive training in the administration and coding of the SCID-I; they were closely supervised by a clinical psychologist who is an established depression researcher and coauthor of this article (Howard Tennen). Interviews were conducted over the phone and audiotaped, with participants' knowledge and consent (see Zautra et al., 2007, and Conner et al., 2006, for a more detailed description of depression assessment procedures). Telephone interviews have been shown to be equivalent to face-to-face interviews for the measurement of Axis I depressive disorders (Rohde, Lewinsohn, & Seeley, 1997; Simon, Revicki, & VonKorff, 1993). A major depressive episode could not be due to normal bereavement, injury, illness, alcohol/drugs, or medication. In necessary cases, SCID-I evaluators sought consultation from an advising consulting liaison psychiatrist, who assisted in determining whether prior depressive symptoms could have been due to medication and/or drug use.

Because we had found evidence that the RA participants in the current study with two or more episodes of major depression were more vulnerable to pain and stress than those without a history of recurrent depression (Zautra et al., 2007), we examined differences in treatment effects between those RA participants as a function of depression history. The hypotheses regarding recurrent depression were not truly a priori because the Pre data informed these predictions. In these analyses, we treated the number of depression episodes as a continuous variable in initial analyses, with scores that ranged from 0 (*no history*) to 5 (*five or more past episodes*). We then probed significant interactions between depression history and intervention group type by dichotomizing depression history to contrast those participants with two or more episodes of depression with those who had either no history or a single episode.

Outcome Variables: Diary Measures

After completing the SCID-I assessment, participants were sent a packet of 30 paper diary questionnaires and 30 postage-paid envelopes and contacted by a research staff member who provided instructions. Participants were asked to fill out the diaries half an hour before bedtime each day. To ensure compliance in completing the diaries on a daily basis, we instructed participants to place the previous night's completed diary in the prepaid envelope in the mail each morning. Postmark verification was monitored to substantiate compliance with instructions. After satisfactory completion of the diary portion of the study, participants were compensated up to $90 for their time: $2 for each diary completed, with a bonus of $1 per diary if they completed more than 25 diaries. Overall, the rate of completion was 94%. Among other questions, the daily diary contained measures of the following primary outcome variables: daily pain, positive and negative affect, depressive symptoms, coping efficacy, catastrophizing, and pain control. For each outcome variable, the daily reports were averaged across the 30 days prior to the intervention and following the intervention. No diary data were collected during the intervention.

Pain. Daily pain was measured in each diary with the standard instruction for a numerical rating scale (Jensen, Karoly, & Braver, 1986; Zautra et al., 2001): "Please choose a number between 0 and 100 that best describes the average level of pain you have experienced today due to your RA. A zero (0) would mean 'no pain' and a one hundred (100) would mean 'pain as bad as it can be.'" Test–retest reliabilities were computed across days to yield an average day-to-day correlation of .75.

Positive and negative affect. We measured positive and negative affect in the daily diary using the Positive and Negative Affect Schedule (Watson, Clark, & Tellegen, 1988). Participants rated 10 standard mood adjectives each for positive and negative affect using a 5-point scale from 1 (*very slightly or not at all*) to 5 (*extremely*). Cronbach's alphas were .96 for positive affect (both Pre and Post) and .93 for negative affect (Pre and Post), calculated from items aggregated across 30 days.

Depressive symptoms. We assessed depressive symptoms by averaging scores for six items: lack of interest in the day's activities, increase or decrease in appetite, feeling "restless" or "slowed

down," fatigue or loss of energy, feeling down on oneself, and difficulty concentrating or making decisions (Conner et al., 2006). Participants responded with an answer of "yes" or "no" to each item. Cronbach's alphas were .80 (Pre) and .81 (Post).

Coping efficacy for pain. Coping efficacy was assessed with two items. The first asked participants to rate how satisfied they were with how they coped with their pain at its worst that day on a scale of 1 (*very dissatisfied*) to 5 (*very satisfied*). The second item asked for their rating of their degree of certainty that they could "adjust well" to the same level of pain again in the future on a scale of 1 (*very uncertain*) to 5 (*very certain*). Both items were used with well-established validity in prior studies (Reich & Zautra, 1991; Zautra & Wrabetz, 1991). Cronbach's alphas for pain coping efficacy scores averaged across days were .91 (Pre) and .92 (Post).

Pain catastrophizing. Participants were asked to rate their level of agreement with the following two statements: "I worried about whether my pain would ever end" and "I felt my pain was so bad I couldn't stand it any more," taken from the Coping Strategies Questionnaire (Rosentiel & Keefe, 1983). Ratings were made on a scale of 1 (*strongly disagree*) to 5 (*strongly agree*). Daily catastrophizing scores were computed by averaging the scores for the two items. Cronbach's alphas were .90 (Pre) and .94 (Post) for these aggregate scores.

Pain control. Participants rated the degree of their perceived control over pain each day on a scale of 1 (*no control at all*) to 10 (*complete control*; Tennen, Affleck, & Zautra, 2006).

Outcome Variables: Laboratory Assessment

Prior to the intervention, half of the participants ($n = 74$) in each treatment condition were randomly assigned to attend a laboratory session at the cooperating VA hospital. All participants were administered the Post laboratory assessment. The laboratory protocol was conducted in the afternoon for all participants to control for time-of-day effects on physiological variables. Each session lasted approximately 2 hr. This design created a Solomon six-group design, which allowed us to evaluate possible effects of testing on subsequent performance in the laboratory stress-induction procedures. (No testing effects were found for the outcome variables reported in this article.) The examination of treatment differences in stress reactivity was beyond the scope of this study. Therefore, only Pre and Post scores taken at baseline, prior to stress induction, were used for the analysis of treatment effects.

Physicians' assessment. Upon arrival at the testing site, participants received detailed instructions regarding the laboratory procedures, submitted a second informed consent, and underwent a joint examination conducted by one of three VA rheumatologists. The rheumatologist palpated 28 joints taken from the Disease Activity Score-28 (DAS28) arthritis measure (Prevoo et al., 1995) to evaluate both joint swelling and tenderness. For each of 28 joints, the examining rheumatologist rated the degree of swelling on a 3-point scale from 0 (*no swelling*) to 3 (*significant joint swelling*). To rate tenderness, they asked participants to rate their pain on a 0 (*no pain*) to 3 (*severe pain*) scale for each joint when palpated. Sum scores were computed and yielded Cronbach's alphas of .95 (Pre) and .93 (Post). Physicians' ratings were available for 82% of participants with Pre lab data and for 98% of those with Post lab data.

Stimulated IL-6 production assays. To examine the production of IL-6, we collected 10 ml of blood into a heparinized syringe (1 ml), maintained it at room temperature, and processed it within 3 hr of collection. Peripheral blood mononuclear cells (PBMCs) were sedimented on Ficoll-Hypaque (Pharmacia, Piscataway, NJ), washed 3 times with phosphate-buffered saline (Gibco Life Technologies, Grand Island, NY), and resuspended in a 1:1 mixture of RPMI 1640 medium supplemented with 10% fetal calf serum (Hyclone, Logan, UT; inactivated 1 hr in 56° C water bath), 4 millimolars (mM) glutamine, 20 mM HEPES buffer solution (Sigma, St. Louis, MO), 50 mg/ml penicillin, and 50 mg/ml streptomycin. Isolated PBMCs (1×10^6 cells/ml) were incubated for 24 hr at 37° C with lipopolysaccharide (LPS; 100 pg/ml; Sigma) along with three concentrations of hydrocortisone (i.e., 10^{-6}, 10^{-7}, and 10^{-8} M). Immediately following culture, supernatants were aspirated and stored at −80° C and subsequently assayed in batches. We measured concentrations of IL-6 from the stimulated cell cultures using commercially available enzyme-linked immunosorbent assay kits (ELISAs; R&D Systems, Minneapolis, MN), which have an intra-assay coefficient of variation (CV) of 3.1%, an inter-assay CV of 2.5%, and sensitivity of < 0.7 pg/ml. These procedures thus produced 4 values of IL-6 for each participant from the baseline blood draw, reflecting LPS-stimulated monocyte IL-6 production alone and its inhibition by exposure to three concentrations of glucocorticoids. IL-6 values were expressed as nanograms per milliliter and log transformed prior to analysis.

Analytic Strategy

The study used a three-factor mixed design: treatment group, with three levels (P, M, and E); a continuous variable (number of depressive episodes) that after reanalysis became a two-level variable for recurrent depression (RD+, RD−); and a within-subjects factor reflecting Pre versus Post assessments for diary, questionnaire, and laboratory outcomes. All participants were included in the analysis of treatment effects, following intent-to-treat guidelines (Altman et al., 2001).

Multilevel modeling was used as the primary data analytic tool. This method is particularly useful for the linear analysis of data that have a nested hierarchical structure with both between- and within-subjects predictors, some of which are continuous variables, are missing data due to data collection errors, and/or have planned missing observations (i.e., for the Pre laboratory testing). All multilevel analyses were conducted using SAS PROC MIXED (Littell, Milliken, Stroup, & Wolfinger, 1996). To illustrate, the basic equation that was initially specified was as follows for joint tenderness assessed during the lab:

$$\begin{aligned}\text{Joint tenderness} &= \beta_0 + \beta_1(\text{Group}) \\ &+ \beta_2(\text{Recurrent Depression History; RD}) \\ &+ \beta_3(\text{Lab; Pre vs. Post}) + \beta_4(\text{Lab} \times \text{RD}) \\ &+ \beta_5(\text{Lab} \times \text{Group}) + \beta_6(\text{Lab} \times \text{Group} \times \text{RD}) + r.\end{aligned}$$

β_0 yields an estimate of the intercept for joint tenderness, and $\beta_1 - \beta_6$ provide slope estimates of the effects of predictor variables. The model specifications followed Singer's (1998) recommendations to identify the best fitting model of the variances and covariances of the variables under study. The dependent variables

Table 1
Demographic Characteristics of the Study Participants

Characteristic	History of recurrent depression (RD+)			No history of recurrent depression (RD−)		
	M (N = 6)	P (N = 17)	E (N = 14)	M (N = 41)	P (N = 35)	E (N = 30)
Gender, *n*						
Male	1	2	3	19	14	7
Female	5	15	11	22	21	23
Ethnicity, *n*						
White	5	15	12	37	31	25
Other	0	2	1	4	4	4
Age in years, *M* (*SD*)	46.17 (12.70)	51.00 (10.74)	51.43 (13.89)	57.29 (15.29)	56.11 (13.49)	52.43 (12.96)
Years with RA diagnosis, *M SD*)	15.83 (19.17)	17.00 (14.41)	12.07 (17.17)	10.13 (8.20)	14.06 (13.46)	11.69 (12.11)
Median family income	$55,000	$27,500	$27,500	$35,000	$35,000	$45,000

Note. There were no significant treatment group differences or Treatment Group × RD differences for any demographic variable. The RD+ group was younger and comprised of more females than the RD− group. M = mindfulness meditation and emotion regulation; P = cognitive behavioral therapy for pain; E = education control; RA = rheumatoid arthritis.

were modeled as random variables, and a first-order autoregressive parameter was introduced to model the within-subjects variance shared among scores collected close in time to one another.

Results

Overview

Table 1 displays the demographic profiles of the study sample across the six study conditions. The average duration of the participants' RA was 11.59 years for women and 15.43 years for men. The mean age was 50.62 years for women and 62.11 years for men. For race/ethnicity, 86% of the women and 80% of the men were Caucasian. The men had an average yearly family income between $21,000 and $24,000, and the women, $30,000 and $39,000, an income level somewhat lower than the median household income of $42,000 for Arizona residents (DeNavas-Walt, Proctor, & Lee, 2005). Participants with a history of recurrent depression tended to be female, $F(1, 137) = 4.42$, $p < .05$, and younger, $F(1, 137) = 4.16$, $p < .05$. There were no demographic differences between intervention groups, and there were no demographic differences when comparing means of the six subgroups.[2] Our reanalysis of the data, treating gender and age as covariates, had no influence on the significance tests or effect sizes for any of the outcomes in this study. The influence of clustering was examined first through a series of one-way analyses of variance on Pre and Post scores for the outcome variables and then through the calculation of the average intraclass correlations from the results of those analyses. These intraclass correlation coefficients averaged .018 for diary and lab variables. No significant differences on the Pre scores of the outcome measures due to cluster were observed (all ps > .15). Cluster was introduced as a covariate in the evaluation of Post scores and had no discernable effect on the findings.

The outcome analyses are presented in two segments with accompanying tables of means and standard errors: first, the Pre–Post 30-day diary data, and second, the lab Pre–Post data on physicians' ratings and IL-6. To provide an orderly presentation, we report the results beginning with the main effects of time (Pre, Post), followed by the Time × Group and Time × Group × Recurrent Depression (RD) interactions. Inferences regarding treatment effects depend on the significance tests for the three-way and two-way interactions that involve group and time. Findings for RD × Time interactions do not provide tests of differential treatment effects;[3] more data are available from Alex J. Zautra upon request. In the examination of potential moderating effects of depression history, we first evaluated the effects of using depression history as a continuous variable, followed by tests of differences between those with recurrent depression and those without. The multilevel analysis of recurrent depression history as a dichotomous variable was pursued only after significant moderating effects were found for depression history as a continuous variable. The F values provided in the text are for tests of recurrent depression when treated as a dichotomous variable to be consistent with the means in the tables and figures. Differences in significance

[2] Pretreatment differences across groups on outcome measures were examined. One preexisting difference was found as a function of group: Coping efficacy was significantly higher at Pre for M than for P or E. Participants with a history of current depression differed from those participants without recurrent depression on several pretest measures, including diary measures of depressive symptoms, pain, and negative affect, and physicians' assessment of tenderness. These differences were not unexpected and were not sources of invalidity, in themselves, of observed Pre–Post differences due to the intervention. We also inspected Pre differences in recurrent depression within and between intervention group assignment because such differences in depression for the M and/or P conditions could be a source of bias, introducing regression to the mean effects as alternative explanations of the findings. We found no differences in Pre scores as a function of depression by intervention group assignment that could account for the findings obtained.

[3] The following is a summary of the RD × Time interactions. Analyses of diary data revealed that daily pain ratings decreased from Pre to Post more for RD− participants than RD+ participants, $F(1, 126) = 8.42$, $p < .01$. Similarly, RD− participants reported greater increases in pain control from Pre to Post than did RD+ participants, $F(1, 126) = 13.08$, $p < .001$. Coping efficacy for pain, however, increased for RD+ individuals compared to RD− individuals, $F(1, 122) = 3.12$, $p < .05$. No other diary outcomes yielded significant Time × RD interactions. We found a significant RD × Time interaction for IL-6 production, $F(1, 370) = 8.72$, $p < .01$, indicating that IL-6 production changed differentially from Pre to Post in the two RD groups. RD− individuals showed a significant decrease, $F(1, 293) = 5.70$, $p < .02$, but RD+ individuals showed a significant increase, $F(1, 103) = 6.99$, $p < .01$. Physicians' tenderness ratings decreased to a significantly greater extent from Pre to Post for RD+ individuals compared with RD− individuals, $F(1, 605) = 29.70$, $p < .001$.

emerging from dichotomizing depression history are noted when they occur. Cohen's *d* (Cohen, 1988) was used to provide an estimate of effect size, calculated on key mean differences reported in the tables between the two active treatment groups when those differences were statistically significant. These values are found in Tables 2 and 3.

Diary Analyses

Across groups, daily pain scores significantly diminished from Pre ($M = 33.50$, $SE = 1.53$) to Post ($M = 28.63$, $SE = 1.54$), $F(1, 133) = 73.89$, $p < .001$. There was no Time × Group interaction, $F(2, 131) = 1.13$, $p = ns$, or Time × Group × RD interaction, $F(2, 122) = 0.64$, $p = ns$.

Positive affect increased across all participants as a function of time, $F(1, 132) = 46.57$, $p < .001$. A Time × Group interaction, $F(2, 130) = 6.74$, $p < .001$, indicated that the M (Pre: $M = 2.83$, $SE = 0.10$; Post: $M = 3.02$, $SE = 0.10$) and P (Pre: $M = 2.54$, $SE = 0.10$; Post: $M = 2.70$, $SE = 0.10$) conditions both produced significant increases in positive affect compared to the E condition (Pre: $M = 2.85$, $SE = 0.10$; Post: $M = 2.88$, $SE = 0.10$). A triple interaction was also observed for positive affect ($p < .001$ for RD as a continuous variable), with RD+ participants in the M condition showing a greater increase in positive affect from Pre to Post, $F(2, 121) = 8.63$, $p < .001$, than participants in other groups (see Table 2).

Negative affect did not change either as a function of time alone, $F(1, 132) = 0.39$, $p = ns$, or as a function of Time × Group, $F(1, 130) = 2.33$, $p = ns$ (but $p < .001$ for Time × Group with RD as a continuous variable). A significant triple interaction emerged for negative affect, $F(2, 121) = 6.51$, $p < .01$ ($p < .025$ for RD as a continuous variable), such that RD+ people in the M condition reported greater decreases in negative affect from Pre to Post compared with participants in other treatment groups (see Figure 2). Daily depression symptoms decreased as a function of time from Pre ($M = 1.22$, $SE = 0.08$) to Post ($M = 1.08$, $SE = 0.08$), $F(1, 130) = 6.11$, $p < .02$, but no group differences or Time × Group × RD interactions emerged.

Coping efficacy for pain increased across participants from Pre ($M = 3.91$, $SE = 0.06$) to Post ($M = 4.04$, $SE = 0.06$), $F(1, 122) = 35.71$, $p < .001$. A significant double interaction emerged, $F(2, 122) = 8.33$, $p < .01$, such that participants in both the M and P conditions experienced greater increases in pain coping efficacy from Pre to Post than did those in the E condition. RD moderated this effect, $F(2, 122) = 3.12$, $p < .05$ ($p < .001$ for RD as a continuous variable), yielding a triple interaction indicating that RD+ individuals in the M condition experienced greater improvements in their pain coping efficacy than did participants in other groups (see Figure 3). For catastrophizing, there were significant Time × Group, $F(2, 122) = 17.76$, $p < .001$, and Time × Group × RD interactions, $F(2, 122) = 15.20$, $p < .001$ ($p < .001$

Table 2
Means (Standard Errors) of Diary Outcome Measures Across Groups

Outcome measure	History of recurrent depression (RD+)			No history of recurrent depression (RD−)			Pre–Post differences
	M	P	E	M	P	E	
Pain							Post < Pre***
Pre	43.19 (7.38)	39.56 (4.52)	35.59 (4.83)	25.99 (3.06)	35.29 (3.10)	33.71 (3.30)	*d*=0.27
Post	40.38 (7.39)	37.08 (4.52)	33.28 (4.84)	21.72 (3.08)	28.68 (3.11)	25.88 (3.32)	
Positive affect							M/RD+ > P, E***
Pre	2.48 (0.28)	2.35 (0.17)	2.64 (0.18)	2.95 (0.11)	2.63 (0.12)	2.95 (0.12)	*d* = 0.78
Post	2.91 (0.28)	2.40 (0.17)	2.77 (0.18)	3.14 (0.11)	2.86 (0.12)	2.93 (0.12)	
Negative affect							M/RD+ < P, E**
Pre	1.34 (0.11)	1.45 (0.06)	1.39 (0.07)	1.22 (0.04)	1.26 (0.04)	1.21 (0.05)	*d* = −0.89
Post	1.22 (0.11)	1.48 (0.06)	1.43 (0.07)	1.26 (0.04)	1.21 (0.04)	1.21 (0.05)	
Depressive symptoms							Post < Pre***
Pre	1.46 (0.35)	1.95 (0.21)	1.64 (0.23)	0.98 (0.14)	1.08 (0.15)	1.04 (0.16)	*d* = 0.16
Post	1.05 (0.35)	1.81 (0.21)	1.66 (0.23)	0.90 (0.15)	0.85 (0.15)	0.95 (0.16)	
Coping efficacy							M/RD+ > P, E*
Pre	3.90 (0.22)	3.77 (0.14)	3.79 (0.15)	4.26 (0.09)	3.91 (0.09)	3.85 (0.10)	*d* = 0.65
Post	4.25 (0.23)	3.90 (0.14)	3.80 (0.15)	4.36 (0.09)	4.04 (0.09)	3.86 (0.10)	
Catastrophizing							M/RD+ < P, E***
Pre	2.49 (0.28)	2.12 (0.17)	2.07 (0.18)	1.96 (0.12)	2.03 (0.12)	2.03 (0.13)	*d* = −0.18
Post	1.94 (0.28)	2.06 (0.17)	2.25 (0.18)	1.97 (0.12)	1.92 (0.12)	2.07 (0.13)	
Pain control							P, E > M*
Pre	6.89 (0.87)	5.59 (0.53)	6.15 (0.57)	7.31 (0.36)	6.08 (0.37)	5.91 (0.39)	*d* = −0.44
Post	6.62 (0.87)	5.39 (0.53)	6.03 (0.57)	7.38 (0.36)	6.46 (0.37)	6.36 (0.39)	

Note. Means (and standard errors) provided for all diary outcomes were obtained from the LSMEANS procedure in SAS. Standard errors were adjusted for the covariance parameters in the model (Littell, Milliken, Stroup, & Wolfinger, 1996). Highest order significant effects are described as a function of time in the far right column. For effects described in the far right column, Cohen's *d* effect sizes are provided between key contrasting groups. M = mindfulness meditation and emotion regulation; P = cognitive behavioral therapy for pain; E = education control; Pre = preintervention; Post = postintervention.

* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 3
Means (Standard Errors) of Lab Outcome Measures Across Groups

Outcome measure	History of recurrent depression (RD+)			No history of recurrent depression (RD−)			Pre–Post differences
	M	P	E	M	P	E	
Swelling							M/RD+ < P, E***
Pre	14.78 (3.42)	7.88 (2.10)	7.01 (2.19)	9.41 (1.38)	11.59 (1.44)	12.92 (1.53)	$d = -0.62$
Post	6.33 (3.27)	11.13 (2.00)	8.29 (2.14)	10.46 (1.36)	10.60 (1.40)	8.57 (1.49)	
Tenderness							M/RD+ < P, E***
Pre	59.29 (9.40)	42.35 (5.78)	38.04 (6.02)	18.50 (3.80)	22.96 (3.96)	25.95 (4.22)	$d = -0.83$
Post	25.67 (8.99)	43.25 (5.51)	32.29 (5.89)	20.50 (3.74)	16.26 (3.84)	18.84 (4.10)	
IL-6							P < M, E**
Pre	8.68 (0.51)	7.99 (0.41)	8.46 (0.34)	8.38 (0.19)	9.29 (0.23)	8.99 (0.25)	$d = 0.21$
Post	8.69 (0.41)	8.94 (0.30)	8.83 (0.32)	8.58 (0.18)	8.04 (0.20)	9.10 (0.22)	

Note. Means (and standard errors) provided for all diary outcomes were obtained from the LSMEANS procedure in SAS. Standard errors were adjusted for the covariance parameters in the model (Littell, Milliken, Stroup, & Wolfinger, 1996). Highest order significant effects are described as a function of time in the far right column. For effects described in the far right column, Cohen's *d* effect sizes are provided for key contrasting groups. M = mindfulness meditation and emotion regulation; P = cognitive behavioral therapy for pain; E = education control; IL-6 = interleukin-6; Pre = preintervention; Post = postintervention.
** $p < .01$. *** $p < .001$.

for RD as a continuous variable), showing a greater benefit of the M treatment for RD+ individuals in a manner similar to that found for coping efficacy.

Pain control showed a significant time effect, $F(1, 133) = 8.37$, $p < .01$, such that participants reported increased pain control from Pre to Post. Unlike other variables analyzed thus far, the Time × Group interaction, $F(2, 131) = 3.91$, $p < .05$, did not favor the M group. Participants in both the P condition (Pre: $M = 5.83$, $SE = 0.30$; Post: $M = 6.13$, $SE = 0.30$) and the E condition (Pre: $M = 5.98$, $SE = 0.32$; Post: $M = 6.24$, $SE = 0.33$) reported greater pain control from Pre to Post than did people in the M condition (Pre: $M = 7.11$, $SE = 0.03$; Post: $M = 7.04$, $SE = 0.32$). RD did not moderate this effect, $F(2, 122) = 0.25$, $p = ns$ ($p = ns$ for RD as a continuous variable).

Laboratory Analyses

An analysis of physicians' ratings of tenderness revealed a time effect, $F(1, 605) = 26.72$, $p < .001$, with lower tenderness ratings from Pre to Post across the board, and significant Group × Time, $F(2, 605) = 16.93$, $p < .05$, and Group × Time × RD effects, $F(2, 605) = 53.48$, $p < .001$ ($p < .001$ for RD as a continuous variable). As shown in Table 3 and displayed in Figure 4, the M treatment for RD+ led to a greater reduction in tenderness from

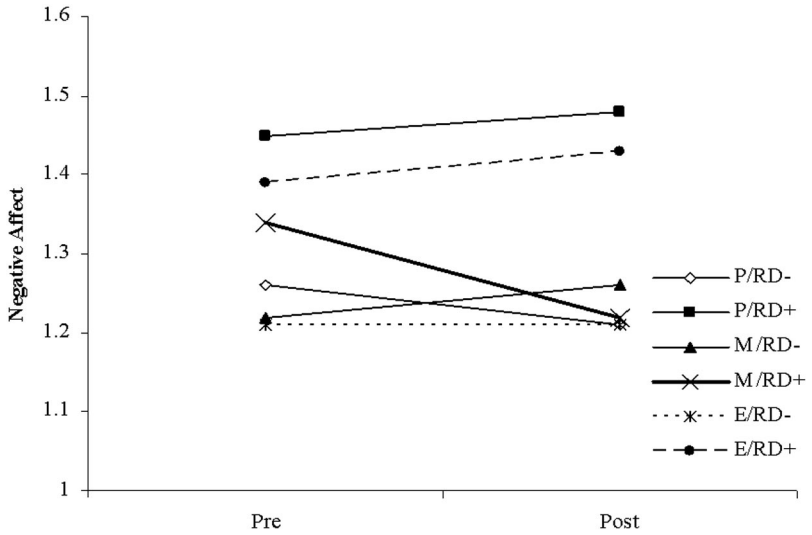

Figure 2. Self-reported scores on negative affect (i.e., recurrent depression) aggregated across diary days by group at pre- and posttreatment. P/ RD− = cognitive behavioral therapy for pain without recurrent depression history; P/RD+ = cognitive behavioral therapy for pain with recurrent depression history; M/RD− = mindfulness meditation and emotion regulation without recurrent depression history; M/RD+ = mindfulness meditation and emotion regulation with recurrent depression history; E/RD− = education control without recurrent depression history; E/RD+ = education control with recurrent depression history.

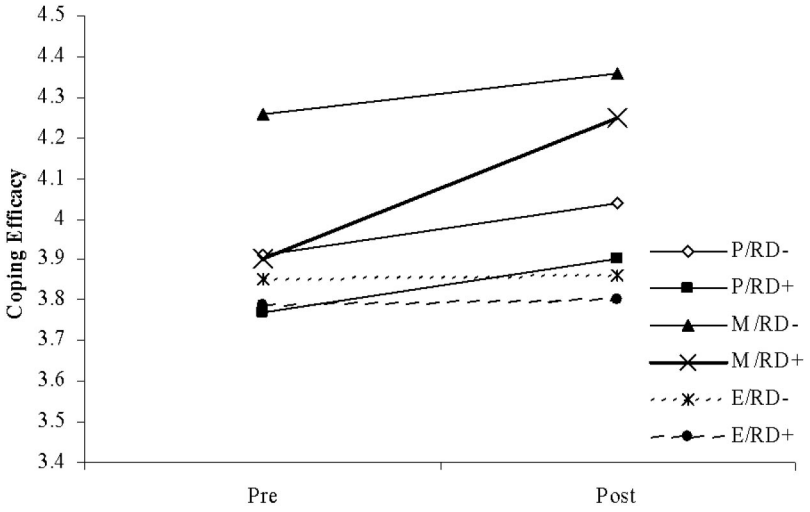

Figure 3. Self-reported scores on coping efficacy for pain aggregated across diary days at pre- and posttreatment. P/RD− = cognitive behavioral therapy for pain without recurrent depression history; P/RD+ = cognitive behavioral therapy for pain with recurrent depression history; M/RD− = mindfulness meditation and emotion regulation without recurrent depression history; M/RD+ = mindfulness meditation and emotion regulation with recurrent depression history; E/RD− = education control without recurrent depression history; E/RD+ = education control with recurrent depression history.

Pre to Post than it did in other groups. Similar findings were found in the analysis of joint swelling made by physicians. A Group × Time × RD effect was found, $F(2, 605) = 51.46$, $p < .001$ ($p < .001$ for RD as a continuous variable), favoring the M treatment for RD+.

Data for the production of IL-6 by LPS-stimulated immune cells were available for 68% of participants with Pre lab data ($n = 54$) and for 68% of those with Post lab data ($n = 84$). IL-6 levels were at four levels of LPS-stimulation/hydrocortisone inhibition on blood drawn at baseline prior to the laboratory session. The findings indicated that IL-6 production decreased from Pre ($M = 8.94$, $SE = 0.23$) to Post ($M = 8.51$, $SE = 0.18$) only for the P group: Group × Time interaction, $F(2, 420) = 4.27$, $p < .02$. There were only 2 participants with IL-6 data at pretest who were in the M condition and who had a history of recurrent depression, precluding a reliable test of the three-way interaction to consider the

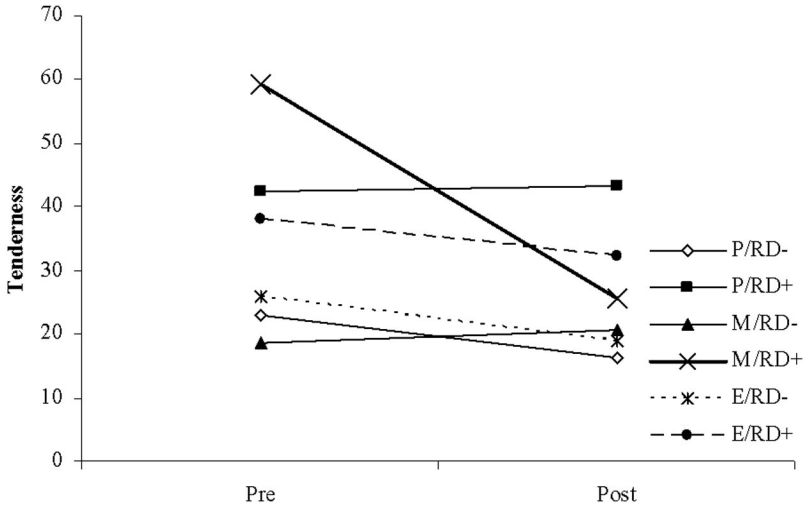

Figure 4. Physician-rated scores on tenderness obtained once at both pre- and posttreatment. P/RD− = cognitive behavioral therapy for pain without recurrent depression history; P/RD+ = cognitive behavioral therapy for pain with recurrent depression history; M/RD− = mindfulness meditation and emotion regulation without recurrent depression history; M/RD+ = mindfulness meditation and emotion regulation with recurrent depression history; E/RD− = education control without recurrent depression history; E/RD+ = education control with recurrent depression history.

effects of multiple episodes of depression on IL-6 values Pre to Post. An analysis of the moderating effects of at least one episode of clinical depression yielded a main effect for depression on IL-6 scores, $F(1, 339) = 11.37$, $p < .001$, and a Depression × Time interaction, $F(1, 338) = 15.58$, $p < .001$, indicating higher scores for depressed participants that were sustained Pre to Post but no moderating influence on intervention effects.

Discussion

In this study, we asked whether interventions that provided cognitive behavioral methods of coping with pain or that alternatively focused on improving emotion regulation and promoting positive affect would strengthen adaptation to the chronic burdens of RA. In doing so, we targeted cognitive–affective and behavioral processes that we suspected would underlie individual differences in disease course and adjustment to RA. We employed two different methodologies and a variety of measures to assess the effects of these interventions. The analyses showed that both cognitive behavioral and affective interventions were useful, but in different ways. Further, it appears that the relative merits of the two approaches also depend on participant history of depression.

As we seek to understand the underlying factors responsible for the results obtained, we first review the findings for the coping measures, because they provide some clues about the differential effects of pain and mindfulness interventions. Both diary measures of pain coping efficacy and catastrophizing indicated a consistent pattern. Patients with recurrent depression in the M group showed a greater shift Pre to Post in their efficacy expectations for coping successfully with pain and less catastrophizing compared to the other groups. There is a clear affective contribution to these coping outcomes. Efficacy judgments ask directly for ratings of satisfaction and estimates of coping capacity, which were found to be associated with greater positive and less negative affect in prior studies (Zautra & Wrabetz, 1991), and arthritis patients who engage in more catastrophic coping tend to report more negative affect (Zautra et al., 1995). Ratings of pain control are heavily infused with cognitive language favoring the kind of interventions offered in CBT for pain and pain education programs. In contrast, mindfulness meditation methods encourage awareness, not control. Seen from this perspective, the findings provide some consistent evidence that the interventions were helpful in different ways; P provided better cognitive control, and M provided better emotion regulation, something of considerable value to those coping with recurrent depression.

The distinctions between rheumatoid arthritis patients with versus without a history of recurrent depression take on added significance in the context of prior findings obtained in analyses of Pre data on the same sample (Conner et al., 2006; Zautra et al., 2007). Lower positive affective responding and more negative affect was found in the Conner et al. (2006) study in response to pain, and in Zautra et al. (2007) affective disturbance accounted for differences in stress-related pain found between depression history groups. In the current study, the mindfulness intervention appeared to have a strong influence on these emotions for those with recurrent depression, as revealed in the greater enhancement in positive affect and reduction in negative affect compared with the other two intervention conditions. The potential for boosting positive affective experience while also lowering negative affective responding may be further developed in emotion regulation therapies, particularly for participants with a history of depression. Chronic pain patients without vulnerability to affective disorder may benefit from a more streamlined cognitive behavioral approach.

Of interest also are the findings from the laboratory sessions. Clinical assessment of history of depression identified a subset of patients who showed significant improvements Pre to Post in physician-assessed joint swelling and tenderness if they received M rather than one of the other two interventions. These findings follow those recently reported by us in the analysis of only Pre data on the same sample, in which we found recurrent depression was a risk factor for reports of pain (Zautra et al., 2007). Apparently, M made a greater difference in reducing pain for those patients, and the effect sizes were substantial. However, the findings for the diary pain measure did not reveal the same results as those from the laboratory data. For that measure, all groups showed improvement Pre to Post. Earlier we reported that recent reviews have shown that the effect sizes for reductions in pain as a consequence of cognitive therapies are small and often nonsignificant (e.g., Dixon et al., 2007). Seen within that broader context, the current study's findings are not surprising. Nevertheless, it is useful to speculate about what might be responsible for the differences on pain as a function of method. First, the measures themselves were different. The physicians' ratings were based on 28 ratings taken from joints on both sides of the body. These ratings provided a much greater range of scores and likely more accurate accounts than those provided by the simple one-item numerical rating scale used in the diary. We conclude that the M intervention had effects on pain, but those effects depended on both depression history and the pain assessment method.

The diary measure of depressive symptoms indicated a shift toward less depression at Post, even for the control group. We suspect that the education group may have provided some benefit beyond that of expectancy. A recent study by Buszewicz et al. (2006) found reductions in anxiety as well as enhanced self-efficacy for those participants involved in a self-management course in arthritis in comparison to those provided with only an education manual. The current study did not include a no-treatment control, which might have provided more clues as to the nature of the effects observed for the education-only condition.

Our assessment of outcomes extended beyond self-report and physicians' ratings to include a physiological marker of disease activity, the proinflammatory cytokine IL-6. The change in IL-6 Pre to Post indicates that standard P may lower inflammatory processes that underlie RA. Comparable results were not found for the other conditions. Two central questions arise from these findings. First, what mechanisms underlie these effects? We suspect that P may reduce cognitive and subsequent physiological reactivity to pain, consistent with some prior findings (Dixon et al., 2007; Giesecke et al., 2005). The lack of beneficial effects on IL-6 for M is not consistent with recent reviews that have suggested a role for emotion regulation in cytokine activation (Pressman & Cohen, 2005), and this finding does not support one of the primary hypotheses of this study.

Methodological differences may account for differences in the relative impact of the treatment conditions. P is a well-established intervention, whereas the M intervention was developed for this study and may not have had comparable fidelity. There is no

evidence from attendance records of differences in patient preferences for one or another treatment or of their expectations of benefit, results that strengthen the case for the internal validity of the differences found between groups. A direct assessment of expectation of improvement and satisfaction with treatment would have been preferable to assess equivalence between groups in garnering positive mindsets about recovery.

We suspect that the beneficial effects of the mindfulness-based emotion regulation intervention on IL-6 were limited to those with recurrent depression. However, we were able to obtain and assay blood samples from only two thirds of our sample, leaving too few respondents with recurrent depression in the emotion regulation intervention with Pre scores on IL-6 to permit a reliable analysis of treatment effects moderated by depression history. It is noteworthy that depression history did influence IL-6. We found significant main effects of depression history on IL-6, consistent with prior studies (Zautra et al., 1999, 2005), and a history by time effect (see Footnote 2), suggesting that those with recurrent depression sustained elevated cytokine levels throughout the study. To better test for mindfulness effects, future studies would need to use stratified sampling to assure an equivalent number of participants with recurrent depression across treatment conditions. Though we had anticipated that depression history would be an important factor, only our analyses of Pre data in a prior study alerted us to the strong influence of recurrent episodes of depression on pain and suffering in RA.

Our method of probing the effects of depression history provided us with confidence that the findings are not artifactual. Graphs of the patterns of means shown in the figures are not consistent with regression to the mean effects, and analysis of Pre scores did not reveal differences on any of the outcome measures as a function of group or group by depression history assignment. Depression history did show main effects on Pre scores of several measures, so some caution is advisable in the interpretation of effects. By treating depression as a continuous variable in the initial analyses, as we have done here, we help resolve questions that may arise regarding the validity of dichotomizing depression history. We examined the effects of recurrent depression as a dichotomous variable only when there were significant moderator effects using the continuous scoring. This method of analysis provides support for the inference that depression history matters. The focus on recurrent episodes here relies on our finding that the differences in outcomes were retained when we contrasted the scores of those with recurrent episodes against those with either one episode or no history. We could not test for differences in outcome by contrasting those with just one episode of depression with those with two or more episodes, due to limitations in the size of the sample (i.e., $n = 6$ for mindfulness participants with recurrent depression), so some uncertainty remains regarding the importance of multiple depressive episodes in defining differences found between treatment conditions.

Our findings do indicate that depression history is an important person characteristic to consider in future intervention studies involving individuals with chronic pain. Had we not assessed depression history, we would have been unable to detect some of the beneficial effects of mindfulness treatment on participants who had a history of recurrent depression. One recent study found modest effects of a mindfulness intervention for RA patients and no benefit in the first 2 months (Pradhan et al., 2007) when compared to waiting-list control participants. By chance, all those with a history of clinical depression were assigned to the control condition. Our findings suggest that greater benefits of mindfulness would have been observed in that study had more RA patients with a history of depression received it. History of recurrent depression may also be a significant factor in studies of pain and current depression. Because many people with current major depression also have a history of depression, researchers could potentially misattribute pain-related patterns rooted in depression history to the current depression (Conner et al., 2006). Moreover, if participants with a history of depression are not identified among a currently healthy control group, they may add systematic error to the data. Finally, these findings suggest that clinicians should consider including depression history as a factor in pain-related assessments and treatment planning.

What may account for the beneficial effects of the M intervention, particularly for those with a history of recurrent depression? A number of mechanisms have been proposed that may have been operating here (Baer, 2003; Shapiro, Carlson, Astin, & Freedman, 2006). For example, the M group was intended to develop the capacity to engage in nonjudgmental observation of thoughts, sensations, and emotions, a perspective that allows patients to consider their current state as a passing mental event rather than an all-encompassing, enduring experience. Teasdale et al. (2002) have termed this perspective "metacognitive awareness" and found it to be a significant predictor of sustained recovery among residually depressed patients. By promoting increased awareness and acceptance of present experience, the M intervention was designed to counter habitual tendencies to escape or suppress difficult experiences. Thus, increased exposure and desensitization to the experience of pain and distress may have contributed to less pain catastrophizing and better pain coping efficacy without a change in pain control (Kabat-Zinn, 1990). An important feature of the M treatment, and one that distinguishes it from other mindfulness approaches and from CBT for pain, was its emphasis on cultivation and savoring of positive emotional and social resources. An improvement in the ability to recognize, create, and draw on such positive resources may have accounted for the greater increases in positive affect among individuals with a history of depressive episodes in the M group compared to the other groups.

Several limitations diminish our confidence in the reproducibility of these findings with other samples. The sample of males was small and of low income in comparison to the community as a whole. The Pre score data offer a mixed picture regarding the sample's level of pain and impairment. Overall, the scores on illness severity reveal a sample of RA participants who had low to moderate levels of pain and low to moderate levels of inflammation and tenderness. In sum, the clinical picture is varied, characterizing older RA patients who remain capable of leaving home to attend group sessions. More impaired RA patients may have responded differently to the interventions.

Many variables were analyzed in these analyses, raising questions regarding alpha inflation. The number of variables and possible Type I errors should be balanced against the use of two distinct methodologies, each of which includes a standard number of measures within its portfolio. A review of the tables that display those effects revealed that many of the results for the three-way interactions remained significant even if we divided the family-wise alpha by the number of tests. Of particular importance for this

study was the consistency of the effects of the three-way interactions across methods. Such patterns in the data are not attributable to alpha inflation and, therefore, invite inferences along the lines presented here.

In sum, the present results offer qualified support for mindfulness meditation in addition to pain management skills training offered in standard methods of CBT for pain. To our knowledge, this is the first published randomized clinical trial that has compared a mindfulness-based intervention with an empirically supported psychological treatment for chronic pain. Our findings contribute to the body of work accrued over the past 20 years that has provided evidence suggesting that mindfulness-based approaches provide significant benefits to patients with chronic health problems (for reviews, see Baer, 2003; Bishop, 2002; Grossman, Niemann, Schmidt, & Walach, 2004). It is important that the data highlight the value of recognizing and managing depression in RA patients because those with a history of depression appear to have a differential response to intervention approaches emphasizing self-management strategies than do those without such a history. Although considerable research literature supports the use of cognitive behavioral interventions for RA (Astin et al., 2002), prior studies have not addressed the problem of matching therapies to individual differences, nor has a model guiding the examination of this important question been proposed. Nevertheless, prior work and theory led us to predict differential influence of a focus on emotion regulation for those with a history of depressive disorder. Replication of these findings will strengthen our confidence in them, and we encourage further study of the value of treatments for chronic pain focused on emotion regulation in contrast to standard cognitive behavioral treatments for pain management.

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