Which treatment worked better for whom? Moderators of group cognitive behavioral therapy versus adapted mindfulness based stress reduction for anxiety disorders

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ABSTRACT

Objective: Identifying treatment moderators facilitates treatment matching and personalized medicine. No previous studies have investigated treatment moderators for a mindfulness-based versus traditional cognitive behavioral therapy (CBT) for anxiety disorders to determine for whom each is most effective. The current study examined three putative moderators of principal anxiety disorder severity outcomes for adapted mindfulness based stress reduction (MBSR) and group CBT – baseline depression symptoms, anxiety sensitivity, and diagnostic severity.
Method: Seventy-one patients with a DSM-IV anxiety disorder were randomized to adapted MBSR or group CBT and assessed at baseline, post-treatment, and 3-month follow up.
Results: CBT outperformed adapted MBSR among those with no to mild depressive symptoms and, at post-treatment only, among those with very high anxiety sensitivity. At follow up, adapted MBSR outperformed CBT among those with moderate to severe depressive symptoms and among those with average anxiety sensitivity (for this sample). Baseline severity affected post-treatment outcomes differently in CBT than in adapted MBSR.
Conclusion: Baseline levels of depression, anxiety sensitivity, and to some extent diagnostic severity, differentially moderated outcomes in CBT and adapted MBSR for anxiety disorders. Recommendations and clinical implications are discussed.

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Beyond establishing treatment efficacy, a key question for psychotherapy research centers on which treatments work best for whom. Tackling this question involves identifying treatment moderators, or baseline characteristics that identify the subgroups of patients who respond *differently* to one treatment over another (Kraemer, Frank, & Kupfer, 2006). Investigating treatment moderators supports the National Institutes of Health's call for personalized medicine. Until recently, however, researchers have had little success at demonstrating treatment moderation among different psychotherapies (Simon & Perlis, 2010) – perhaps partly because relatively few studies have compared distinct psychotherapies, a required first step.

Within the context of anxiety disorders, however, the last several years have produced an increasing number of studies comparing two distinct psychotherapies or interventions. Such studies provide the necessary data for examining treatment moderation. Our recent work (Arch et al., 2012, 2013), for example, compares mindfulness and acceptance-based versus traditional cognitive behavioral (CBT) treatments for anxiety disorders, revealing similar outcomes particularly at post-treatment (Arch et al., 2012). Upon demonstrating the comparative efficacy of both treatments, we now have the opportunity to address whether certain types of patients are better served by one treatment over the other.

Acceptance and mindfulness therapies and (traditional) CBT[2] for anxiety disorders differ in ways that may have implications for treatment matching. CBT focuses on treating thoughts and behaviors related to anxiety and fear; mindfulness and acceptance-based interventions focus more broadly on shifting relationship to internal experience – anxiety-related and otherwise. Cognitive

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[2] To simplify language, traditional CBT will henceforth be referred to as 'CBT'.

model-based components of CBT purport to target the *content* of anxiety-related thinking; acceptance and mindfulness based treatments purport to target our *relationship* with thinking altogether (see Arch & Craske, 2008). CBT aims for mastery and control of anxiety; acceptance and mindfulness based treatments aim for acceptance of anxiety. Given these and other purported differences, it is reasonable to expect that some patients might respond better to one approach over the other.

For anxiety disorders, the only known study to date examining treatment moderation for CBT versus an acceptance or mindfulness-based treatment compared CBT and acceptance and commitment therapy (ACT; Hayes, Strosahl, & Wilson, 1999, 2012) for heterogeneous anxiety disorders (Wolitzky-Taylor, Arch, Rosenfield, & Craske, 2012). Findings revealed that heterogeneous anxiety disorder patients with moderate anxiety sensitivity and those without comorbid mood disorders improved more in CBT than ACT, whereas patients with comorbid mood disorders improved more in ACT than CBT. These findings suggest that CBT was superior at helping patients with focused anxiety symptoms whereas ACT was superior at helping patients with broader emotional dysfunction. The emergence of anxiety sensitivity as a moderator suggests that fear of anxiety-related sensations may serve different roles within CBT versus ACT for anxiety disorders. These findings, if replicated, provide an important foundation for informing the personalized treatment of anxiety disorders.

The current study builds on this initial study by examining treatment moderation within CBT versus a mindfulness intervention adapted from Mindfulness Based Stress Reduction (MBSR; Kabat-Zinn, 1990) for heterogeneous anxiety disorders. In contrast to ACT, a multicomponent acceptance and mindfulness-based intervention (see Hayes, Luoma, Bond, Masuda, & Lillis, 2006), adapted MBSR concentrates predominantly on mindfulness training – cultivating receptive awareness and attention to present moment experience (Brown & Ryan, 2003) – facilitating a more focused comparison with CBT. Whereas the ACT protocol in our previous study utilized behavioral exposure (Arch et al., 2012; Eifert & Forsyth, 2005), the current adapted MBSR protocol did not – providing a sharper contrast with (exposure based) CBT. Finally, our previous treatment moderation study compared individual therapies conducted in a university setting (Wolitzky-Taylor et al., 2012), whereas the current study compares group interventions conducted in a community setting.

We first examined whether the moderators that previously distinguished treatment response to CBT and ACT – anxiety sensitivity and mood disorder symptoms (Wolitzky-Taylor et al., 2012) – also distinguished response to group CBT and adapted MBSR. Similar to ACT, mindfulness-based stress reduction represents a broad intervention that does not focus narrowly on anxiety disorder symptoms as does CBT. We therefore hypothesized that adapted MBSR would be more helpful than CBT for anxiety disorder patients with broader emotional dysfunction characterized by symptoms of depression, whereas CBT would be more helpful than adapted MBSR for patients with low or absent depression symptoms. Based on our previous study (Wolitzky-Taylor et al., 2012) we hypothesized that anxiety sensitivity would be a more significant moderator within CBT than adapted MBSR, and that CBT would be more helpful than adapted MBSR for patients with moderate (mean) levels of anxiety sensitivity. Finally, we explored whether baseline diagnostic severity of the principal anxiety disorder differentially impacted treatment outcomes in CBT and adapted MBSR. Previous CBT studies have reported mixed findings regarding whether baseline severity impacts outcomes (Aiken & West, 1991; Marks et al., 1993), and our previous study found that baseline severity neither moderated nor generally predicted ACT or CBT outcomes (Wolitzky-

Taylor et al., 2012). Thus, we did not put forth hypotheses about whether baseline diagnostic severity would moderate outcomes in CBT or adapted MBSR. Based on our previous finding that (continuous) moderators had non-linear relationships with treatment outcomes (Wolitzky-Taylor et al., 2012), we assessed both linear and non-linear relationships between moderators and outcomes.

Methods

Participants

Patients (Ps) were veterans referred for treatment between October 2009 and April 2011 at the Anxiety Disorders Clinic at the VA San Diego Healthcare System Medical Center, an outpatient clinic that specializes in the behavioral treatment of anxiety disorders. Ps were eligible for the study if they (a) met criteria for a principal (or dual principal) DSM-IV diagnosis of one of more anxiety disorders on the MINI International Neuropsychiatric Interview (MINI) for DSM-IV (Sheehan et al., 1998); (b) were between 18 and 75 years old; and (c) were English speaking. Exclusion criteria included (a) a principal diagnosis of military-related post-traumatic stress disorder, which required referral to a specialized military PTSD clinic; (b) active suicidal ideation; (c) active substance use disorders within the past 3 months; (d) current participation in other CBT or mindfulness-based treatments for anxiety disorders. For additional participant and study design details please see Arch et al. (2013). Of the patients who began treatment ($n = 105$), seventy-one patients completed at least one post-treatment or follow-up assessment and thus could be included in the moderator analysis. See Table 1 for sociodemographic and clinical characteristics of the current sample.

For anxiety and mood disorder diagnoses, diagnostic status ratings from the MINI (yes, no) were enhanced with a dimensional clinical severity rating (CSR) made on a 0 to 8 scale based on current symptom severity, distress, and disablement (0 = none, 2 = subclinical, 4 = clinically significant, 6 = moderately severe, 8 = most severe). Disablement was characterized by behavioral interference in valued/central life activities. A CSR of "4" or above for 1 + anxiety disorders meeting DSM-IV criteria on the MINI was required for study entrance (Arch et al., 2012; Craske, DeCola, Sachs, & Pontillo, 2003; Craske et al., 2007). We have established good to excellent inter-rater agreement for dimensional CSR ratings (e.g., social anxiety disorder and obsessive compulsive disorder ICC = 1.00, panic disorder ICC = .91, generalized anxiety disorder ICC = .85, and specific phobia ICC = .75, and CSRs across all principal diagnoses, ICC = .65, Arch et al., 2012), as have Brown, Campbell, Lehman, Grisham, & Mancill (2001). See Arch et al. (2013) for details of blind assessor training and ratings.

Measures

Outcome measure
Severity of the principal disorder (clinical severity ratings or CSR). Diagnostic severity was ascertained with the blind assessor-derived CSR ratings for the principal anxiety disorder diagnosis from the MINI (see above). If Ps had dual principal anxiety disorders at baseline (e.g., two of equal CSR severity), we averaged the CSRs across both disorders.

Putative moderators
Baseline severity. Baseline severity of the principal diagnosis was defined by the CSR on the MINI for DSM-IV (see Outcome measure, above) and rated on a 0–8 scale.

Table 1
Sample Demographic and clinical characteristics.

Characteristic	Total ($n = 71$)[a]	MBSR ($n = 32$)	CBT ($n = 39$)	t value or χ^2	p
Male	79.41% (54/68)	70.97% (22/31)	86.49% (32/37)	2.49	.12
Race/ethnicity					
White/Caucasian	68.66% (46/67)	70.00% (21/30)	67.57% (25/37)	.05	.83[b]
Hispanic/Latino/a	10.45% (7/67)	6.67% (2/30)	13.51% (5/37)		
African-American/Black	4.48% (3/67)	3.33% (1/30)	5.41% (2/37)		
Asian-American/Pacific Islander	7.46% (5/67)	10.00% (3/30)	5.41% (2/37)		
Other	8.96% (6/67)	10.00% (3/30)	8.11% (3/37)		
Age, *in years*	46.59 (14.24)	45.35 (13.85)	48.06 (14.78)	.78	.44
Education, *in years*	13.79 (1.35)	13.61 (1.36)	13.95 (1.33)	1.02	.31
Professional/white collar	33.33% (22/66)	36.67% (11/30)	30.56% (11/36)	.28	.60
Unemployed or disabled	50.00% (34/68)	41.94% (13/31)	56.76% (21/37)	.91	.34
Married/Cohabiting	57.35% (39/68)	64.52% (20/31)	51.35% (19/37)	1.32	.25
Children, *average number*	1.06 (1.37)	1.13 (1.63)	1.00 (1.12)	−.38	.71
Principal anxiety disorder[c]:					
PD/A	30.99% (22/71)	34.38% (11/32)	28.21% (11/39)	.31	.58
GAD	36.62% (26/71)	37.50% (12/32)	35.90% (14/39)	.02	.89
SAD	15.49% (11/71)	6.25% (2/32)	23.08% (9/39)	3.80	.05
PTSD (civilian)	16.90% (12/71)	21.88% (7/32)	12.82% (5/39)	1.03	.31
OCD	5.63% (4/71)	9.38% (3/32)	2.56% (1/39)	1.53	.22
Moderators at Pre:					
CSR for principal anxiety disorder (0–8 scale)	6.05 (.99)	5.88 (1.13)	6.19 (.86)	1.35	.18
ASI	34.25 (14.38)	35.85 (16.01)	32.95 (12.99)	.82	.42
BDI	25.31 (12.62)	27.95 (11.02)	23.23 (13.53)	1.55	.13

[a] Demographic data was missing for up to 5 patients, depending on the variable.
[b] The analysis for race/ethnicity compared the portion of white versus minority Ps. Small cell sizes precluded group comparisons for other race/ethnicity categories.
[c] Four patients had dual primary anxiety disorders (defined as two anxiety disorders with equally highest CSR ratings), and thus were included twice, once on each primary disorder.

Anxiety sensitivity. The Anxiety Sensitivity Index[3] (ASI; Peterson & Reiss, 1992; Reiss, Peterson, Gursky, & McNally, 1986) assesses fear of anxiety-related bodily sensations (e.g., shortness of breath, rapid heart beat) based on the belief that such sensations are harmful or embarrassing. The ASI shows elevation across all of the anxiety disorders (except specific phobia; Taylor, Koch, & McNally, 1992) relative to nonanxious controls (Peterson & Reiss, 1992). In the current sample, Ps with panic disorder (principal or principal/comorbid combined) did not significantly differ in ASI scores from Ps without panic disorder, $ps > .16$. Further, CBT and adapted MBSR did not differ in the portion of patients with panic disorder

(principal or principal/comorbid combined), $ps > .55$. For the ASI, current sample αs were .91 (Pre) and .93 (Post and FU).

Depression symptoms. Depression symptoms were assessed with the widely-used Beck Depression Inventory-II (BDI; Beck, Steer, & Brown, 1996). Current sample αs were .91 (Pre) and .95 (Post), and .96 (FU).

Procedure
Design. The diagnostic interview and questionnaires were administered at baseline (Pre), post-treatment (Post), and 3-month follow up (FU, i.e., 3 months after Post). For treatment dropouts, we scheduled an assessment within 2–3 weeks, the results of which were substituted for the Post assessment.

Treatments: shared features. Ps were randomized to CBT or adapted MBSR. Each group met weekly for 90 min for 10 weeks for a total of 10 sessions, with the exception of a single 3-h onsite mindfulness retreat in week 7 of adapted MBSR that served as the treatment session for that week. Due to the retreat, adapted MBSR offered 1.5 more total hours of treatment than CBT, although there were no group differences in completed treatment hours (see Arch et al., 2013). Both treatments utilized patient workbooks with didactic handouts, homework, and in-session exercises. See Arch et al. (2013) for more details on randomization and therapists.

Group CBT. The CBT protocol consisted of a group version of a manual originally authored by Craske (2005) and used successfully in previous trials (Arch et al., 2012). To treat Ps with heterogeneous anxiety disorders, the CBT manual used a branching mechanism that provided cognitive restructuring and behavioral exposure content guidelines for each anxiety disorder, using the methodology developed by Craske, Rose, et al. (2009; 2011) for treating anxiety disorders in primary care. Session 1 consisted of psycho-education, identifying treatment targets, and self-monitoring. Session 2 introduced breathing retraining and cognitive restructuring, which were reinforced in Sessions 3–4. At the end of Session 4, Ps constructed an in-vivo exposure hierarchy. Sessions 5–9 centered on conducting in-session in-vivo, interoceptive, and imaginal exposures appropriate to each P. CBT therapists tailored exposure content to individual P's principal anxiety disorder as much as possible such that group members were often focusing on different exposures both in and out of session. Exposures were conducted within the group therapy room as well as in various public locations at the VA medical center. Session 10 focused on relapse prevention. Please see Arch et al. (2012) for additional details of treatment content.

Group adapted MBSR. Adapted MBSR for anxiety disorders followed a manualized protocol written by the first author (J.J.A.) in collaboration with three experienced MBSR instructors, and reflected MBSR protocols from the University of Massachusetts Center for Mindfulness (Kabat-Zinn, 1990). Relative to official MBSR, our manual responded to concerns from previous MBSR groups at the San Diego VA that group sessions, the retreat, and mindfulness home practice meditations were too long to sustain veterans' attention,[4] with few veterans practicing meditation between sessions (Ramel, Goldin, Carmona, & McQuaid, 2004). See Arch et al. (2013) for details of our adaptations, which included briefer group sessions, home practice, and retreat than typical MBSR, and

[3] We used the original ASI because we simultaneously conducted another study comparing traditional CBT with a mindfulness and acceptance-based treatment (Arch et al., 2012) that began before the ASI-3 (Taylor et al., 2007) was published, and wished to maintain consistency in outcome measures for internal comparisons between the two studies.

[4] Given the high rates of PTSD and psychiatric comorbidities among many veterans, PTSD symptoms or other co-morbid conditions may have contributed to veterans' difficulties sitting still and focusing for long periods.

extending the number of group sessions from 8 to 10 to match the number of CBT sessions. Given these adaptations, ours is more accurately characterized as an adapted MBSR approach.

Adapted MBSR session 1 introduced two mindfulness practices (mindfulness of raisin eating and body scan) and psychoeducation about fear and anxiety. Session 2 continued with mindfulness practice (body scan). Session 3 introduced formal sitting meditation and mini-breathing meditations, and discussed stress reactivity versus mindful responding. Session 4 introduced mindful yoga and discussed reactive avoidance. Session 5 continued with mindful yoga and sitting meditation, and introduce the notion of "judging mind". Session 6 continued with mindful yoga, sitting meditation, and/or the body scan and prepared Ps for the 3-h meditation retreat in Session 7. The retreat in Session 7 consisted of continuous silence while participating in various formal mindfulness practices. Session 8 continued with sitting meditation and mindful yoga, and debriefed the retreat. In Session 9, participants continued with formal meditation, and helped Ps to reflect on and live mindfully from a place of personal virtue. Session 10 helped Ps to continue integrating mindfulness practice into their daily lives.

Statistical analyses

To test potential moderators, we used hierarchical linear regression to examine the variance attributed uniquely to each predictor. We constructed separate models for Post and FU outcomes. In all models, pre-treatment CSR (severity of the principal anxiety disorder at baseline) was entered first to account for individual differences in diagnostic severity. In each regression model, the pre-treatment score on the putative moderator was entered into the first block along with pre-treatment CSR, Group and the putative moderator main effect terms were entered into the second block, and the Group × putative moderator interaction was entered on the third block. Because associations between psychological variables are often non-linear, as affirmed by our recent moderator work (Wolitzky-Taylor et al., 2012), we also explored whether the moderating relations were non-linear. Thus, quadratic main effects for the moderator (moderator^2) and the quadratic interaction term (moderator^2 x Group) were entered into a fourth and fifth block, respectively. Scatterplots and residuals were inspected for influential outliers, which were removed prior to final modeling. Less than 5% of data (e.g., influential outliers ≥ 3SD from the mean) was removed, which did not significantly impact findings.

When a significant moderator × Group interaction was observed, we did not report main effects because the effect of each variable depended on the level of the other variables in the interaction. Rather, we examined the effect of Group at relevant levels of the moderator variable in the interaction, and vice versa. Specifically, when a Group × moderator^2 interaction was observed (i.e., a moderated effect), we investigated the specific nature of the interaction from two perspectives: (1) the effect of the moderator within each Group, and (2) the effect of Group at different levels of the moderator. To assess the effect of the moderator within each Group, simple within-Group slopes were computed by dummy coding, in turn, one treatment group as 0, and the other as 1 (e.g., CBT = 0, adapted MBSR = 1; Aiken & West, 1991). To assess the effect of Group at different levels of the moderator, simple slopes for Group (e.g., between group differences) were computed at different levels of the moderator. The moderator was "centered" alternately at "low" and "high" levels, thus allowing the calculation of the effect of Group at low (i.e., 1 and 1.5 SD below the mean) and high (i.e., 1 and 1.5 SD above the mean) levels of the moderator (thus deriving the effect of treatment for those low in depression symptoms and the effect of treatment for those high in depression symptoms, for example). This procedure for investigating simple effects at different levels of the moderator (or for the different

treatment groups) included *all* participants in the data analysis, and produced *model based estimations* of the relation between Group and the outcome for patients at the "centered" level of the moderator (see Wolitzky-Taylor et al., 2012). This model based approach is preferred to the typical "subsample" approach of examining Group effects for patients low in depression, in which one would only select those with low depression levels (1SD below the mean or lower) and examine the Group effect within this smaller subsample. The subsample approach often yields less reliable and replicable results because it is based on smaller, partial samples (see Marchand et al., 2012).

When a significant Group × moderator interaction was not observed, we assessed simplified models without the interaction (and without the main effects of Group or moderator^2 if they were nonsignificant) to assess whether the putative moderator served as an overall predictor of treatment outcome.

A significant portion of patients with data at Post did not complete the FU assessments ($n = 18$, 29.51%); therefore, we used multiple imputation procedures to impute the missing data for these patients. Although we cannot know for certain if our results would differ if we had original FU data for these patients, we could assess whether our results would change if imputed FU data for these patients were added to the models. In SPSS 19.0, we performed multiple imputation using "full condition specification" for all relevant variables in the models (all IVs and DVs), computing 10 imputations. We used the dataset with the imputed values to run the same set of moderator analyses at FU, and reported the "pooled" results as a secondary approach to analyzing the data.

Results

Baseline group differences

According to the treatment moderation guidelines outlined by Kraemer and colleagues (Kraemer, Wilson, Fairburn, & Agras, 2002), potential moderators must not correlate with group. We used independent *t*-tests to examine group differences at baseline on putative moderators (baseline severity, ASI, BDI), demonstrating a lack of group differences on all putative moderators, $ps > .12$, see Table 1.

Group differences in outcome

Both CBT and adapted MBSR led to large improvements in the outcome variable (principal diagnosis severity) from Pre to FU, $ds > -3.50$, $ps < .001$, with no differences between groups at Post thru FU, $p = .33$ (see Arch et al., 2013). Thus, groups demonstrated similar improvements on the outcome measure.

Therapist competence, treatment integrity, and treatment credibility

Twenty percent of group session videotapes were randomly selected for therapist integrity and adherence ratings (see Arch et al., 2013; for details of tape selection, rater training, and scales). Therapists in CBT and adapted MBSR did not differ in competence ($p = .18$); both were rated as "very good to excellent". As expected, cognitive therapy adherence scores were higher in CBT than adapted MBSR, $F(1, 15) = 723.88$, $p < .001$, $p\eta^2 = .98$, whereas MBSR adherence scores were higher in adapted MBSR than CBT, $F(1, 15) = 49.72$, $p < .001$, $p\eta^2 = .77$. Treatment credibility ratings (see Arch et al., 2013), revealed no differences between adapted MBSR ($M = 5.63$, $SD = 1.75$) and CBT ($M = 5.38$, $SD = 1.51$), $t(59) = .59$, $p = .56$; both treatment ratings approached 'mostly credible'.

Differences between patients with and without missing data

To examine whether Ps with missing data for Post or FU CSRs differed on putative moderators from Ps without missing data, we ran a MANOVA with baseline levels of CSR and the other putative moderators (BDI and ASI scores) as dependent variables, and Post or FU data status (present versus missing) as the independent variable. We found no significant differences on the putative moderators between Ps with versus without missing data at Post ($p = .48$) or FU ($p = .18$).

Depression as a moderator

Depression moderating outcomes at Post

A significant Group $\times$ BDI^2 interaction predicted diagnostic severity at Post, $b = -.008$, $SE = .004$, $t = -2.18$, $p < .05$, $\Delta R^2 = .05$, showing that baseline depression levels moderated Post outcomes in a nonlinear manner that differed between groups. Simple effects tests revealed nonsignificant quadratic BDI effects within CBT, $p = .19$, and trending quadratic BDI effects within adapted MBSR, $p = .09$ − nonetheless, the significant Group $\times$ BDI^2 interaction demonstrates that the quadratic effects within each group differed from one another, see Fig. 1. Consistent with our hypothesis that CBT would be more helpful than adapted MBSR for those with low or absent depression symptoms, CBT outperformed adapted MBSR for those with low depression scores 1.5 SD below the BDI mean, $p < .05$, see Fig. 1. However, our hypothesis that adapted MBSR would be superior for patients with higher baseline depression symptoms was not supported − no group differences emerged at any other point along the BDI continuum, including at 1 and 1.5 SD above the BDI mean.

Depression moderating outcomes at follow up

A large and significant Group $\times$ BDI^2 interaction predicted diagnostic severity at FU, $b = .018$, $SE = .006$, $t = 3.16$, $p < .01$, $\Delta R^2 = .16$, demonstrating that baseline depression levels moderated FU outcomes in a nonlinear manner that differed between groups. Simple effects tests revealed significant quadratic BDI effects within adapted MBSR, $p < .01$, such that low BDI scores were associated with higher diagnostic severity at FU whereas moderate to high BDI scores were associated with lower diagnostic severity. In CBT, quadratic BDI effects were non-significant, $p = .34$, although linear BDI effects were significant, $p < .05$, with higher BDI scores associated with higher diagnostic severity outcomes. Consistent with our hypothesis that CBT would be better for those with low depressive symptoms whereas adapted MBSR would be better for those with high depressive symptoms, CBT outperformed adapted
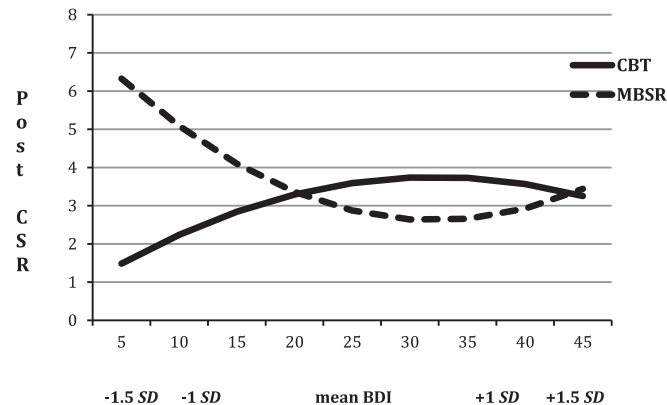
MBSR among those with lower BDI scores, including 1 SD below the mean ($p < .05$) and 1.5 SD below the mean ($p < .01$). Adapted MBSR outperformed CBT among those with moderate to high BDI scores, including at the mean ($p = .01$) and at 1 SD above the mean ($p < .01$).

Anxiety sensitivity as a moderator

Anxiety sensitivity moderating outcomes at Post

A significant group $\times$ ASI^2 interaction predicted diagnostic severity outcomes at Post, $b = .01$, $SE = .003$, $t = 3.12$, $p = .003$, $\Delta R^2 = .10$, indicating that baseline anxiety sensitivity moderated Post outcomes in a nonlinear manner that differed by group. Consistent with our hypothesis that anxiety sensitivity would serve as a more important moderator in CBT than in adapted MBSR, ASI exerted a quadratic moderation effect in CBT, $p < .01$, but exerted neither a quadratic nor linear effect in MBSR ($ps > .18$), see Fig. 2a. In contradiction with our hypothesis that CBT would be more helpful for those with moderate (e.g., mean) levels of anxiety sensitivity, the quadratic effect of ASI within CBT showed that those with mean ASI scores evidenced *greater* Post diagnostic severity than those with low or high ASI − at least within CBT. Group differences, however, did not reach significance at the mean or 1 SD above or below the mean, $ps > .11$. CBT outperformed MBSR at 1.5 SD below the ASI mean, $p = .08$, and at 1.5 SD above the mean, $p < .01$, indicating that those with low or high anxiety sensitivity did better in CBT than in adapted MBSR.

Anxiety sensitivity moderating outcomes at follow up

A large and significant Group $\times$ ASI^2 interaction predicted diagnostic severity outcomes at FU, $b = .01$, $SE = .004$, $t = 3.12$,
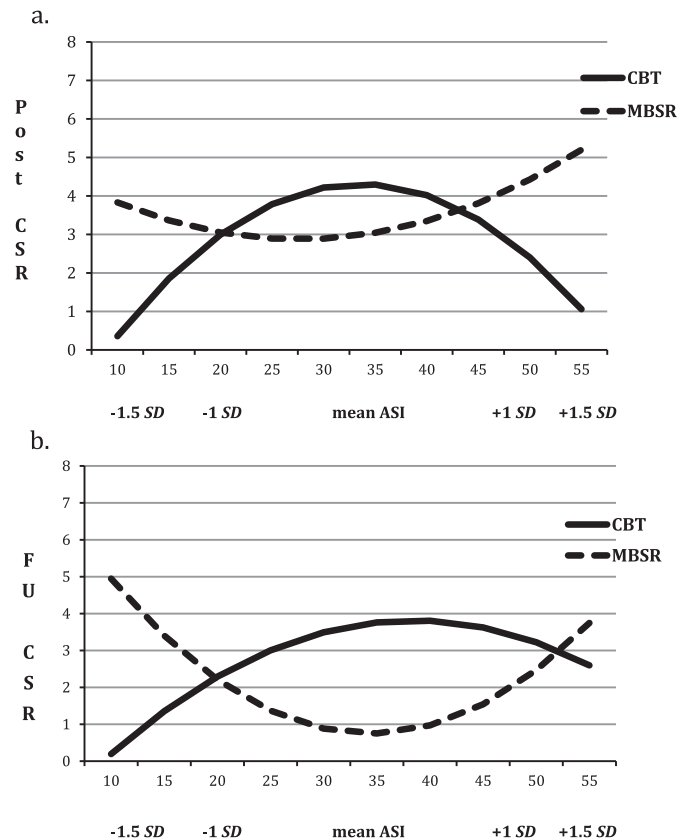
a.

b.

Fig. 2. a. Baseline anxiety sensitivity (ASI) as a moderator of diagnostic severity at Post. b. Baseline anxiety sensitivity (ASI) as a moderator of diagnostic severity at FU.

Fig. 1. Baseline depression (BDI) as a moderator of diagnostic severity at Post.

$p < .01$, $\Delta R^2 = .16$, such that baseline anxiety sensitivity moderated FU outcomes in a nonlinear manner that differed by group. Contrary to our hypothesis that anxiety sensitivity would moderate outcomes more in CBT than adapted MBSR, simple effects tests showed that the quadratic ASI effect was significant within adapted MBSR, $p < .05$, such that those with moderate ASI showed lower diagnostic severity at FU than those with low ASI and to some extent, high ASI, see Fig. 2b. The quadratic ASI effect was nearly significant in CBT, $p = .05$ such that those with low ASI showed lower diagnostic severity than those with moderate or high ASI. Examining group differences a function of ASI scores, significant or nearly significant group differences were found among those with ASI scores at the mean ($p < .01$), with adapted MBSR outperforming CBT, and at 1.5 SD below the mean ($p = .06$), with CBT outperforming MBSR. The finding that adapted MBSR outperformed CBT at mean ASI levels contradicted our hypothesis that CBT would be more helpful than adapted MBSR for patients with moderate (e.g., mean) levels of anxiety sensitivity. No group differences were observed at 1 SD below the mean or 1 or 1.5 SDs above the mean, $ps > .31$.

Baseline severity as a moderator

Baseline severity moderating outcomes at Post

A significant Group $\times$ baseline severity^2 interaction predicted diagnostic severity outcomes at Post, $b = -1.97$, $SE = .97$, $t = -2.04$, $p < .05$, $\Delta R^2 = .05$, showing that baseline severity levels moderated Post diagnostic outcomes in a nonlinear manner that differed by group. As shown in Fig. 3, simple effects tests revealed that within CBT, the quadratic effects of baseline severity were significant, $p = .03$, such that low to moderate baseline severity predicted lower Post severity, but higher baseline severity predicted exponentially higher Post severity. Within adapted MBSR, the quadratic effects of baseline severity were nonsignificant, $p = .88$, although a significant linear effect, $p = .04$, indicated that higher baseline severity predicted higher Post severity overall. Group differences approached significance among those with mean baseline severity, $p = .07$, with CBT outperforming MBSR whereas at 1.5 SD above the mean adapted MBSR outperformed CBT, $p = .05$. No group differences emerged at other points of baseline severity (1 SD above the mean, 1 and 1.5 SDs below the mean).

Baseline severity predicting outcomes at follow up

The Group $\times$ baseline severity^2 interaction did not moderate diagnostic severity outcomes at FU, $b = -1.48$, $SE = 1.21$, $t = -1.23$, $p = .23$, $\Delta R^2 = .03$ – nor did the Group $\times$ linear baseline interaction. In a simplified model without group or baseline severity^2, baseline severity trended toward significance as a predictor of FU severity, $b = .67$, $SE = .38$, $t = 1.75$, $p < .09$, $\Delta R^2 = .06$. In summary, baseline

Fig. 3. Baseline diagnostic severity (CSR) as a moderator of diagnostic severity at Post.

severity somewhat predicted (across both groups) but did not moderate (differently between groups) outcomes at FU.

Multiple imputation for the follow-up analyses

For the pooled results from the multiply imputed dataset, the significant higher order interactions predicting diagnostic severity at FU were replicated for ASI^2 x Group ($p < .05$), and for BDI^2 x Group ($p < .05$). Thus, the multiple imputation results replicated and reinforced those from our non-imputed FU analyses.

Discussion

In an effort to inform treatment matching and personalized medicine for the group treatment of heterogeneous anxiety disorders, the present study investigated moderators of treatment outcome among patients randomized to group CBT or adapted MBSR. Both treatments led to similarly large reductions in principal anxiety disorder severity (Arch et al., 2013). With regard to treatment outcomes, however: "equal on average does not mean equal for everyone" (Simon, 2001, p. 3003). We therefore aimed to identify treatment moderators that would predict differential efficacy (see Simon & Perlis, 2010) for patients in CBT versus adapted MBSR. Based on our previous findings (Wolitzky-Taylor et al., 2012), we identified three baseline clinical characteristics − depressive symptoms, anxiety sensitivity, and diagnostic severity − and investigated their impact on post-treatment and follow-up diagnostic severity of the principal anxiety disorder. All three moderated diagnostic severity outcomes at Post, and two out of three moderated diagnostic severity outcomes at Follow Up. These findings inform treatment-matching efforts in the context of group treatment for mixed anxiety disorders.

Depression as a moderator

Based on our previous finding (Wolitzky-Taylor et al., 2012), we predicted that adapted MBSR would be more helpful than CBT for anxiety disorder patients with significant depression symptoms, whereas CBT would be more helpful for anxiety disorder patients with relatively few depression symptoms. Our findings generally supported this hypothesis. Among those with no to mild depressive symptoms, CBT outperformed adapted MBSR at both post-treatment and follow up. Among those with 'average' to high levels of depressive symptoms, adapted MBSR led to better outcomes than CBT at follow up, though not at post-treatment. The 'average' baseline depression symptoms in the current sample indicated moderate depression (see Table 1); therefore, adapted MBSR outperformed CBT at follow-up among those with moderate to severe depression symptoms. Why this finding emerged only at follow-up is unclear. To speculate, it is possible that the finding for CBT superiority among low-depression patients (found across both time points) was more robust than the finding for adapted MBSR superiority among moderate to high-depression patients (found only at follow-up). Alternatively, participating in a group may have reduced depressive symptoms for patients with comorbid depression through meaningful social contact and other nonspecific group factors that were common to both group-based interventions. At follow-up, significantly after this source of peer contact ended, treatment-specific differences in efficacy for patients with comorbid depressive symptoms may have been easier to detect.

These findings echo our previous finding that ACT outperformed CBT among anxiety disorder patients with co-occurring mood disorders, whereas CBT outperformed ACT among those without co-occurring mood disorders (Wolitzky-Taylor et al., 2012). Although the current study examined adapted MBSR rather than
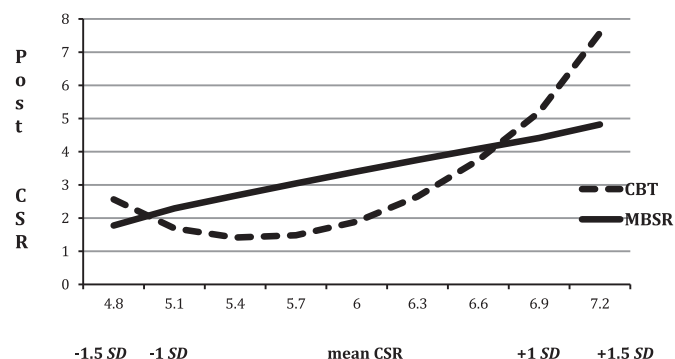
ACT, these interventions share an emphasis on mindfulness and acceptance. Two characteristics of acceptance and mindfulness-based interventions may account for its tendency to be more successful for anxiety disorders with co-occurring depression. First, both MBSR and ACT focus *broadly* on shifting relationship to internal experience rather than *narrowly* on anxiety disorder symptoms as in CBT. Second, mindfulness and acceptance-based treatments teach self distancing from thought content, known as cognitive defusion (Hayes et al., 1999) or decentering (Fresco et al., 2007), which represents a central proposed mechanism of action in mindfulness-based treatments for depression (Teasdale et al., 2002). These treatments thus tap into an important component of an evidence-based treatment for depression and related relapse (e.g., Mindfulness Based Cognitive Therapy, Teasdale et al., 2000). In contrast, the focus on anxiety symptoms in CBT likely accounts for its superiority among anxiety disorder patients who *lack* comorbid depression. The concentrated emphasis on anxiety disorder symptom improvement in CBT may allow those without mood disorder comorbidity to make faster and more sustained progress toward this aim. In summary, findings from two studies point to the possibility that anxiety disorder patients with comorbid depression diagnoses or symptoms tend to do better – at least at follow up – in mindfulness and acceptance-based treatments whereas anxiety disorder patients lacking comorbid depression diagnoses or symptoms tend to do better in CBT. Additional data are now needed to further replicate and refine this hypothesis by comparing groups over more extended time periods (e.g., multiple years) and across additional outcomes.

Anxiety sensitivity as a moderator

Baseline anxiety sensitivity moderated outcomes at post-treatment and follow-up, although not in the predicted direction. Based on our previous study (Wolitzky-Taylor et al., 2012), we hypothesized that 1) anxiety sensitivity would be a more significant moderator within CBT than adapted MBSR, and that 2) CBT would be superior to adapted MBSR for patients with mean levels of anxiety sensitivity. Contrary to our first prediction, anxiety sensitivity moderated outcomes within both CBT *and* adapted MBSR (though only at follow-up for the latter). Contrary to our second prediction, those with 'mean' levels of anxiety sensitivity did better in adapted MBSR than CBT, at least at follow-up. *Within* CBT, those with 'mean' anxiety sensitivity did *worse* than those with more extreme (low or high) anxiety sensitivity. In fact, those with more extreme levels of anxiety sensitivity tended to improve more in CBT than in adapted MBSR.

Our previous investigation (Wolitzky-Taylor et al., 2012) found the seeming opposite: CBT outperformed ACT among those with mean levels of anxiety sensitivity, and within CBT, those with more extreme (low or high) anxiety sensitivity did *worse* than those with mean levels. What accounts for the different findings between the two studies? First, regarding the divergent between-group findings, one major difference between adapted MBSR and ACT is that the former represents a more body-based intervention. That is, adapted MBSR focused nearly exclusively on body-based practices – the body scan meditation, mindful yoga, following the sensations of breathing in the belly or chest – whereas ACT did not. Perhaps the emphasis on body-based practices in adapted MBSR was overly arousing for patients with high levels of anxiety sensitivity and less interesting or relevant for those with low levels. Further, the current sample commonly reported medical comorbidities such as chronic obstructive pulmonary disease that may have made focusing on breathing anxiety-provoking. Patients with high anxiety sensitivity appear to have been better served by a treatment emphasizing direct confrontation of anxiety-related

misappraisals and promoting habituation to anxiety sensations, as in CBT.

Second, our mean anxiety sensitivity scores were *higher* in the current sample than in the previous sample by 3–6 points per group, representing a quarter to half *SD* or greater difference between the two samples (Rapee, Brown, Antony, & Barlow, 1992). In fact, mean anxiety sensitivity in the current sample was higher than in a large, recent sample of panic disorder with agoraphobia patients (Kampfe et al., 2012). Anxiety sensitivity severity differences may help to explain the different findings *within* CBT between the two studies. For example, if we map our patients onto the previous sample, the curve shifts upwards such that our 'mean' (and least-improved) CBT patients move to above the mean for anxiety sensitivity – more akin to our previous findings.

Third, we used total anxiety sensitivity scores based on the original ASI rather than the revised ASI-3. Although adequate as a global measure of anxiety sensitivity (as used here), our measure did not assess the three facets of anxiety sensitivity assessed by the ASI-3 (physical, social, and cognitive concerns). Had we examined the individual facets of anxiety sensitivity as moderators of treatment outcome – more precise ways to characterize anxiety sensitivity – we may have found more consistent findings between studies.

Diagnostic severity as a moderator

Across both groups, greater baseline diagnostic severity predicted greater severity at post-treatment and follow-up (although $p < .09$ at Follow Up). Baseline severity more dramatically predicted outcomes within CBT than adapted MBSR, such that high baseline severity resulted in exponentially higher severity at post-treatment. The current findings replicate several previous CBT studies for panic disorder, which found relations between pre- at post-treatment severity (e.g., Kampman, Keijsers, Hoogduin, & Hendriks, 2008; Ramnero & Ost, 2004) but not pre-treatment and follow-up severity (Ramnero & Ost, 2004). Overall, however, findings have been mixed for the association of pre-treatment severity with CBT for anxiety disorder outcomes – at least for panic disorder and obsessive compulsive disorder (Steketee & Shapiro, 1995). Inconsistent findings may stem in part from a failure to investigate nonlinear relationships between baseline moderators at treatment outcomes. On the other hand, our previous study examined nonlinear moderators of anxiety disorder outcomes in CBT and ACT and failed to find an association between baseline severity and treatment outcomes (Wolitzky-Taylor et al., 2012). Perhaps the greater baseline severity and complexity of the current sample resulted in a stronger relationship between baseline severity and outcomes.

Study strengths and limitations

We focused the current investigation on putative clinical moderators – depression and anxiety sensitivity – with demonstrated importance in the one previous study comparing moderation within an acceptance and mindfulness based treatment and traditional CBT for anxiety disorders (Wolitzky-Taylor et al., 2012). We also assessed baseline diagnostic severity as a potential moderator of treatment outcome, given its frequent examination in previous CBT studies (Steketee & Shapiro, 1995). Our selection of putative moderators, therefore, was both theoretically and empirically driven – a strength. Kraemer et al. (2006) argue that every randomized trial should examine sex, race, ethnicity, and age as possible treatment moderators as well. Our focus on clinical moderators and the small number of women (only 9 at Follow Up) and ethnic/racial minorities (only 15 with specified minority groups) in

the sample, divided across two treatment groups, precluded doing so at present. Future studies, therefore, should examine putative sociodemographic moderators in addition to putative clinical moderators. Similarly, we limited the putative clinical moderators to those identified in our previous work (Wolitzky-Taylor et al., 2012); future studies would benefit from examining a broader range of putative moderators, particularly those related to baseline levels of acceptance, experiential avoidance, cognitive fusion, daily mindfulness, and other constructs with relevance to mindfulness based interventions. We speculate that patients who show at least moderate deficits at baseline in psychological constructs or skills (acceptance and daily mindfulness, for example) that are targeted strongly and specifically by a particular intervention (e.g., MBSR) would respond better to that intervention than to an intervention that does not target those constructs or skills as directly (e.g., CBT). Convergently, we recently demonstrated that anxiety disorder patients low in behavioral willingness (assessed behaviorally) did better in ACT (than CBT) whereas patients high in behavioral willingness did better in CBT (Davies, Niles, Pittig, Arch, & Craske, submitted for publication).

Second, likely due to the complex clinical and disadvantaged socioeconomic status of the sample (e.g., many patients did not answer the phone or have access to alternative methods of being reached) coupled with the lack of significant financial incentives, many patients could not be reached for follow up. Although we cannot know for certain how complete follow-up data would have affected the results, computations based on a conservative multiple imputation approach suggested that the follow-up results were robust to missing data. Similarly, considering the complex and severe nature of the patient sample, the limited dose of active therapy components (five exposure sessions in CBT and minimal daily meditation practice in adapted MBSR), and the public hospital setting, the findings better generalize to similar treatment settings – community mental health centers, veterans medical centers and other public treatment settings – than to private practice or academic settings. On the other hand, the depression moderator results replicated our previous findings (at follow up), which were obtained through a longer course of individual therapy at an academic clinic. Data from a broad variety of individual and group treatment settings would further elucidate the generalizability of the findings.

Third, the relatively small heterogeneous anxiety disorder sample prohibited investigating moderators within each anxiety disorder – an important task for future studies. However, the mixed sample reflected shared features across the anxiety disorders (Craske, Rauch, et al., 2009) and growing interest in transdiagnostic treatments for anxiety disorders and emotional disorders (Arch et al., 2012; Barlow, Allen, & Choate, 2004) and increases the ease with which treatment findings can inform work in community settings. Finally, although we aimed to match CBT exposure content to each patient's principal anxiety disorder, the group setting limited the extent to which exposure content could be tailored fully to each patient. On the other hand, patients provided one another with peer support and encouragement around doing exposures, a possible strength of the group setting.

The nature of the findings – significant *nonlinear* moderator by group interactions in 5 of 6 analyses – points to the importance of examining nonlinear associations between putative moderators and treatment outcomes. The significant nonlinear interactions, moreover, were medium to large in magnitude. The non-linear moderators parallel our previous report, in which (continuous) moderator relationships also were non-linear (Wolitzky-Taylor et al., 2012). Previous difficulties in identifying clinical moderators of treatment outcome (e.g., Simon & Perlis, 2010) may stem in part from a failure to examine such non-linear relationships. Of

course, the more complex nature of nonlinear associations may complicate efforts to replicate findings. Conversely, replication of non-linear moderation may represent a particularly strong form of scientific reinforcement.

Conclusions

The current study represents the first effort to identify treatment moderators for outcomes of CBT versus a mindfulness-based treatment for anxiety disorders. Findings indicated that baseline levels of depression, anxiety sensitivity, and to a lesser extent diagnostic severity, differentially moderated outcomes in CBT compared to adapted MBSR. Together with results from our previous related investigation (Wolitzky-Taylor et al., 2012), these findings lead to a preliminary conclusion. First, anxiety disorder patients with significant depression symptoms or unipolar mood disorders appear to enjoy better outcomes following acceptance and mindfulness-based treatments – ACT and adapted MBSR – than CBT, at least at follow-up. On the other hand, anxiety disorder patients without significant mood disorder symptoms appear to enjoy better outcomes following CBT. If further replicated, these findings hold clinical relevance, given the frequent co-occurrence of anxiety and mood disorders (Kessler, Chiu, Demler, & Walters, 2005). Findings for anxiety sensitivity as a moderator were complex and failed to replicate those in our previous study (even for CBT); we conclude that anxiety sensitivity requires additional study as a moderator of treatment outcome. Use of the subscales on the ASI-3 would help to clarify what consistent role, if any, anxiety sensitivity plays in moderating treatment outcomes in CBT compared to mindfulness or acceptance based treatments for anxiety disorders. Future studies are now needed to replicate that baseline depression levels moderate anxiety disorder outcomes (in larger and single-disorder samples) and pending additional replication, to conduct clinical trials that randomize anxiety disorder patients to particular treatments based on baseline depression characteristics and assess the extent to which outcomes incrementally improve.

Acknowledgments

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