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Identifying Moderators of the Adherence-Outcome Relation in Cognitive Therapy for Depression

Katherine E. Sasso^{a,*}, Daniel R. Strunk^a, Justin D. Braun^a, Robert J. DeRubeis^b, and Melissa A. Brotman^c

Robert J. DeRubeis: derubeis@psych.upenn.edu; Melissa A. Brotman: brotmanm@mail.nih.gov

^aDepartment of Psychology, The Ohio State University, 1835 Neil Avenue, Columbus, OH 43210

^bDepartment of Psychology, University of Pennsylvania, 3720 Walnut Street, Philadelphia, PA 19104; Tel: +1 215 573 5804

^cMood and Anxiety Disorders Program, National Institute of Mental Health, 15K North Drive, Room 208, Bethesda, MD 20892

Abstract

Objective—Little is known about the influence of patients' pretreatment characteristics on the adherence-outcome relation in cognitive therapy (CT) for depression. In a sample of 57 depressed adults participating in CT, we examined interactions between pretreatment patient characteristics and therapist adherence in predicting session-to-session symptom change.

Method—Using items from the Collaborative Study Psychotherapy Rating Scale, we assessed three facets of therapist adherence: Cognitive Methods, Negotiating/Structuring, and Behavioral Methods/Homework. Two graduate students rated sessions 1–4 for adherence. Symptoms were assessed prior to each session with the Beck Depression Inventory-II. Moderators were assessed as part of patients' intake evaluations.

Results—After correcting for multiple comparisons, patient sex remained a significant moderator of the relationship between Cognitive Methods and next-session symptom change; Cognitive Methods more strongly predicted greater symptom improvement for women as compared to men. Pretreatment anxiety and number of prior depressive episodes were significant moderators of the relationship between Behavioral Methods/Homework and next-session symptom change, with greater Behavioral Methods/Homework predicting symptom improvement more strongly among patients high in pretreatment anxiety and among patients with relatively few prior depressive episodes.

Conclusions—This is the first study to provide evidence of how therapist adherence is differentially related to outcome among depressed patients with different characteristics. If replicated, these findings may inform clinical decisions regarding the use of specific facets of adherence in CT for depression with specific patients.

*Corresponding author. Tel: +1 440 452 6423; fax: +1 614 688 8261; sasso.9@buckeyemail.osu.edu.

Keywords

therapist adherence; cognitive therapy; moderation

Identifying Moderators of the Adherence-Outcome Relation in Cognitive Therapy for Depression

In order to account for variability in how patients respond to a given treatment, psychotherapy process researchers have examined a number of therapeutic processes hypothesized to cause symptom change. One such process variable, therapist adherence, refers to the degree to which a therapist implements the manual-specified techniques for a given treatment. While a recent meta-analysis failed to find a significant relation of adherence and outcome over a variety of treatments for different disorders (Webb, DeRubeis, & Barber, 2010), studies examining the effects of adherence in cognitive therapy (CT) for depression specifically have each found some evidence of a relation between therapist adherence and subsequent reductions in depressive symptoms (DeRubeis & Feeley, 1990; Feeley, DeRubeis, & Gelfand, 1999; Strunk, Brotman, & DeRubeis, 2010; Strunk, Cooper, Ryan, DeRubeis, & Hollon, 2012). As we highlight in this paper, each of these studies examined the overall adherence-outcome relation without examining whether the strength of this relation varied as a function of patient characteristics. To facilitate a more personalized view of the key ingredients for producing change in psychotherapy, research must examine whether process variables are more or less important for different kinds of patients (Whisman, 2008).

While no empirical research has focused primarily on patient characteristics as potential moderators of adherence-outcome relations in CT for depression, two studies have examined patient characteristics as moderators of the relation between other process variables (competence and the alliance) and outcome in CT for depression. In the study examining therapist competence (Strunk, Brotman, DeRubeis, & Hollon, 2010), the competence-outcome relation was found to vary as a function of three of four moderators examined (i.e., anxiety, age of onset, and chronicity). A stronger competence-outcome relation was evident among patients high in anxiety, with an earlier age of onset and with a chronic form of depression. In the study examining the alliance, Lorenzo-Luaces, DeRubeis, and Webb (2014) examined 23 pretreatment variables as potential moderators of the relation between alliance and subsequent symptom change. After applying the Benjamini-Hochberg correction for multiple tests (Benjamini & Hochberg, 1995), interactions with anxiety and number of prior depressive episodes remained significant, such that the alliance-outcome relationship was stronger among patients with higher levels of baseline anxiety and relatively few prior episodes. In a model testing both interactions simultaneously, only the interaction between alliance and prior episodes remained significant.

While it has often been acknowledged that patient variables may moderate the strength of the adherence-outcome relation (for a discussion, see DeRubeis, Gelfand, German, Fournier, & Forand, 2014), no previous empirical study has focused specifically on examining patient characteristics as potential moderators of this relation in psychotherapy for depression. We

are aware of only two published reports that include tests of pretreatment patient characteristics as moderators of the adherence-outcome relation. In the context of cognitive behavioral therapy for panic disorder, Huppert, Barlow, Gorman, Shear, and Woods (2006) reported an analysis in which therapists' ratings of patient motivation served as a moderator of the adherence-outcome relation, with higher levels of adherence predicting less marked symptom improvements among patients rated as low in motivation and being unrelated to symptoms among patients high in motivation. Similarly, Webb and colleagues (2012) sought to explain differential process-outcome relations among two samples of CT patients by testing an interaction between intake depressive symptom levels and variables that reflected therapist behaviors in the prediction of changes in depressive symptoms. They found a nonsignificant trend for this interaction, such that therapist adherence to concrete (i.e., symptom-focused) CT techniques tended to be more strongly predictive of subsequent symptom improvement for patients who entered treatment with more severe symptoms. Inspired in part by these studies, we examine patient pretreatment variables as potential moderators the relation between therapist adherence and symptom change in CT for depression.

The work we describe in this paper builds on our previous analyses of adherence-outcome relations in the same dataset. Previously, we examined the main effects of within-and between-patient variability in adherence scores on patients' session-to-session symptom severity (Sasso, Strunk, Braun, DeRubeis, & Brotman, 2014). In those analyses, we found higher within-patient variability in therapist adherence to Cognitive Methods at a given session predicted greater next-session symptom improvement ($p = .002$). For the other two aspects of within-patient therapist adherence we examined (i.e., Negotiating/Structuring Activities and Behavioral Method Homework), we did not find a significant relation with next-session symptom change (p -values of .08 and .58 respectively). As we later discuss, focusing on within-patient variability in adherence allows us to rule out any stable patient characteristics as potentially confounding variables. Having characterized the average within-patient adherence-outcome relations, we now turn to considering possible moderators of these relations.

Selecting Potential Moderators of the Adherence-Outcome Relation

As this paper reports the first empirical investigation focused primarily on examining potential moderators of the adherence-outcome relation in CT for depression, our analyses are necessarily exploratory. In light of this and the risk of Type I errors, we chose to limit our focus to six pretreatment patient characteristics selected a priori on the basis of prior research suggesting these characteristics are related to either the course of depression or treatment response. In the absence of more specific evidence, we focused on variables related to patients' prognosis as DeRubeis and colleagues (2014) have recently suggested such variables may be useful for identifying moderators of process-outcome relations. The six pretreatment patient characteristics we selected were: age, sex, depressive symptom severity, number of prior depressive episodes, diagnosis of personality disorder (PD), and anxiety symptom severity.

Older age has been found to predict prolonged time to recovery, poorer treatment outcomes, and higher risk of relapse (Keller, Lavori, Lewis, & Klerman, 1983; Thase et al., 1997). As has been reported in previous analyses of data from the same trial we utilize in this paper, older age predicted a less robust response to either CT or antidepressant medication (see Fournier et al., 2009). Similarly, compared to men, women have been found to be at greater risk for recurrent depression, poorer treatment outcome, and increased reliance on problematic ruminative coping strategies (Solomon et al., 2000; Thase et al., 1997; Nolen-Hoeksema, Parker, & Larson, 1994). With regard to features of patients' depression, higher initial symptom severity is the most well-established moderator of treatment response (Driessen, Cuijpers, Hollon, & Dekker, 2010). Both initial severity and the number of prior major depressive episodes have been found to predict higher rates of relapse and a more chronic course of depression (Thase et al., 1992; Keller et al., 1983, Solomon et al., 1997; McDowell et al., 2004).

As for the remaining two variables (i.e., PD diagnosis and severity of anxiety symptoms), meta-analytic evidence indicates that patients with a PD tend to have a less favorable response to treatment for depression than those without a PD (Newton-Howes, Tyrer, & Johnson, 2006). In a previous report using data from the trial we examine in this study, Fournier and colleagues (2008) found a treatment-by-PD-status interaction, with PD patients experiencing larger symptom reductions in the medication condition and non-PD patients experiencing larger symptom reductions in the CT condition. Severity of patients' anxiety symptoms at intake has also been related to differential therapeutic outcomes, with pretreatment anxiety predicting greater or more rapid changes in depressive symptoms in CT (Forand, Gunthert, Cohen, Butler, & Beck, 2011; Smits, Minhajuddin, Thase, & Jarrett, 2012; Forand & DeRubeis, 2013).

Purpose of This Study

We examine six pretreatment variables as potential moderators of the adherence-outcome relation in CT for depression. Employing the approach we have used in our previous examination of the adherence-outcome relation (Sasso et al., 2014) we focused on the relation of within-patient variability in adherence scores and session-to-session symptom change. This approach offers the following advantages: (1) it rules out possible bias in the adherence-outcome relation due to any stable patient characteristics (Curran & Bauer, 2011; Allison, 2005), and; (2) it examines symptom change over the relatively brief time periods (i.e., the time between one session and the next) early in treatment when symptom change is likely to be great (Feeley et al., 1999) and therapeutic activities are most likely to facilitate symptom improvement (Tang & DeRubeis, 1999; Tang, DeRubeis, Beberman, & Pham, 2005).

Method

Participants

Patients were 57 of 60 adults who were randomly assigned to the CT condition of a two-site (University of Pennsylvania and Vanderbilt University) clinical trial of CT, pharmacotherapy, and placebo for moderate to severe depression (DeRubeis et al., 2005).

The trial was approved by local Institutional Review Boards. All patients had a primary Axis I diagnosis of major depressive disorder and met criteria for a current episode of depression according to the Structured Clinical Interview for DSM-IV diagnosis (SCID-I; First, Spitzer, Gibbon, & Williams, 2001). As our analytic procedures to isolate within-patient variation in adherence scores require at least three observations per patient, three of the 60 patients lacked adequate data for inclusion, resulting in a sample of 57 (Sasso et al., 2014). In this sample, 56% were female with ages ranging from 19 to 68 ($M = 41$, $SD = 11.50$) and depression onset occurred most typically in the mid-20s ($M = 24.42$, $SD = 13.00$). Most patients were Caucasian (77%), with 12% being African American, and 11% being other ethnicities. The majority had at least some college education (14.60 years of education on average). For additional details on sample characteristics, full inclusion and exclusion criteria, treatment protocols, and main clinical outcomes, see DeRubeis et al. (2005).

Therapists—CT was provided by six therapists (two of whom were female), with three therapists being at each site respectively. Therapists were thoroughly trained in CT, with five being licensed Ph.D. level psychologists and one being a psychiatric nurse practitioner (MSN). Of the 57 patients examined, the number per therapist ranged from 8 to 12, with a mean of 9.5. All therapists followed the procedures outlined in standard texts of CT for depression (Beck, Rush, Shaw, & Emery, 1979; Beck, 1995).

Measures

Depressive symptoms—The Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) is a widely used and well-validated 21-item self-report measure. Patients completed the BDI-II prior to each therapy session. In this study, patients' BDI-II scores at each of the first five sessions were used in the assessment of session-to-session symptom change.

Therapist adherence—The Collaborative Study Psychotherapy Rating Scale (CSPRS; Hollon et al., 1988) was used to measure therapist adherence at each of the first four sessions of CT. On any given item, a higher score indicates more extensive therapist engagement in manual-specified CT behavior. We examined therapist adherence to the same three CSPRS subscales reported in Strunk, Brotman, and DeRubeis (2010) and Sasso and colleagues (2014). The subscales were constructed on the basis of a factor analysis of a larger dataset (Strunk et al., 2012). The 9-item Cognitive Methods (CM) subscale evaluates therapists' efforts to help patients identify their automatic thoughts and evaluate the accuracy of these thoughts strategically (i.e., by examining evidence and realistic consequences of thoughts). The 8-item Negotiating/Structuring (NS) subscale evaluates therapists' efforts to structure the therapy session, collaborate with patients, and negotiate therapy content. Finally, the 5-item Behavioral Methods/Homework (BH) subscale evaluates therapists' use of behavioral strategies and therapists' assigning and reviewing of homework, including but not limited to homework involving behavioral interventions.

Six potential moderators—Personality disorder diagnoses were determined at intake using the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II; Spitzer, Williams, Gibbon, & First, 1990). For analyses, we used a categorical variable

reflecting whether or not patients met diagnostic criteria for at least one personality disorder. Anxiety symptom severity was assessed at intake using the Hamilton Rating Scale for Anxiety (HAM-A; Hamilton, 1959). Pretreatment depressive symptoms were assessed at intake using patients' scores on the 17-item Hamilton Rating Scale for Depression, with selected items modified to include the assessment of atypical symptoms (HRSD; Hamilton, 1960; for modification details, see Reimherr et al., 1998). HRSD interviews were conducted by trained assessors (intraclass correlation coefficient = .96; DeRubeis et al., 2005). The number of prior depressive episodes, patients' age, and sex were all assessed at patients' intake evaluation using the SCID-I for DSM-IV Axis I Disorders (First et al., 2001).

Procedure

Two advanced graduate students trained in CT independently observed and rated each therapy session recording. The raters, who were blind to outcome, provided ratings for each of the first four sessions of CT. Therapy sessions were both audio and video recorded. Audio recordings were used when video recordings were unavailable or damaged (for further details on rating procedures, see Strunk, Brotman, & DeRubeis, 2010). As calculated and reported in Sasso and colleagues (2014), random effects intraclass correlation coefficients (ICCs) showed that the two independent raters achieved moderate to strong inter-rater reliability on each adherence scales examined here (ICCs ranging from .60 – .71).

Analytic Strategy

We disaggregated within-patient variation in patients' observed scores on the three adherence subscales (i.e. CM, NS, and BH) using the procedure described in Sasso et al. (2014) and shown here in equation 1. Specifically, for a given adherence subscale we regressed the subscale scores (*represented by z_{ti} in equation 1, where t = session and i = patient*) on session (mean-centered), separately for each patient in the sample using ordinary least squares.

$$z_{ti} = b_{0i} + b_{1i} \text{Session}_{ti} + e_{ti} \quad (1)$$

We then retained the session-specific residuals (e_{ti}) from these models as an estimate of within-patient variation in that subscale. As Curran and Bauer (2011) have argued, this approach “de-trends” any person-specific change in the adherence over time and therefore avoids violating the assumption of stationarity¹ (i.e., no change in the repeated measures predictor across time; Falkenström et al., 2013). We refer to these within-patient adherence scores using the following abbreviations: Cognitive Methods (CM-within), Negotiating/Structuring Activities (NS-within), and Behavioral Methods/Homework (BH-within). For more details on the advantages (and limitations) of the procedure used, please see Sasso et al. (2014).

We then used repeated measures regression models implemented in SAS PROC MIXED to examine predictors of next session depressive symptoms (BDI_{t+1i}). As shown in equation 2,

¹As noted in Sasso et al. (2014), the average slope of change in adherence scores was: significantly positive for Cognitive Methods ($b = .12, SE = .03, t(56) = 3.75, p = .0004$), not significant for Behavioral Methods/Homework ($p = .63$), and significantly negative for Negotiating Structuring ($b = -.08, SE = .03, t(56) = -2.96, p = .005$).

the predictors in these models were: (1) patients' BDI-II scores at the current session (β_1); (2) the study site² (β_2); (3) within-patient variation in the adherence subscale (e_{ti} from equation 1) at the current session (β_3); (4) the moderator (β_4), and; (5) the interaction of the moderator and within-patient-variation in the adherence subscale at the current session (β_5).

$$BDI_{t+1i} = \beta_0 + \beta_1(BDI_{ti}) + \beta_2(Site_i) + \beta_3(e_{ti}) + \beta_4(Moderator_i) + \beta_5[(Moderator_i)(e_{ti})] + \epsilon_{ti} \quad (2)$$

We examined each potential moderator by adherence subscale interaction in a separate model. In these models, we modeled the variance-covariance matrix of repeated BDI-II scores across patients (i.e., the R matrix). While we did not specify random effects in these models, modeling the variance-covariance matrix of patients' repeated dependent variable values is equivalent to a random intercept only model (see Kiernan, Tao, & Gibbs, 2012). For all models (i.e., the model depicted in equation 2), we used maximum likelihood (ML) as the estimation method. We also examined several different covariance structures (viz., autoregressive (AR), heterogeneous AR, compound symmetry, toeplitz, and unstructured) and selected the structure that provided the best fit. Compound symmetry was determined to have the best fit across all information criteria indices.

For any given adherence and moderator combination, a significant interaction would indicate that within-patient variation in the adherence subscale is differentially related to symptom improvement as a function of patients' score on the moderating variable. All continuous predictor variables were mean-centered and dichotomous variables recoded (i.e., plus or minus .5). Within-patient scores did not need to be centered as these scores each had a mean of zero. We corrected for multiple comparisons using the Benjamini-Hochberg approach (Benjamini & Hochberg, 1995; false discovery rate of $p < .05$ for each set of 6 tests; with one set for each of 3 adherence subscales). To probe the interactions, we applied the Johnson-Neyman (J-N) technique to identify cut-points in the moderator at which the relation of the predictor (i.e., adherence) variable and outcome (i.e., next session BDI-II scores) changes from statistically significant to non-significant (see Preacher, Curran, & Bauer, 2006).

Results

Descriptive statistics for the pretreatment variables of interest are provided in Table 1. Before testing our primary moderation models, we examined the role of therapist and the magnitude of symptom improvement across the early sessions. In comparing the fit of models in which therapist was or was not included as a random effect (as described by West, Welch, & Galecki, 2007), we found that the inclusion of therapist failed to significantly improve fit. In addition, modeling therapist as a random effect failed to change the statistical significance of any of the interactions of interest in our primary repeated measures regression models (equation 2). To examine the magnitude of symptom change experienced,

²Site was included as a fixed effect in all analyses as the primary outcome paper reporting on this trial found a significant site by treatment interaction. In our primary models (see equation 2), site was not significant (all $ps > .2$). Additional analyses failed to show evidence of any adherence by site interactions (all $ps > .4$). Finally, each of the three significant adherence by moderator interactions that survived the correction for multiple comparisons were significant in models in which site was not included as a predictor (and survived the same multiple comparison correction).

we first compared BDI-II scores in sessions 1 and 5. This revealed an average improvement of 5.2 points ($t(48) = 5.92, p < .0001$, using a paired t-test; $d = .56$). As shown in Table 2, the average session-to-session change for the four intervals we studied ranged from $-.2$ to 2.4 , with the SDs around those means ranging from 4.7 to 5.9 . It is the variability in BDI scores across these early session-to-session intervals that we are attempting to account for in our primary models. Specifically, these models examine how variability in BDI-II improvement from session-to-session might be predicted by the interaction of patients' pretreatment characteristics and specific forms of therapist adherence.

After conducting our primary moderation analyses for each moderator by adherence subscale combination (see equation 2) and correcting for multiple comparisons, three interactions remained significant (detailed results provided in Online Supplement A). All other interactions were either non-significant or failed to survive the correction.³ In the first of the significant interactions, patient sex moderated the relationship between CM-within and next-session symptom change (see Figure 1). Higher than expected adherence to Cognitive Methods at a given session significantly predicted a greater next-session symptom reduction for women (simple slope of CM-within on next-session symptoms $b = -6.50$, $SE = 1.51$, $t = -4.30$, $p < .001$, where female coded as $-.5$), and was unrelated to next-session symptom change for men (simple slope of CM-within on next-session symptoms $b = -.22$, $SE = 1.61$, $t = -.14$, $p = 0.89$, where male coded as $.5$). In the second and third interactions, both anxiety symptoms (see Figure 2) and number of prior episodes (see Figure 3) moderated⁴ the relationship between BH-within and next-session symptom change. Higher than expected adherence to Behavioral Methods/Homework at a given session predicted a greater improvement in symptoms at the next-session for patients who were high in pretreatment anxiety and had fewer prior depressive episodes. Because we identified multiple interactions involving BH-within, we also examined a model containing BH-within, anxiety symptoms, number of prior episodes, and interaction terms for each of the two moderators with BH-within. In this model, anxiety severity remained a significant moderator of the relation between BH-within and next-session symptom change ($t(153) = -2.31$, $b = -.44$, $SE = .19$, $p = .02$) as did number of prior episodes ($t(153) = 2.43$, $b = 1.40$, $SE = .58$, $p = .02$).

There were no significant main effects of any patient characteristics in the three models in which we found a significant interaction. Across all of the primary models (i.e., equation 2), only PD status exhibited a main effect on session-to-session symptom change, with PD status being related to less marked symptom improvement. This main effect of PD was comparable across all three adherence subscale models (bs ranged from 1.04 – 1.06 ; all $ps < .05$). To place our results in context, we also examined the relation of patient characteristics and raw adherence scores. Adherence scores were remarkably unrelated to patient

³While not a primary focus, we also examined the patient specific intercepts shown in equation 1 (b_{0i}) in place of within-patient adherence scores in our primary moderation analyses (equation 2). Following the correction for multiple tests, no significant interactions emerged for any combination of patient characteristics and average adherence scores (i.e., intercepts).

⁴In a supplementary analysis to examine whether the three interactions that survived the correction were specific to therapist adherence, we examined sex, prior episodes, and anxiety severity as moderators of the relation among within-patient variation in alliance total scores and session-to-session symptom change. None of the interactions were significant (all $ps > .16$; for details on the alliance ratings utilized, see Strunk, Brotman, & DeRubeis, 2010).

characteristics. When examining these correlations separately at each session, only 3 of 72 tests (< 5%) were statistically significant, none involving our significant moderators (see Online Supplement B). Thus, for the three significant interactions we identified, there were no main effects for the patient characteristics involved and adherence scores were quite independent of these patient characteristics.

We used the J–N technique (Preacher et al., 2006) in order to identify the regions of significance for HAM-A and prior episodes in which the effect of BH-within on symptom change was significantly negative, non-significant, or significantly positive. To characterize the effects obtained, we then recoded our continuous prior episodes and HAM-A variables based on the cut points for these regions of significance. We then ran the two interaction models for prior episodes and HAM-A using these categorical variables and calculated the simple slopes of BH-within on symptom change for each different category of HAM-A, and each category of the prior episodes variable, as identified by the regions of significance. These models involved predicting the BDI-II score at the beginning of the next session, controlling for the BDI-II score obtained just before the start of the session that was the basis of the BH-within score. As a result, the simple slopes we report characterize the relation of the adherence score and the BDI-II score for the next session after statistically controlling for prior session BDI-II scores.

For the interaction involving prior episodes, we identified 1.5 to 4.1 as cut-points for the region of prior episodes values outside of which the simple slope of BH-within on next-session symptom change is statistically significant. We recoded our continuous prior episodes variable accordingly. The first region included 22 patients with zero to one prior episode, the second region included 22 patients with two to three prior episodes, and the third region included 13 patients with four or more prior episodes. When we re-ran the interaction model using this categorical prior episodes variable⁵ and calculated the simple slope of BH-within in these regions, we found the following: higher BH-within scores at a given session predicted a significantly greater next-session symptom improvement among the subgroup of patients with zero or one prior episode (simple slope $b = -4.71$, $SE = 1.51$, $t = -3.13$, $p = .003$), were unrelated to symptom improvement among patients with two or three prior episodes (simple slope $b = -.28$, $SE = .84$, $t = -.33$, $p = .74$) and predicted less symptom improvement among patients with four or more prior episodes (simple slope $b = 4.16$, $SE = 1.61$, $t = 2.58$, $p = .01$).

For the interaction involving intake HAM-A, we identified 10.11 to 18.11 as cut-points for the region of HAM-A scores outside of which the simple slope of BH-within on next-session symptom change is statistically significant and recoded our continuous HAM-A variable accordingly. The first region included 8 patients with HAM-A scores ≤ 10 , the second region included 31 patients with scores ranging from 11 to 18, and the third region included 18 patients with scores ≥ 19 . When we re-ran the interaction model using this categorical HAM-A variable, and calculated the simple slope of BH-within in these regions,

⁵It is important to note that we still rely on the continuous prior-episodes and HAM-A variables for our primary tests of interaction effects; however, since we rely on categorical variables in order to characterize the effects of these interactions in the different regions of significance, we note here that both the prior episodes*BH-within and HAM-A*BH-within interactions were still significant predictors of next-session symptom change when the categorical variables were used ($p = .001$ and $.001$ respectively).

we found the following: higher BH-within scores at a given session predicted significantly weaker next-session symptom improvement among patients with the lowest pretreatment anxiety severity scores (simple slope $b = 5.29$, $SE = 1.97$, $t = 2.69$, $p = .01$), were unrelated to symptom improvement among patients with average levels of anxiety (simple slope $b = .54$, $SE = .89$, $t = .60$, $p = .55$) and predicted greater symptom improvement among patients high in pretreatment anxiety (simple slope $b = -4.22$, $SE = 1.42$, $t = -2.96$, $p = .005$).

Discussion

After correcting for the risk of false discovery, our examination of six potential moderators of the relation of three facets of adherence to symptom change in CT for depression identified three instances of moderation. Specifically, the relation between CM-within and next-session symptom change varied as a function of sex, and the relation of BH-within and symptom change varied as a function of both anxiety symptoms and patients' number of prior depressive episodes. After correcting for multiple tests, we failed to find any evidence that the relation between NS-within and next-session symptom change varied as a function of the pretreatment patient characteristics we examined. As all of our models controlled for patients' current BDI-II scores in predicting their next session BDI-II scores, these interactions cannot be attributed to patients' current symptom-severity. Furthermore, because we examined within-patient variability in adherence specifically, our results cannot be attributed to any stable patient characteristics we may have failed to include in our models. Insofar as the moderating effects we identified are robust, the evidence we obtained suggests that previous characterizations of adherence-outcome relations without consideration of individual patient characteristics failed to account for important systematic variability in adherence-outcome relations across patients.

We found that for women, higher within-patient therapist adherence to CM at a given session predicted greater next session symptom improvement; whereas for men, it was unrelated to next session symptom improvement. While to our knowledge, this is the first finding suggesting that therapists' use of cognitive strategies may have different consequences for men and women, there is other evidence that cognitive vulnerabilities are differentially related to outcomes in men and women. In two studies examining the relation of pessimistic biases in the prediction of future life events and depressive symptoms, bias was found to be more strongly related to depressive symptoms among women than men (Strunk, Lopez, & DeRubeis, 2006; Strunk & Adler, 2009). Our finding that therapist adherence to CM predicts a significant reduction in next-session symptoms among women suggests one of two possibilities. First, these methods may be particularly well-suited for targeting and changing the maladaptive thinking patterns underlying the pessimistic biases common among depressed women. Second, even if the methods are similarly effective in producing cognitive change, such cognitive change may be more likely to impact symptoms among women as compared to men. While our data do not allow us to tease apart these possibilities regarding the mechanisms of effects, the results do suggest that cognitive methods predict symptom change differentially among women and men. As Fournier and colleagues (2009) examined the sample currently under investigation and found no sex differences in symptom change across the 16 weeks of CT and we found no sex differences in early symptom change, it is possible that other aspects of treatment might account for

change in men. Alternatively, it is possible that CM-adherence scores do not adequately differentiate Socratic vs. didactic use of cognitive strategies and men respond to a more Socratic style. We await future studies that aim to replicate the results presented here or test these notions experimentally.

In the second of the three interactions we identified, within-patient variation in therapist adherence to BH predicted symptom change differentially as a function of pretreatment anxiety. BH-within predicted symptom change most strongly among patients high in pretreatment anxiety. Among those with the lowest levels of pretreatment anxiety, higher BH-within at a given session predicted a smaller degree of next-session symptom change. Previous research on the role of anxiety among patients in CT may aid in our understanding of such relations. In the sample currently under investigation, Forand and DeRubeis (2013) found that patients higher in anxiety showed more rapid early (i.e., up to week 8 of acute treatment) change in depressive symptoms but also greater vulnerability to relapse than those low in pretreatment anxiety. As noted previously, Strunk, Brotman, DeRubeis, and Hollon (2010) found that the relation between therapist competence and early subsequent symptom change was largest among highly anxious patients. In considering these findings with our results, it may be that increased adherence to BH is most effective for highly anxious patients because their depressive symptoms are particularly responsive to the specific behavioral strategies it represents (i.e., effect of enhancement in treatment specific mechanisms).

In the final interaction identified, we found that higher BH-within predicted symptom change differentially as a function of patients' number of prior depressive episodes. Higher BH-within was most strongly predictive of symptom change among patients with zero or one prior depressive episodes and was related to less symptom change for patients with four or more prior episodes. The relation of stressful life events and risk of depressive recurrence varies as a function of number of depressive episodes, with the relation being smallest among patients with the largest number of episodes (Monroe & Harkness, 2005). As such, environmental factors and intervention strategies leveraging such factors might be expected to have more limited effects among patients with more prior episodes (for a discussion of this issue, see Lorenzo-Luaces et al., 2014). Consistent with this line of reasoning, interventions focused primarily on changing patients' cognitive vulnerabilities (i.e., Mindfulness-Based CT and cognitive group therapy for the prevention of relapse / recurrence) have been found to have the greatest long-term benefits for patients with more prior episodes of depression (Bockting et al., 2005; Bockting, Spinhoven, Wouters, Koeter, & Schene, 2009).

As one considers evidence of stronger adherence-outcome relations among certain patients, it is important to consider that the moderating relations we found also identified groups of patients for whom adherence was remarkably unrelated to symptom change. What accounts for the symptom improvement observed among these patients? As Fournier and colleagues (2009) examined the sample currently under investigation and found no differences in symptom change across the 16 weeks of CT as a function of baseline HAM-A scores or prior depressive episodes, and we found no evidence of significant differences in symptom change across the first five sessions among these patients, other aspects of treatment must

account for how these patients managed to achieve comparable outcomes. With this in mind, we looked at therapists' relative adherence to CM vs. BH (see Online Supplement C) to try to identify the strategies that are beneficial for these patients (i.e., those with more prior episodes or lower anxiety). As detailed in the supplement, we found that for patients low in initial anxiety and higher in prior depressive episodes, a tendency to adhere more to CM than to BH at a given session predicted greater next-session symptom improvements. This suggests that therapists might be able to maximize outcome by utilizing more cognitive methods in working with patients for whom behavioral methods / homework were not predictive of greater symptom improvements. We regard these supplementary analyses as preliminary. If replicated in future studies, these effects could be used to aide clinicians in deciding whether to focus more on cognitive vs. behavioral techniques early in treatment.

Limitations

It is important to note a few key limitations of this study. As adherence was not experimentally manipulated, we cannot establish a definitive causal relationship between the adherence and outcome. However, by focusing on within-patient variation in the patients' adherence scores, we were able to rule out any stable third variables as alternative explanations for the relations we identified. What we still cannot rule out is the possibility that an unanticipated *time-varying* characteristic accounted for the significant interactions obtained.

Although we were selective in choosing moderators to examine, our hypotheses regarding their interactions with the three subscales of adherence were exploratory and we stress the need to replicate these findings. Additionally, given our sample size, we may have been inadequately powered to detect some interactions of patient characteristics and adherence. Our test of initial depressive symptom severity may have also suffered from a restriction of range as only moderately to severely depressed outpatients were eligible to participate. Our sample size may have also limited our ability to detect therapist effects. Future investigations in larger samples are needed to address these issues. As our analyses focus on early sessions of CT for depression specifically, the significant interactions obtained may not generalize to later sessions or to other forms of treatment. We did not examine the possibility that "delayed effects" influenced symptom change (i.e., as these effects do not conform to our one-lag session-to-session model, see Sasso et al. (2014) for further discussion on this issue). Lastly, our analyses of within-patient adherence relied on adequate variability in these scores (Sasso et al., 2014). This means that the non-significance of any of the interaction terms may have been partly a function of limited variability in within-patient scores. Future studies using data simulations are needed to evaluate the power to detect interactions terms such as those we examined.

Conclusions

To our knowledge, this is the first empirical investigation to examine potential moderators of the adherence-outcome relation in psychotherapy for depression, and in CT for depression specifically. Our results showed that therapist adherence to Cognitive Methods early in treatment may be particularly predictive of next-session symptom reductions when working with women. Therapist adherence to Behavioral Methods/Homework was particularly

predictive of next-session symptom reductions for patients high in anxiety and those with fewer prior depressive episodes. These findings lead us to consider several clinical implications. First, when adhering to Cognitive Methods, it may be important for therapists to consider patients' sex. Future research is needed to identify whether and what types of cognitive approaches are most beneficial for men. Additionally, our findings raise the possibility that therapists could maximize outcome by utilizing fewer behavioral strategies (and perhaps more cognitive strategies) for patients with a larger number of prior episodes and those low in anxiety. We encourage future research examining moderators of adherence-outcome relations so that efforts to adapt psychotherapy to specific patients can be better informed by research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Public health significance

This study suggests that therapist adherence in cognitive therapy for depression is not uniformly related to outcome across all patients. The relation of specific aspects of adherence and outcome varied as a function of patients' sex, level of pretreatment anxiety, and prior depressive episodes. If replicated, these findings will facilitate personalizing the delivery of cognitive therapy on the basis of patient characteristics.

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Figure 1.

Association between Therapist Adherence to Cognitive Methods-Within and Next-Session Symptom Change Across Patient Sex

Note: High and low values of within-patient Cognitive Methods scores are ± 1 SD from the mean (CM-within $M = 0$, $SD = .33$) Results depicted were obtained using a model such as that shown in equation 2 with one modification: patients' next-session BDI-II scores ($M = 24.1$) were centered to zero. Plotted values represent deviations from the mean in BDI-II units. Gender was coded as Female = $-.5$ and Male = $.5$.

Figure 2.

Association between Therapist Adherence to Behavioral Methods/Homework-Within and Next-Session Symptom Change Across Anxiety Severity

Note: Results depicted were obtained using a model such as that shown in equation 2 with one modification: patients' next-session BDI-II scores ($M = 24.1$) were centered to zero. Points plotted represent deviations from the mean BDI-II scores for patients with scores of ± 1 SD from the mean on the Hamilton Rating Scale for Anxiety (HAM-A) and ± 1 SD from the mean of Behavioral Methods / Homework-within patient. For the HAM-A, the low and high values are 10.6 and 22.8, respectively. For the Behavioral Methods / Homework-within, the low and high values are $-.43$ and $.43$, respectively.

HW = homework.

Figure 3.

Association between Therapist Adherence to Behavioral Methods/Homework-Within and Next-Session Symptom Change Across Prior Depressive Episodes

Note: Results depicted were obtained using a model such as that shown in equation 2 with one modification: patients' next-session BDI-II scores ($M = 24.1$) were centered to zero.

Points plotted represent deviations from the mean BDI-II scores for patients with scores of ± 1 SD from the mean on prior episodes and ± 1 SD from the mean of Behavioral Methods / Homework-within patient. For the prior episodes, the low and high values are .41 and 4.02, respectively. For the Behavioral Methods / Homework-within, the low and high values are $-.43$ and $.43$, respectively.

HW = homework.

Table 1

Descriptive Statistics for the Six Pretreatment Variables Examined as Moderators of the Within-Patient Adherence-Outcome Relationships

	Mean	%	(SD)	N
Age	40.5	-	11.5	-
Female %	-	56%	-	32
HRSD at intake	24.0	-	3.4	-
Number of prior depressive episodes	2.2	-	1.8	-
Anxiety severity – HAM-A (0 – 48)	16.7	-	6.1	-
Personality disorder %	-	44%	-	25

Note. N = 57. HRSD – Hamilton Rating Scale for Depression. All values above reflect Mean and SD of un-centered variables. N reflects the number of patients in the sample who were female and had a Personality Disorder diagnosis respectively.

Table 2

Descriptive Statistics for Patients' BDI-II Scores Across Sessions 1 Through 5

BDI-II scores at each session, M (SD)		Improvement in BDI-II scores for each session-to-session interval, M (SD) of differences	
Session 1	28.3(9.0)		
Session 2	25.8(9.3)	Session 1–2	2.4(4.7)
Session 3	24.7(10.3)	Session 2–3	1.1(4.7)
Session 4	22.7(11.1)	Session 3–4	1.9(5.0)
Session 5	22.9(10.6)	Session 4–5	–.2(5.9)

Note: Improvement scores are mean differences in patients' BDI-II scores at the earlier of the two sessions minus their score at the following session. A positive value reflects a decrease in self-reported symptom severity.