Predicting Response to Depression Treatment: The Role of Negative Cognition

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Repeated experiences with major depressive disorder (MDD) may strengthen associations between negative thinking and dysphoria, rendering negative cognition more accessible and pronounced with each episode. According to cognitive theory, greater negative cognition should lead to a more protracted episode of depression. In this study of 121 adults with MDD, number of previous episodes was associated with slower change in depression across inpatient and outpatient treatment. Further, although pretreatment negative cognition and pretreatment family impairment both uniquely predicted slower change in depressive symptoms, only negative cognition mediated the association between depression history and depression change. Findings suggest that repeated MDD episodes are specifically associated with increased negative cognition, which in turn contributes to a more pernicious course of symptom change during treatment for depression.

Keywords: treatment response, mediators, negative cognition, depression

Several decades ago it was observed that treatment response often varies across individuals (i.e., the patient uniformity myth; Kiesler, 1966). Despite this recognition, relatively few studies have examined how symptoms change during depression treatment, and perhaps more important, few studies have identified predictors of symptom change. Such analyses are critical because they provide information about who is most likely to benefit (or not) from treatment. Identifying such individuals may be particularly important for depression, as treatments are only effective for approximately two thirds of those who receive them (Hollon, Thase, & Markowitz, 2002). The purpose of the present study was to examine whether depression recurrence predicts poor treatment response and, if so, to identify factors that explain this relationship.

There is considerable evidence suggesting that number of previous episodes of depression will predict treatment response. In naturalistic, longitudinal studies, depression history is often correlated with the duration of the current episode, with more prior episodes predicting longer episode duration (D. A. Solomon et al., 1997). More prior episodes also predict rates of relapse leading to hospitalization and whether patients receive antidepressant medication (Kessing, Hansen, & Andersen, 2004). Moreover, Reynolds et al. (1998) reported that age at first onset of depression among an elderly sample was associated with a slower speed of remission from the index depressive episode during pharmacologic treatment. The authors speculated that age at first onset could be a proxy for number of previous depressive episodes. Similarly, Klein et al. (1999) found that depression history was a significant predictor of symptom course among people with chronic depression.

Although the association between depression history and symptom course is well established, considerably less research has sought to explain this relationship. Cognitive models of depression offer one possible explanation. Specifically, the differential activation hypothesis (Teasdale, 1988) states that depression is maintained by negatively biased information processing. Depressed mood states can facilitate negative information processing by increasing accessibility to negative beliefs and memories, negatively biasing how situations are perceived and interpreted, and negatively influencing expected outcomes for future events. These cognitive biases, in turn, serve to reinforce a depressed mood. Mutual entrainment between negatively biased information processing and depressed mood serves to create a persistent depressed mood that contributes to the onset and maintenance of a depressive episode.

Building on work by Post (1992), Segal, Williams, Teasdale, and Gemar (1996) have argued that repeated episodes of depression may cognitively sensitize an individual, such that each episode serves to reinforce the mutual entrainment between information processing bias and depressed mood. Strengthening this association then facilitates activation of and accessibility to negative thinking patterns in the presence of depressed moods. With repeated episodes, negative cognition becomes more closely associated and tightly interconnected. The activation of one element within this associative network can then lead to the activation of others. In a highly sensitized individual, one negative thought is likely to activate a wide variety of related negative thinking. Thus, a person who has experienced many episodes of depression will likely experience more dysfunctional thinking than someone who has experienced fewer episodes of depression. As predicted by the differential activation hypothesis (Teasdale, 1988), greater activation of negative cognition should serve to maintain an episode of depression.
This conceptualization suggests a mediational model for understanding symptom change: Repeated episodes of depression should lead to greater negative cognition, which in turn should predict a more pernicious course of depressive symptoms. The purpose of this study was to test this idea within the context of depression treatment. Specifically, we first modeled initial depression severity and depression symptom change during treatment using latent growth curve analyses. Once we established the best fitting model for symptom change, we then examined whether negative cognition mediated the relationship between depression history and symptom change during treatment. To test the specificity of this model, we also examined whether family functioning, another factor thought to contribute to a poor course of symptoms, also mediated the effect of depression history on symptom change. Although family impairment has been shown to predict poorer symptom change (Miller et al., 1992), there is limited evidence that family functioning is influenced by repeated episodes of depression. Thus, we expected negative cognition to be a specific mediator of the link between depression history and change in depressive symptoms.

Method

Design

The present study is a secondary analysis of a study examining the efficacy of combined pharmacological and psychosocial treatments for the posthospital care of patients with severe depression (Miller et al., 2005). Because the methodology of the treatment study has been described in more detail elsewhere (Miller et al., 2005), we will provide only a brief summary. Patients were recruited during admission to a psychiatric hospital. Hospital treatment consisted of pharmacotherapy and milieu treatment. Average length of inpatient treatment was 2 weeks. Following discharge, participants were randomized to 6 months of outpatient pharmacotherapy or pharmacotherapy plus psychosocial treatment. Participants were randomized to outpatient treatment regardless of their symptom severity at the end of inpatient treatment. The psychosocial treatments provided were family (Epstein & Bishop, 1981), cognitive–behavioral (Beck, Rush, Shaw, & Emery, 1979), or combined cognitive–behavioral and family treatment. Participants were randomized to treatments that either matched or mismatched patients’ pattern of cognitive distortion and family impairment. Miller et al. (2005) reported that matched treatment led to significantly more improvement in depressive symptoms among patients who were symptomatic at discharge from hospitalization. They also found that patients who received family treatment also reported greater symptom improvement compared with those who received other forms of treatment.

Because the current article is a secondary analysis, it is important to identify how this article differs from findings reported in the original outcome study. Analyses within the current article differ from the Miller et al. (2005) study in a number of ways. First, to investigate differences in efficacy between outpatient treatments, Miller et al. (2005) focused on differences between randomized outpatient treatments for individuals who were symptomatic at discharge from inpatient hospitalization. Because the current study was focused on predictors of treatment response regardless of treatment received, we used the full sample of participants (N = 121), all of whom were symptomatic upon study entry. We then examined predictors of subsequent symptom change. That is, we used information collected prior to inpatient treatment (i.e., negative cognition and depression history) to predict symptomatic change from hospital admission to the end of outpatient treatment. By including data collected during inpatient and outpatient treatment, we obtained a comprehensive assessment of depression change. Further, all participants were randomly assigned to outpatient treatment regardless of their depression severity at discharge from hospitalization. This allowed us to easily account for the effect of treatment on change in depression over time, if necessary. Most important, the Miller et al. (2005) study did not focus on predictors of treatment response, but instead focused on the effect of treatment on symptom change and end-point functioning.

Participants

Participants consisted of 121 patients admitted to a private psychiatric hospital. Upon admission, all participants (a) met criteria for major depressive disorder according to the Structured Clinical Interview for DSM–III–R diagnoses, patient version (SCID–P; First, Spitzer, Williams, & Gibbon, 1995); (b) had Modified Hamilton Rating Scale for Depression (MHRSD; Miller, Bishop, Norman, & Maddever, 1985) and Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) scores greater than 17; (c) were between 18 and 65 years of age; (d) had sufficient reading skills to complete questionnaires; (e) were currently living with one or more family members; and (f) along with their family, provided informed consent to participate in the project. Patients were excluded from the study if they (a) met DSM–III–R criteria (Spitzer, Williams, Gibbon, & First, 1990) for bipolar disorder, alcohol or drug dependence, somatization disorder, or schizophrenia; (b) met criteria for dementia or displayed significant cognitive impairment; or (c) presented with a medical illness severe enough to contraindicate antidepressant medication.

Measures

MHRSD (Miller, Bishop, et al., 1985). The 17-item MHRSD is a widely used interview-based measure of depression severity with acceptable reliability and validity (Miller, Bishop, et al., 1985). The MHRSD has been demonstrated to have excellent interrater reliability and to correlate highly with the original Hamilton Rating Scale for Depression (Miller, Bishop, et al., 1985). Assessors for this study were trained clinical raters.

The MHRSD was completed upon admission for inpatient treatment, upon discharge from inpatient treatment, and on a monthly basis during a 6-month course of outpatient treatment. Assessments conducted during the inpatient phase were completed in person. Monthly MHRSD assessments were conducted by telephone. Phone assessments were completed to reduce participant burden and subsequently to minimize missing data given the frequent assessments (i.e., monthly). Research suggests that depression assessments conducted via the phone produce very similar results to those conducted in person (Simon, Revicki, & VonKorff, 1993). Indeed, in a subset of participants from the current study (n = 99), the correlation between an MHRSD interview conducted via the phone and in person at the end of treatment was .83.
Depression history. Number of previous depressive episodes was obtained during the mood disorders module of the SCID–P interview. Interviewers were careful to ensure that episodes were discrete (i.e., separated by at least 2 months). A subset of participants was unable to recall the number of previous episodes (n = 20). Maximum-likelihood (ML) procedures (see below for further detail about these methods) were used to estimate values for individuals who could not recall their depression history. Those who could not recall the number of past episodes did not differ in patient age, gender, or length of stay in the hospital (ps > .14). However, they were more depressed at admission to the hospital (MHRSD: M = 27.10, SD = 4.19, vs. M = 23.60, SD = 4.52), F(1, 119) = 10.02, p < .05, and tended to be younger at the onset of their first MDD episode (years of age: M = 21.90, SD = 11.21, vs. M = 29.08, SD = 13.04), F(1, 119) = 5.30, p < .05.

Disfunctional Attitudes Scale (DAS; Weissman, 1979). The DAS Form A has 40 statements to which participants respond on a 7-point scale (i.e., totally agree, agree very much, agree slightly, neutral, disagree slightly, disagree very much, and totally disagree). The DAS assesses dysfunctional beliefs that are thought to reflect a person’s self-evaluation. DAS items measure concerns about approval from others, prerequisites for happiness, and perfectionist standards. The DAS has been used widely in depressed and psychiatric control populations (Oliver & Baumgart, 1985). The DAS has good internal consistency (α = .85; Oliver & Baumgart, 1985) and test–retest correlation of .84 over an 8-week period (Weissman, 1979). Internal reliability in the current study was very good (α = .91).

Cognitive Bias Questionnaire (CBQ; Krantz & Hammen, 1979). The CBQ was used to assess negatively biased, self-referent information processing. The CBQ presents four vignettes (8 to 12 sentences each) that are ambiguous in outcome (e.g., employer gives potentially negative feedback on employee’s work). Participants imagine themselves in each situation and then select one of four response options to four questions per vignette. Options for each question represent depressed–distorted, nondepressed–distorted, depressed–nondistorted, and nondepressed–nondistorted cognitive styles. The current study was consistent with previous studies in that it focused on the Depressed–Distorted subscale, which has exhibited good reliability and validity (Krantz & Hammen, 1979; Miller & Norman, 1986; Norman, Miller, & Klee, 1983). Internal reliability in the present sample was adequate (α = .80).

Hopelessness Scale (HS; Beck, Weissman, Lester, & Trexlter, 1974). The HS is a 20-item true–false self-report questionnaire that assesses participants’ negative expectations regarding the future. Scores on the HS range from 0 to 20, with higher scores indicating higher levels of hopelessness. The HS has high internal reliability, is moderately correlated with depressive symptoms, and has been shown to prospectively predict suicide attempts (Beck, Brown, Berchick, Stewart, & Steer, 1990). Internal reliability in the present study was good (Kuder–Richardson 20 = .92).

Family Assessment Device (FAD; Epstein, Baldwin, & Bishop, 1983). The FAD is a 60-item self-report questionnaire that assesses six areas of family functioning, including problem solving, communication, roles, behavior control, affective responsiveness, affective involvement, and overall functioning. The FAD has good psychometric properties (Byles, Byrne, Boyle, & Offord, 1988; Kabacoff et al., 1990; Miller, Epstein, Bishop, & Keiter, 1985) and cutoff scores that discriminate between families rated as healthy and dysfunctional by experts (Miller, Epstein, et al., 1985). The General Functioning subscale of the FAD was used for the purposes of the present study. Internal reliability for this subscale in the current study was good (α = .82).

McMaster Structured Interview for Family Functioning (McSIFF; Bishop, Epstein, Keiter, Miller, & Zlotnick, 1980). The McSIFF is a structured interview that was designed to assess problem solving, communication, roles, behavior control, affective responsiveness, affective involvement, and overall functioning. The McSIFF is scored with the McMaster Clinical Rating System (MCRS; Miller et al., 1994). The MCRS is a seven-item rating scale that includes ratings of each of the six dimensions as well as an overall global functioning score. Each of the dimensions is rated on a 7-point scale; a 1 represents most unhealthy or disturbed functioning, and a 7 represents the most healthy or effective functioning possible. The MCRS has acceptable interrater and test–retest reliability (Miller et al., 1994). The MCRS also shows good correspondence with the self-report FAD (Fristad, 1989; Hayden et al., 1998; Miller et al., 1994) and with independently rated family behavior (Hayden et al., 1998). The McSIFF takes approximately 90 min to administer. For the purposes of the present study, the Overall Functioning scale was used. In addition, to be consistent with the FAD scoring, we reverse scored McSIFF scores so that higher scores represent more family impairment.

Timing of Assessments

The SCID–P, MHRSD, DAS, CBQ, HS, FAD–Global Functioning, and McSIFF assessments were conducted at hospital admission. All 121 participants completed these assessments. MHRSD assessments were also completed upon discharge from inpatient treatment (and prior to outpatient treatment) and then in monthly intervals during the 6 months of outpatient treatment. Of the 121 participants, 121, 119, 114, 108, 103, 104, and 100 completed MHRSD assessments at discharge from inpatient treatment and Months 1–6, respectively.

Missing Data

ML estimation was used to estimate missing data (Little & Rubin, 1987). A recent review suggested that ML is a “state-of-the-art” procedure for estimating missing data (Schafer & Graham, 2002). This approach assumes that data missing at random can be estimated by nonmissing data. This technique uses all available raw data for each participant and estimates missing data with the use of multiple imputation procedures. See Little and Rubin (1987) for more detail on ML estimation procedures. Across all variables used in the current analyses, less than 9% of the data were missing. The patterns of missing data in the current study were consistent with the assumption that the data are missing at random, as determined by Little’s (1988) MCAR test, χ²(192) = 194.87, p = .43. ML was thus an appropriate estimator for our missing data.

Statistical Model

Latent curve analysis (LCA; Curran & Hussong, 2002) was used to model change in depression over time. LCA uses structural equation modeling (SEM) to estimate the intercept and slope...
(often referred to as latent growth trajectory) for repeated measurements collected from the same individual over time. Because SEM methods were used, observed intercepts and slopes were not assessed. Rather, unobserved latent variables thought to underlie the observed intercept and slope were computed.

One benefit of LCA is that different growth curve trajectories (e.g., linear, quadratic, nonlinear) can be modeled for the same data. Fit indices can then be compared among models, and the model that provides the best fit can be established. This process helps to determine the type of symptom change that best fits the data. Several indices are used to determine quality of model fit. The most commonly used are chi-square, comparative fit index (CFI), root-mean-square error of approximation (RMSEA), and standardized root-mean-square residual (SRMR). Model fit that includes a chi-square/degree of freedom < 2, CFI ≥ .90, RMSEA ≤ .10, and SRMR ≤ .08 is generally acceptable (see Kline, 1998). These criteria were used in the present study.

Once the best-fitting model has been established, the latent intercept and slope become the focus of subsequent analyses. For instance, we first examined whether depression history was associated with initial depression severity (latent intercept) and change in depression over time (latent slope). We then examined whether other latent variables, specifically negative cognition and family functioning, could explain associations between depression history and the depression intercept and slope. If support for mediation is found, additional analyses can be completed to determine whether full or partial mediation provides a better fit for the data.

In the context of intervention research, two types of variables related to treatment outcomes are predictors and moderators (Kraemer, Wilson, Fairburn, & Agras, 2002). Predictors and moderators are assessed prior to treatment and alter treatment response. Predictors alter treatment response regardless of treatment modality. Moderators alter treatment outcome for specific interventions.

Results

Patient Characteristics

See Table 1 for descriptive statistics of participant and treatment characteristics. Participants were predominantly female, middle aged, Caucasian, and high school educated. On admission, patients exhibited high levels of depression (MHRSD M = 24.18, SD = 4.46) and reported an average of 3.50 previous episodes of depression in their lifetime (SD = 3.17). Average length of hospital stay for the current episode was approximately 2 weeks. Following discharge from the hospital, the majority of patients received combined pharmacological and psychosocial treatment. Most patients completed a full course (6 months) of outpatient treatment.

Descriptive Statistics

Correlations among depression severity assessments ranged from moderate to strong (see Table 2). Negative cognition assessments were strongly associated with each other, as were family functioning assessments. Negative cognition and family functioning were only moderately associated with each other. Associations between pretreatment cognitive functioning and depression severity tended to become stronger as the interval between assessments increased. Finally, number of previous episodes of MDD was moderately associated with the negative cognition assessments and weakly associated with family functioning.

LCA for Depressive Symptoms

Linear model. We first examined whether a linear trajectory in depressive symptoms provided a good fit for the data. To do so, we tested a latent growth model with two latent variables, an intercept and a linear slope. Each latent variable had direct effects that emanated to each assessment of depression severity. For the latent intercept variable, each path was set to 1. For the linear slope, each of the seven assessments was given a value that corresponded with the assessment period and ranged from 0 to 7. Therefore, the admission MHRSD was assigned the value of 0, discharge MHRSD was assigned a value of 1, Month 1 MHRSD was assigned a value of 2, and so on through Month 7. This linear model of depression growth did not fit the data well, $\chi^2(31) = 246.07$, $p < .001$ (CFI = .45, RMSEA = .24, $p < .001$, SRMR = .57).

Quadratic model. We next examined whether a quadratic trajectory provided a good fit for the data. We tested a model that was

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<th>M</th>
<th>SD</th>
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<td>90</td>
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<td>Male</td>
<td>31</td>
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<tr>
<td>Caucasian</td>
<td>113</td>
<td>93.4</td>
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<td>Other ethnicities</td>
<td>8</td>
<td>6.6</td>
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<td>Married</td>
<td>82</td>
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<td>Age (years)</td>
<td>37.97</td>
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<td>Education (years)</td>
<td>13.28</td>
<td>2.69</td>
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<td>Age of onset for first episode of depression (years)</td>
<td>27.90</td>
<td>12.99</td>
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<td>Duration of index episode (months)</td>
<td>16.18</td>
<td>43.56</td>
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<td>Inpatient treatment</td>
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<td>Length of hospital stay (days)</td>
<td>13.97</td>
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<td>Outpatient treatment (Months 1–6)</td>
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<td>Pharmacological treatment only</td>
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<td>74.4</td>
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<td>Completed full course of treatment</td>
<td>74</td>
<td>61.2</td>
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identical to the linear model, with the addition of a latent quadratic slope. From the latent quadratic slope, direct effects emanated to the intercept and slope in Equation 1 represent the means of the latent intercept and latent slope, respectively. Because this is a nonlinear change coefficient, the values for time t were estimated from the data, except for the first two values, which were set to 0 and 1 to provide a metric for the latent variable. The values for t were 0, 1.00, 1.03, 1.18, 1.29, 1.34, 1.41, and 1.36. As can be seen in Figure 1, depressive symptoms had a steep drop from admission to discharge from hospitalization, and then gradually decreased during Months 1 through 6.

**Predictors of Change in Depression: Depression History, Negative Cognition, and Family Functioning**

We next sought to examine predictors of change in depression during treatment. However, before doing so, since outpatient treatment was randomly assigned, we examined whether it was necessary to control for the effect of outpatient treatment in our analyses. Although effects for treatment matching and family treatment were observed among a subgroup of symptomatic patients (for more detail, see Miller et al., 2005), there was no evidence for differential nonlinear change in depression in the full sample as a function of randomization of outpatient treatment to (a) matched versus mismatched treatment ($\beta = -0.02, ns$), (b) cognitive therapy versus no cognitive therapy ($\beta = -0.07, ns$), or (c) family therapy versus no family therapy ($\beta = -0.17, ns$). We thus collapsed across groups to examine change in depression during treatment more generally. Given that we collapsed across treatments for the LCA, variables associated with change in depression are predictors and not moderators of treatment.

**Predictor analyses.** We then examined whether previous episodes of depression were associated with initial depression severity and change in depression. We conducted these analyses to

$$E(\text{MHRSD}) = 24.16 - 9.47^t,$$ (1)

where $E(\text{MHRSD})$ represents expected MHRSD score at time $t$. The intercept and slope in Equation 1 represent the means of the latent intercept and latent slope, respectively. Because this is a nonlinear change coefficient, the values for time $t$ were estimated from the data, except for the first two values, which were set to 0 and 1 to provide a metric for the latent variable. The values for $t$ were 0, 1.00, 1.03, 1.18, 1.29, 1.34, 1.41, and 1.36. As can be seen in Figure 1, depressive symptoms had a steep drop from admission to discharge from hospitalization, and then gradually decreased during Months 1 through 6.

Note. Means and correlations are based on estimates of missing data. Correlations greater than or equal to $|0.18|$ are significant at $p < 0.05$ (two-tailed). MDD = major depressive disorder; MHRSD = Modified Hamilton Rating Scale for Depression; DAS = Dysfunctional Attitudes Scale; CBQ = Cognitive Bias Questionnaire; HS = Hopelessness Scale; FAD = Family Assessment Device; GF = General Functioning; McSIFF = McMaster Structured Interview for Family Functioning.

### Table 2

**Bivariate Correlations, Means, and Standard Deviations Among Depression Severity, Cognitive Functioning, Family Functioning, and Total Number of Previous Episodes of MDD**

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<td>9. DAS (admission)</td>
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<td>11. HS (admission)</td>
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<td>13. McSIFF (admission)</td>
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<td>14. No. of MDD episodes</td>
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<td>14.01</td>
<td>14.51</td>
<td>13.03</td>
<td>12.39</td>
<td>11.80</td>
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<td>11.15</td>
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<td>$SD$</td>
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<td>7.68</td>
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<td>4.76</td>
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Table 2

Bivariate Correlations, Means, and Standard Deviations Among Depression Severity, Cognitive Functioning, Family Functioning, and Total Number of Previous Episodes of MDD
establish that depression history was indeed associated with change in depression. If no such association existed, testing for mediators of this association may not be warranted. To examine this association, we added number of depressive episodes as an observed variable to our nonlinear change model. We then tested direct effects from number of prior depression episodes to the depression intercept and depression change. This model adequately fit the data, $\chi^2(31) = 66.64$, $p < .05$ (CFI = .91, RMSEA = .09, SRMR = .07). Further, depression history was a significant predictor of depression change; more previous episodes of depression were associated with less change in depression (see Figure 2).\footnote{It may at first seem counterintuitive for a positive association to indicate that higher levels of negative cognition were associated with less change in depressive symptoms. However, larger negative values for the depression change parameter reflect more symptom improvement over time. Thus, positive associations with depression change suggest less improvement over time. * $p < .05$.} Depression history was not significantly associated with initial depression severity. This model explained 9.9% of the variance in depression change and less than 1% of the variance in initial depression.

**Mediator analyses.** We next examined whether negative cognition mediates the relationship between number of previous depressive episodes and depression change. To examine these hypotheses, we added negative cognition and family functioning as latent variables to our previous model. Negative cognition consisted of admission scores on the DAS, CBQ, and HS. Family functioning consisted of the General Functioning subscales of the FAD and McSIFF, also measured at admission. Direct effects emanated from number of previous episodes to the other latent variables. Direct effects also emanated from the negative cognition and family functioning latent variables to the depression intercept and depression change latent variables.

This model provided an adequate fit of the data, $\chi^2(81) = 128.51$, $p < .05$ (CFI = .91, RMSEA = .07, SRMR = .08). The three indicators for the cognitive variable adequately loaded on to the latent variable ($\beta$s ranged from .49 to .78). Similarly, the two family functioning indicators loaded adequately well on to the latent variable ($\beta$s ranged from .52 to .96). More important, the direct effect from negative cognition to change in depression was
significant and positive; more negative cognition prior to treatment led to less subsequent change in depressive symptoms during treatment (see Figure 3). A similar pattern emerged for family functioning. Higher family impairment was associated with less subsequent change in depressive symptoms during treatment. Number of previous episodes was significantly associated with negative cognition; more episodes of depression were associated with greater negative cognition. In contrast, number of episodes was not significantly correlated with family impairment, initial depression severity, or depression change. Finally, initial depression severity was strongly associated with negative cognition; more episodes of depression were associated with greater negative cognition. In contrast, number of episodes was not significantly correlated with family functioning, initial depression severity, or depression change. In addition, initial depression severity was strongly associated with negative cognition; more episodes of depression were associated with greater negative cognition. In contrast, number of episodes was not significantly correlated with family impairment, initial depression severity, or depression change. Finally, initial depression severity was strongly associated with negative cognition; more episodes of depression were associated with greater negative cognition. In contrast, number of episodes was not significantly correlated with family functioning, initial depression severity, or depression change. Finally, initial depression severity was strongly associated with negative cognition; more episodes of depression were associated with greater negative cognition. In contrast, number of episodes was not significantly correlated with family functioning, initial depression severity, or depression change.

Additional mediator analyses. To help minimize the probability of committing a Type I error, we tested only two additional SEM models. One model tested whether negative cognition fully mediated the effect of depression history on change in depression. To do so, we tested the model presented in Figure 3, with the exception that the direct effect was removed from number of previous episodes to depression change. Model fit was not significantly different for full mediation compared with partial mediation, $\Delta \chi^2(1) = 3.48, p = .06$. Therefore, the full cognitive mediation model was retained, as it is more parsimonious.

A second model tested whether negative cognition would continue to predict change in depression after directly accounting for the effect of initial depression severity on depression change. To do so, we tested a model identical to the one above (i.e., full cognitive mediation), only this time we modeled an additional direct effect from initial depression severity to change in depression. This model also had adequate fit, $\chi^2(82) = 133.66, p < .05$ (CFI = .91, RMSEA = .07, SRMR = .08). As before, number of previous episodes significantly predicted negative cognition ($\beta = .32, p < .05$) but not family functioning ($\beta = .10, ns$) or initial depression ($\beta = .04, ns$). Negative cognition fell just short of significantly predicting initial depression ($\beta = .25, p < .10$), and family functioning did not predict initial depression ($\beta = -1.5, ns$). More important, initial depression severity was strongly associated with change in symptoms ($\beta = -.47, p < .05$). Further, consistent with our previous analyses was our finding that negative cognition remained a significant predictor of depression change ($\beta = .51, p < .05$); higher negative cognition predicted less change in depression. The association between family impairment and depression change fell short of statistical significance in this model ($\beta = .16, p = .12$). This model explained 9.1% of the variance in initial depression severity and 40.9% of the variance in depression change.

Discussion

The present study examined predictors of depression change during treatment. To summarize, a nonlinear pattern of symptom change fit the data well. Depressive symptoms typically had their

![Figure 3](image-url)
strongest decrease early in treatment and were then followed by less dramatic decreases. However, initial depression and depression change significantly varied across participants. Number of past MDD episodes predicted slower change in depression symptoms. Further, greater negative cognition and worse family functioning both predicted slower change in depression, but only the former was associated with depression history. Thus, negative cognition mediated the relationship between number of past MDD episodes and a poorer response to treatment.

These findings suggest that repeated episodes of depression may lead to greater negative cognition. As episodes accumulate, dysfunctional thought content and biased information processing may become more ingrained and severe. After depression onset, negatively biased information processing and dysfunctional content is readily accessible and apparent in someone who has experienced multiple episodes of depression. Greater negative cognition, in turn, predicts a worse response to depression treatment. It is important to note that this is not simply an epiphenomenon of greater initial depression severity. Negative cognition remained a potent predictor of depression change even when accounting for initial depression severity. These findings strongly suggest that negative cognition has an important role in predicting treatment response, particularly for individuals who have experienced multiple episodes of depression.

Our finding that depression recurrence is associated with greater negative cognition is consistent with the results of previous work. For instance, using an innovative psychological distance scaling task, Dozois and Dobson (2003) reported that negative self-referent information was highly interconnected among people with more previous episodes of depression compared with those with fewer previous episodes. This is also consistent with research documenting that negative cognition is more easily activated by a negative mood in nondepressed people with a history of depression than in individuals who have never been depressed (e.g., Miranda, Gross, Persons, & Hahn, 1998; Segal & Ingram, 1994; A. Solomon, Haaga, Brody, Kirk, & Friedman, 1998). However, the present study is among the first to demonstrate that elevations in negative cognition mediate the relationship between depression recurrence and response to treatment.

Analyses also indicated that negative cognition fully mediated the effect of depression history on treatment response. This suggests that heightened negative cognition could fully explain the association between depression history and slower depression change. Of course, this should not be interpreted to mean that negative cognition is the only predictor of depression change. Other factors may also influence depression change. Indeed, greater family impairment was associated with slower change in depression (when not controlling for initial depression severity). Our results simply suggest that negative cognition can fully explain the effect of depression history on change in depression. However, this conclusion is tempered by the fact that depression history and negative cognition were both assessed during hospitalization. True mediation is difficult to establish, as it is unclear whether past episodes of depression led to greater negative cognition or vice versa. Longitudinal studies with repeated assessments over a longer period of time are needed to address this issue.

Given that depressive symptoms do not always change in a linear fashion, future work examining symptomatic change may be well served to move beyond a linear change model. Indeed, one advantage of an LCA is that several change trajectories can be tested, and model fit for each type of trajectory can be compared. In the present study, linear and quadratic change models did not adequately fit the symptom data. Instead, a nonlinear model, with the majority of symptom change occurring during inpatient hospital treatment followed by more gradual improvement during outpatient treatment, provided a better fit for the data (see Figure 1). Incorporating these types of change estimates into outcome analyses may provide a more accurate and sensitive assessment of change, which could be critical for identifying predictors of change.

The use of growth curve modeling to estimate symptom change is becoming increasingly popular (Cole et al., 2002; Speer & Greenbaum, 1995). Other advantages of this repeated measurements approach in comparison with more traditional approaches include (a) smaller standard errors for the change parameter estimates, (b) flexible data handling that allows for variability in the number of assessments per individual, and (c) an ability to model different types of change (e.g., linear, quadratic, nonlinear), among others. The application of latent growth curve modeling has the additional benefit of assessing the change thought to underlie the observed change. Indeed, this approach is becoming a more popular method for assessing behavioral or symptomatic change (e.g., Beauchaine, Webster-Stratton, & Reid, 2005; Curran, Stice, & Chassin, 1997).

It should also be noted that family functioning was a significant predictor of symptom change during treatment, although this association was diminished somewhat and became nonsignificant when controlling for initial depression severity. Nevertheless, this is consistent with past research documenting that family functioning can influence the course of depressive illness. For instance, Miller et al. (1992) found that participants with dysfunctional families had higher levels of depression, lower levels of overall adjustment, and a lower probability of recovery 12 months after hospitalization than did patients with good family functioning. Of interest, depression history was not associated with family functioning in the present study. Other factors, such as personality pathology, may play a more important role for predicting individual differences in family functioning.

Several limitations of the present work should be noted. Additional research is needed to determine whether these findings generalize to depressed patients with less severe presentations. Participants in the present study were from a study examining the efficacy of combined treatments in the posthospital care of depressed inpatients. Because depression severity was severe enough to warrant inpatient hospitalization and because the larger study examined combined treatment modalities, participants received relatively intensive inpatient and outpatient treatment. Whether these findings apply to less severely depressed populations who receive less intensive treatment is unclear. However, it should be noted that severely depressed people are often excluded from studies of depression, often because of high levels of suicidal ideation. Therefore, although the generalizability of the findings may be questioned, this study does provide important information about a subgroup of depressed patients that is generally understudied.

Another possible limitation is our reliance on self-report assessments of information-processing bias and dysfunctional attitudes, which are susceptible to demand effects. It would be useful for...
future research to examine non-self-report assessments of cognition, such as biased attention, implicit cognition, and other cognitive processes that may be relevant for predicting treatment response (e.g., Gotlib & Neubauer, 2000). Indeed, a comprehensive cognitive assessment would ideally assess the structure, operations, and products of negative cognition (Ingram, Miranda, & Segal, 1998). Other limitations include the uncontrolled nature of treatment during the inpatient portion of treatment and limited statistical power to identify moderators of the specific outpatient treatments offered in the current study. In addition, although this study was longitudinal, it was correlational. Additional factors, such as psychiatric comorbidity, should also be considered potential alternative explanations for the associations observed in the current study.

Despite these limitations, the present work furthers our understanding of why people with recurrent depression often do not respond well to depression treatment. Our data suggest that negative cognition becomes more ingrained, accessible, and prominent as MDD episodes accumulate. This heightened negative cognition, in turn, predicts less change in depressive symptoms during treatment, regardless of treatment modality. Effectively reducing negative cognition may thus be particularly important for improving treatment response among adults with recurrent episodes of depression.

References


Miller, I. W., Keitner, G. I., Ryan, C. E., Solomon, D. A., Cardemil, E. V.,


Received June 26, 2006
Revision received December 13, 2006
Accepted December 19, 2006