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Lena C. Quilty

David J. A. Dozois
University of Western Ontario, ddozois@uwo.ca

Daniela S.S. Lobo

Lakshmi N. Ravindran

R. Michael Bagby

RUNNING HEAD: COGNITION DURING TREATMENT FOR DEPRESSION

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Lena C. Quilty [a, b]

David J. A. Dozois [c]

Daniela S. S. Lobo [a, b]

Lakshmi N. Ravindran [a, b]

R. Michael Bagby [a, b]

[a] Centre for Addiction and Mental Health

[b] University of Toronto

[c] University of Western Ontario

Author Note

This research was supported by the Ontario Mental Health Foundation. Correspondence regarding this article should be addressed to Lena C. Quilty, Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Department of Psychiatry, University of Toronto, 250 College Street, Suite 648, Toronto, ON, M5T 1R8; Lena.Quilty@camh.ca; tel: (416) 535-8501, x34313.

Abstract

Background: Evidence has converged to suggest that cognitive processing and content covary with depression severity, whereas indices of cognitive structure exhibit greater stability and promise as markers of vulnerability for depression. The objective of the current study was to investigate the temporal dynamics and causal role of cognitive structure and processing in treatment for depression. Method: A total of 104 patients with major depressive disorder were randomized to receive cognitive behavioural therapy (CBT; *n*=54) or pharmacotherapy (*n*=50). Patients completed the Hamilton Depression Rating Scale, Beck Depression Inventory-II, Psychological Distance Scaling Task, Redundancy Card-Sorting Task, and Self-Referent Encoding Task before, during, and after treatment. Results: Most cognitive indices exhibited change over treatment to a similar degree across both treatments. Evidence for the mediating role of cognition was limited, and not specific to CBT. Discussion: Results suggest that both cognitive structure and processing may be amenable to change, by both CBT and pharmacotherapy. The role of cognitive structure in the course of depression may require qualification.

Introduction

Major depressive disorder (MDD) is among the most serious public health burdens worldwide; in this context, it is concerning that even empirically-supported treatments delivered according to best practices have limited efficacy, with up to 70% of patients with MDD failing to achieve remission following treatment (Insel, 2006). Efforts to identify the causal mechanisms underlying treatment response are crucial to the development of more powerful, nuanced interventions targeting ingredients critical to short- and long-term symptom amelioration (Kraemer, Wilson, Fairburn, & Agras, 2002). The cognitive mediational model reflects the central theoretical guiding principle of cognitive behavioural therapy (CBT), namely, that change in cognition is responsible and sufficient for the resolution of depressive symptoms (Beck, Rush, Shaw, & Emery, 1979; Clark, Beck, & Alford, 1999). Investigations of the causal role of cognition in treatment for MDD to date have predominantly included measures of cognitive content as compared to cognitive processing or structure (e.g., Quilty, McBride, & Bagby, 2008). In the current study, we investigated the causal role of the latter forms of cognitive functioning in depression, within a randomized controlled trial of CBT versus pharmacotherapy for depression.

Disrupted cognitive functioning associated with MDD includes negative cognitive content as well as maladaptive cognitive structure and processing (Ingram & Wisnicki, 1998; Segal, 1988). Cognitive content in MDD includes situation-specific unbalanced interpretations known as negative automatic thoughts, the logical errors or cognitive distortions that characterize them, and the rigid and maladaptive standards or dysfunctional attitudes that underlie each. Cognitive content in MDD exists within a cognitive structure, in that sets of cognitions are highly interrelated (“I am incompetent,” “I am a failure,” “I am a fraud”) and thus are highly likely to be noticed, attended to, and remembered when any one of those cognitions are brought

to mind. Measures of cognitive structure and processing in depression capture this interconnectedness of cognitive content, and the impact of this organization upon attentional and memory processes.

Empirical evidence has converged to support maladaptive cognitive structure and processing in MDD, most commonly evaluated by performance-based tasks including cognitions about the self in social or achievement domains. The emphasis on these two domains is consistent with the centrality of sociotropy and autonomy in cognitive theory (Beck, 1983; see also Luyten & Blatt, 2011). In a seminal article, Dozois and Dobson (2001b) reported that patients with depression demonstrated greater endorsement, recall, and interrelatedness of negative interpersonal self-descriptors, and lower endorsement, recall, and integration of positive interpersonal self-descriptors. Lack of coherent positive self-view was not found in anxious controls, and so seemingly unique to depression. In a subsequent replication and extension, both samples of patients with depression and with social phobia demonstrated greater interrelatedness of negative interpersonal self-descriptors, and lower endorsement, recall, and integration of positive interpersonal and achievement themed self-descriptors, as compared to anxious and nonclinical controls (Dozois & Frewen, 2006). Other research has demonstrated that patients with more severe or recurrent depression exhibited greater interrelatedness of negative interpersonal self-referent information, and lesser interrelatedness of positive interpersonal self-referent information as compared to those with less severe or fewer episodes of depression (Dozois, 2002; Dozois & Dobson, 2003).

Longitudinal investigations of cognitive functioning in depression suggest that cognitive structure and processing demonstrate differential stability and covariation with depression severity. Dobson and Shaw (1987) reported in early work that cognitive processing changed

markedly in 14 depressed inpatients followed until remission (> 1 month) as compared to those retested while still depressed (two to three weeks). In 45 patients with depression followed over six months, attentional and memory biases resolved with depressive symptoms; however, the organization of negative interpersonal self-descriptors remained stable (Dozois & Dobson, 2001a). In a subsequent replication and extension in 54 patients with depression followed over six months, the organization of negative achievement self-referent information improved with symptom status, whereas the organization of negative interpersonal self-referent information again remained stable (Dozois, 2007). Cognitive structure has also prospectively predicted depressive symptoms in a nonclinical sample. In a longitudinal investigation of 57 undergraduates followed for one year, cognitive organization demonstrated moderate to high stability. Further, interrelatedness of positive and negative self-referent information interacted with negative life events to predict depressive symptom severity (Seeds & Dozois, 2010). Cognitive processing thus appears to covary with symptom severity in a manner similar to cognitive content, whereas cognitive structure may be a more promising vulnerability factor for depression not reflective of current symptom status.

CBT is explicitly designed to target cognitive functioning in depression, and has been associated with decreased risk of relapse and remission as compared to other forms of treatment (Beck & Dozois, 2011; Hollon et al., 2005). It is therefore possible that indices of cognitive structure, although relatively stable as compared to other forms of cognition in MDD, may change following this targeted treatment and result in the sustained treatment response that follows CBT. Dozois and colleagues (2009) evaluated both cognitive content and structure in 42 outpatients with depression randomized to receive cognitive therapy plus pharmacotherapy versus pharmacotherapy alone. Both treatment groups exhibited comparable decreases in

depression severity, automatic thoughts, and dysfunctional attitudes. Patients receiving cognitive therapy plus pharmacotherapy, however, exhibited greater interrelatedness of positive interpersonal content and decreased interrelatedness of negative interpersonal content following treatment. These results suggest that cognitive interventions may impact this vulnerability factor differently than pharmacotherapy which may, in turn, result in the longer-lasting treatment response to this intervention.

The Current Investigation

According to the cognitive mediational model, CBT for depression alters cognition, which includes cognitive structure (interconnectedness), processing (attention, memory), and content (thoughts, attitudes). A marked disconnect exists between theoretical and empirical attention to the cognitive mediational model, as research concerning cognitive structure and processing over the course of treatment has been limited to date. The objective of the current study was to investigate the temporal dynamics and the causal role of cognitive structure and processing during treatment. To our knowledge, only two published studies have evaluated cognitive structure or processing in the context of a treatment trial (Dozois et al., 2009; Segal & Gemar, 1997). Further, no published study to date has evaluated cognitive structure and processing before, *during*, and after CBT compared to pharmacotherapy for depression. This investigation includes numerous design strengths, such as a carefully diagnosed clinical sample, and three well-established tasks using the same set of rigorously tested adjective stimuli to assess cognition. Most importantly, the comparison of cognition across CBT versus pharmacotherapy follows the recommendations of extant reviews of the cognitive meditational model of depression. Whisman (1993) submitted that the cognitive mediational model entails that cognitive change is associated with depression change, and that cognitive change is specific to

CBT. Garratt, Ingram, Rand, and Sawalani (2007) suggested instead that as cognitive change is likely directly or indirectly targeted during most psychosocial treatments, the optimal test of cognitive specificity is a contrast between CBT and antidepressant medication – wherein cognitive change may occur within antidepressant medication, but is not of causal significance. We hypothesized that indices of cognitive processing (endorsement, reaction time, and memory for self-referent information) would improve over the course of treatment similarly across both treatment conditions. For example, we expected the decreased endorsement, increased reaction time, and decreased recall of negative self-descriptors over treatment, and an inverse pattern of results for positive self-descriptors. In contrast, we hypothesized that indices of cognitive structure (redundancy and interrelatedness of self-referent information) would improve in patients receiving CBT compared to those receiving pharmacotherapy. For example, we expected decreased redundancy and interrelatedness of negative self-descriptors, and increased redundancy and interrelatedness of positive self-descriptors, over treatment. We further hypothesized that cognitive structure during treatment would have a causal role in treatment response in patients receiving CBT. In line with previous investigations of cognitive content (Quilty et al., 2008), interpersonal and achievement self-referent information have demonstrated comparable results in investigations of cognitive processing and structure overall. Therefore, we hypothesized that results would be similar for tasks including each type of self-referent content.

Methods

Participants

The sample consisted of 104 participants including 49 males and 55 females ranging in age from 18 to 59 years (M=33.61, SD=9.97). Eligibility criteria included meeting Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychological Association,

1994) criteria for a primary diagnosis of MDD as assessed by the Structured Clinical Interview for DSM-IV (SCID-I/P; First, Spitzer, Gibbon, & Williams, 1995), being between 18 to 65 years of age, being fluent in English, and having the capacity to give informed consent. Exclusion criteria included a diagnosis of bipolar disorder, psychotic disorder, substance dependence disorder, or organic brain syndrome; current treatment with antidepressant medications or electroconvulsive therapy (ECT) in the past 6 months.

A total of 1415 individuals responded to advertisement or referral (see Figure 1). Of these, 455 expressed interest in participating and consented to a brief telephone screen to assess their suitability for participation. Of the 333 telephone screens conducted, 213 individuals were invited to complete a clinic screen to further determine eligibility. Of the 175 clinic screens conducted, 140 individuals were eligible for and interested in participation. A total of 104 patients initiated treatment. Stratified random sampling was employed such that of the 104 patients, 54 were assigned to the CBT treatment condition and 50 to the pharmacotherapy (PHT) treatment condition. Randomization was stratified based on gender and depression recurrence (i.e., single episode versus recurrent). Patients exhibited both Single Episode (n=45) and Recurrent (n=59) MDD, at Mild (n=24), Medium (n=68), and Severe (n=12) levels of intensity. There were no differences across treatment groups for MDD recurrence (χ^2=.42, p=.52) or severity (χ^2=1.64, p=.65) specifiers. Of the 54 patients assigned to CBT, 49 completed at least eight weeks of treatment. Of the 50 patients assigned to PHT, 43 completed at least eight weeks of treatment. Reasons for early withdrawal from treatment included: moving from the city, seeking alternate treatments, and not following through with appointments.

Participants reported an average of 15.91 (SD=2.06) years of education. The majority of participants had never been married (60.4%; n=55); the remaining were married (27.5%; n=25)

or divorced or separated from their marital partner (2.1%; *n*=11). Using Statistics Canada racial groupings, the majority of participants identified as Caucasian (69.2%; *n*=63); the remaining participants identified as South Asian (15.4%; *n*=14), Black (5.5%; *n*=5), Visible Minority (3.3%; *n*=3), Chinese (2.2%; *n*=2), Latin American (2.2%; *n*=2), Arab/West Indian (1.1%; *n*=1), and Aboriginal (1.1%; *n*=1). Co-occurring Axis I disorders as assessed by the SCID-I/P were found in 29.0% (*n*=27) of the sample and included: dysthymic disorder (6.7%; *n*=7), anxiety disorders (20.2%; *n*=21), substance use disorders (1.0%; *n*=1), and eating disorders (1.9%; *n*=2); four participants exhibited more than one comorbid diagnosis. There were no differences across treatment groups for patients with co-occurring disorders (χ^2=.23, *p*=.63).

Procedure

Participants were recruited via a multi-faceted campaign, including online and newspaper advertisements, poster advertisements in local universities and transit, and mail-outs to local health care clinics. Clinic screens were conducted by registered psychologists, doctoral trainees, or experienced research assistants trained in diagnostic interviewing and the administration of the SCID-I/P. All assessments audio recorded; 20% (*n*=35) were independently reviewed by a second interviewer. There was 100% agreement in the diagnosis of MDD between the original and second interviewer. Two registered psychologists and the study coordinator reviewed cases for study eligibility. Participants were randomly assigned to 16 sessions of standardized CBT administered according to the empirically-supported protocol outlined by Beck and his colleagues (Beck et al., 1979) or 16 weeks of pharmacotherapy according to Canadian Network for Mood and Anxiety Treatment (CANMAT) guidelines (Kennedy et al., 2009). CBT was provided by nine study clinicians, including three registered psychologists (including the first author) and six doctoral trainees, all of whom had received graduate training in CBT and were

under the supervision of a registered psychologist. Controlling for pre-treatment score, there was no difference in treatment response across registered psychologists versus doctoral trainees according to both measures of depression severity (ts<1.43, ps>.16). Pharmacotherapy was provided by four psychiatrists. Assessments were conducted at Week 0 (pre-treatment), Week 4, Week 8, and Week 16 (post-treatment). Study clinicians and psychiatrists did not have access to measures of cognitive content, processing or structure collected at Weeks 0, 4, 8, and 16.

Measures

Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996): The BDI-II is a 21-item self-report measure of depression severity. The BDI-II is recognized for its internal consistency, retest reliability and validity (Dozois & Covin, 2004). Coefficient α in the current sample ranged from .84 to .94.

Hamilton Depression Rating Scale (Ham-D_{17}; Hamilton, 1960): The Ham-D_{17} is a semi-structured interview designed to assess depression severity. The Ham-D_{17} is widely used in treatment trials for depression; its psychometric properties are reviewed in detail by Bagby, Ryder, Schuller, and Marshall (2004). Interrater reliability of the Ham-D_{17} based on an independent review of 35 audio recordings of interviews was adequate (ICC=.70). Coefficient α in the current sample ranged from .69 to .86.

The *Psychological Distance Scaling Task* (*PDST*; Dozois, 2002; Dozois & Dobson, 2001b, 2003) is a computer-administered task in which participants characterize the self-relevance and valence of a set of adjectives. The trials of this task were administered in line with the procedures of Dozois and Dobson (2001b). A computer screen displayed a grid, divided by a horizontal and vertical line, with the anchors “not at all like me” and “very much like me” on the left and right of the horizontal line, and the anchors “very negative” and “very positive” on the

bottom and top of the vertical line, respectively. In each trial, participants moved adjectives initially presented at the center of the screen to the position indicating appropriate self-relevance and valence by mouse. Participants completed ten practice trials, and confirmed the position of each adjective before moving to the subsequent trial. The x and y coordinates of each adjective were recorded; average interstimulus distances was computed via a formula involving dividing the mean squared distances of every adjective–adjective combination within a particular adjective list (e.g., interpersonal positive) by the total number of possible distances, and obtaining the square root of this number (see Dozois and Dobson, 2001b). Less distance among adjectives reflects *greater* interconnectedness of self-referent content, and vise versa. Scores were computed separately for positive and negative, and interpersonal and achievement themed adjectives.

The *Redundancy Card-Sorting Task* (*RCST*; Linville, 1987) is a card-sorting task in which participants sort adjectives into clusters that describe self-aspects. In this task, participants generated as many self-aspects as they chose, and described each self-aspect using a set of adjectives presented singly on a deck of cards. Adjectives could be used to describe more than one self-aspect, or not used at all. Attribute redundancy was calculated as the sum of adjective repetitions across self-aspects, controlling for number of self-aspects and of adjectives used. Scores were computed separately for positive and negative, and interpersonal and achievement themed adjectives (see Dozois & Dobson, 2001b).

The *Self-Referent Encoding Task (SRET*; Derry & Kuiper, 1981; Dobson & Shaw, 1987) is a computer-administered task in which participants indicate whether a series of positive and negative adjectives are self-descriptive, and subsequently recall as many adjectives as possible. The trials of this task were again administered in line with the procedures of Dozois and Dobson

(2001b). A computer screen displayed a blank screen. In each trial, the word "ready" was presented for 1 second, and following by a blank screen for .5 seconds. A randomly selected adjective was presented centrally until participants pressed one of two mouse buttons to indicate whether the adjective was or was not self-descriptive. After rating all adjectives, participants were asked to recall as many as possible, in any order. This task yields reaction time between adjective presentation and participant response, endorsement and recall of both positive and negative adjectives. Similar to previous literature, a proportional score was used for recall to control for the influence of yes vs. no response (i.e., recall for positive and negative adjectives was divided by the total number of adjectives endorsed).

Adjectives. The same 80 adjectives were utilized in all three performance-based tasks. These adjectives were drawn from an original list (Myers, 1984), subsequently refined into four adjective sets based on their relevance to sociotropic and autonomous dimensions: interpersonal positive (e.g., admired, encouraged), interpersonal negative (e.g., alone, unwanted), achievement positive (e.g., respected, capable), and achievement negative (e.g., defeated, incompetent). Each adjective set was matched on emotional intensity, imaginability, word length and word frequency (see Dozois, 2007; Dozois & Frewen, 2006).

Statistical Analyses

A total of 19.2% of participants were missing observations from one or more scales; multiple imputation procedures were conducted within SPSS 21.0 to avoid bias associated with listwise deletion and to maximize statistical power. We evaluated change in depression severity and cognition during treatment with a series of repeated measures analyses of variance (ANOVAs). Separate analyses were conducted for each measure of depression severity (BDI-II, Ham-D_{17}), for each adjective type in the PDST and RCST (interpersonal positive, interpersonal

negative, achievement positive, and achievement negative), and for each outcome of the SRET (positive word endorsement, reaction time, and proportionate recall, and negative word endorsement, reaction time, and proportionate recall), which served as dependent variables. Treatment condition served as the independent variable for all analyses. We evaluated the mediational role of cognition with a two step procedure consistent with the recommendations of Kraemer, Wilson, Fairburn, and Agras (2002). First, to evaluate whether the treatment was correlated with the mediator, we conducted a series of linear regressions including treatment condition as the independent variable and each possible mediator as the dependent variable (i.e., each adjective type in the PDST and RCST and each outcome of the SRET at Week 4 and 8) in separate analyses. Second, to evaluate the main effect of mediation and the interactive effects of the mediator with treatment, we conducted multiple linear regressions including treatment condition (coded 1 for CBT and -1 for medication), each possible mediator and treatment condition × mediator interaction in turn as independent variables in separate analyses. Depression severity (i.e., Week 16 BDI-II and Ham-D_{17}) served as the dependent variable in separate analyses.

Results

Participant depression severity and cognitive functioning are displayed in Table 1. Univariate normality of indicators was below established cutoffs for all indices but Week 0 and 8 reaction time indices (skewness ≤ 2.24, kurtosis ≤ 6.37; Curran, West, & Finch, 1996). There were no significant differences across treatment condition in sex (χ^2=.54, p=.56), age (t=56, p=.57), depression severity or cognitive functioning at Week 0 (all ts<1.08, all ps>.28).

Cognitive Change Over Treatment

Results of the repeated measures analyses of variance are displayed in Table 2. There was a significant effect for Time and a Time × Treatment Condition interaction for both measures of depression severity, indicating that depression severity decreased over the course of treatment differently in CBT and PHT conditions. Post-hoc comparisons revealed that depression severity did not differ across treatment conditions at Week 0 or 16 (all ts<1.49, all ps>.14); however, patients receiving medication exhibited an earlier treatment response in the form of lower depression severity at Week 4 according to both indices (BDI-II t=2.74, p<.01, d=.54; Ham-D_{17} t=2.92, p<.01, d=.57), and at Week 8 according to the Ham-D17 (BDI-II t=.57, p=.57; Ham-D_{17} t=2.22, p= .03, d=.44).

There was a significant effect for Time for all adjective types in the PDST, and a Time × Treatment Condition interaction for interpersonal negative words. These findings indicate that distance between positive self-referential content decreased over treatment (i.e., positive content became more interconnected), similarly across both treatment conditions. The distance between negative achievement-themed self-descriptors increased over treatment, also similarly across both treatment types. Post-hoc comparisons revealed that negative interpersonal content distance increased over treatment, but earlier in the CBT condition at Week 8 (t=2.33, p=.02).

There was a significant effect for Time for interpersonal positive, interpersonal negative, and achievement positive adjectives in the RCST. No Time × Treatment Condition interactions were found. These findings indicated that positive attribute redundancy increased over treatment. Interpersonal negative attribute redundancy exhibited an overall increase over treatment as well; results suggested a nonlinear relation, with scores initially increasing and then decreasing during treatment.

There was a significant effect for Time for all indices of the SRET but one (recall of positive content), and a Time × Treatment Condition interaction for negative word endorsement. Reaction time for both word types decreased over treatment, similarly across treatment conditions. As positive and negative word reaction times were kurtotic at Week 0 and 8, analyses conducted on log transformations of reaction time indices; the same pattern of results was found. Further, participants endorsed an increasing number of positive words and recalled a decreasing proportion of negative words, to a similar degree across both treatments. Similar to depression severity, negative word endorsement decreased earlier in the medication condition (Week 4 t=2.43, p=.02; all other ts<1.16, ps>.25).

Cognitive Mediation of Treatment Outcome

Only three cognitive indices covaried with treatment condition in Step 1: Week 4 PDST achievement negative F=5.46, p=.02, β=-.23; Week 8 PDST interpersonal negative F=5.43, p=.02, β=-.23; and Week 4 SRET negative word endorsement F=5.90, p=.02, β=.24. Of these, only Week 8 interpersonal negative (F=8.38, p<.01, β=-.43, t=4.45, p<.01) and Week 4 SRET negative word endorsement (F=5.80, p<.01, β=.34, t=3.56, p<.01) exhibited mediator effects of post-treatment depression severity as assessed by the BDI-II. In both cases, there was a significant main effect of treatment as well (β=-.24, t=2.59, p=.01 and β=-.24, t=2.52, p=.01), indicating partial mediation. No mediator effects were found in analyses including post-treatment depression severity as assessed by the Ham-D_{17}.

Discussion

We believe the current investigation represents an innovative evaluation of cognitive structure and processing before, during, and after treatment with CBT versus pharmacotherapy for depression. Patients treated with pharmacotherapy demonstrated an earlier response than did

patients who received CBT. Consistent with previous research, however, patients in the CBT condition began to exhibit treatment response by Week 8 and treatment outcome was comparable across both treatment modalities at Week 16.

Two measures of cognitive organization revealed significant change in all forms of self-referential content over the course of treatment. Positive self-descriptors became more closely interrelated and positive attribute redundancy increased similarly across both treatment modalities. Further, negative achievement themed self-descriptors became less integrated and negative achievement attribute redundancy decreased similarly across both forms of treatment. These results suggest that cognitive organization may be responsive to pharmacotherapy as well as CBT, particularly when that pharmacotherapy is delivered according to best practices by psychiatrists with expertise in the treatment of depressive illness. This responsiveness to treatment may pose a challenge to models of cognitive structure as a stable vulnerability factor; however, these results should be interpreted in the context of previous research wherein participants largely treated with antidepressant medications did not exhibit similar change in cognitive structure over time. Yet, there appears to be reason to believe that even more enduring risks for depression can be addressed by multiple treatment modalities.

Negative interpersonal self-descriptors again emerged as a distinct domain of cognitive organization. Patients receiving CBT demonstrated earlier improved interrelatedness of negative interpersonal content as compared to those receiving pharmacotherapy; yet, interrelatedness was comparable across both treatment modalities at Week 16. In some contrast, negative interpersonal attribute redundancy *increased* over treatment, overall, displaying an unanticipated nonlinear trend during treatment. It may be that cognitive skills training in the first half of treatment may have resulted in increased insight into areas of interpersonal areas for growth

which then began to be addressed in treatment; yet, this interpretation does not account for the lack of differences across treatment condition.

The current study represents the first investigation of cognitive processing as assessed by the SRET within a treatment trial. Consistent with previous research, all but one indices of cognitive processing demonstrated change over treatment. The comparable decrease in reaction time for positive and negative words over both treatments suggests that this effect may simply reflect participant increasing familiarity with the task and the adjective stimuli. Indeed, the repeated administration of the recall task introduces the possibility that patients approached this task (and the memory component in particular) with greater intention following their first assessment. Yet, negative word endorsement and recall decreased over treatment whereas positive word endorsement increased over treatment. Negative word endorsement in particular exhibited a similar pattern of results to depression severity, as it decreased earlier in the pharmacotherapy condition.

The evidence for the mediational role of cognitive structure in CBT vs. pharmacotherapy was weak. Only one index of cognitive structure covaried with treatment condition: results did support the causal role of the interrelatedness of negative interpersonal self-descriptors, although this role did not differ across treatment condition. Further, an index of cognitive processing also covaried with treatment condition, and Week 4 negative word endorsement also demonstrated an unanticipated causal role which again did not differ across treatments. Thus, the current study provides only limited support for the causal role of cognition in CBT, and does not support the specificity of these effects as recommended by Garratt et al. (2007).

The discrepancies between the results of the current study as compared to previous studies, in particular Dozois et al. (2009), may have resulted from a variety of design and sample

differences. First, Dozois et al. (2009) contrasted cognitive therapy plus pharmacotherapy versus pharmacotherapy alone. Second, although the descriptives of cognitive indices in the current study are comparable to the previous investigations, the means and distributions of depression severity in this sample do differ from the earlier investigation (Dozois et al., 2009). This may have rendered cognitive therapy more powerful in changing cognitive structure in the Dozois et al. trial, whereas both conditions were able to do so in this study.

Although it is possible that the pharmacotherapy provided in this trial was superior to that administered in Dozois et al. (2009), resulting in structural changes in both conditions, this explanation is highly unlikely. The pharmacotherapy reported in Dozois et al. (2009) was rigorously delivered according to CANMAT guidelines as was the case in the current study. It is also possible that the Dozois et al. (2009) trial was underpowered compared to this trial, such that although effects were found for the combined treatment condition, there was not sufficient statistical power to detect effects in those treated by pharmacotherapy alone. These explanations are speculative, however, and further research is necessary to ascertain the mechanisms involved in cognitive structure change and whether such change represents a key ingredient to long-term improvement and relapse prevention.

This study has several strengths, including random assignment of patients with MDD to two evidence-based interventions which were well-positioned to evaluate the specificity of cognitive mediation of treatment response. Well-established, performance-based tasks were administered at numerous occasions over the course of treatment. This study has some limitations as well. First and most importantly, although this investigation has the largest sample of patients of any investigation of cognitive structure to date, our sample size was limited from a statistical perspective and precluded more sophisticated modeling of causal associations between

variables. For example, a full cross-lagged panel analysis in structural equation modeling, which would permit the evaluation of the causal paths between depression severity and cognition while simultaneously modelling the stability of these constructs, could not be conducted. This model includes 34 parameters to be estimated, which results in a participant:parameter ratio well below the liberal threshold of 5:1. Inadmissable solutions and unreliable parameter estimates and model comparison indices would pose problems in analyses under these conditions. Second, the lack of follow-up assessment precluded our ability to evaluate the lasting impact of treatment upon cognitive structure and processing. It was notable that an index of negative cognitive structure changed more quickly within patients treated with CBT, even though indices of cognitive processing and depression severity changed more quickly in those treated with pharmacotherapy. It would therefore be particularly fascinating to learn whether the interrelatedness of negative interpersonal self-descriptors was predictive of relapse or recurrence for example. Finally, patients in randomized controlled trials may differ in qualitative ways from those in routine clinical practice (Kushner et al., 2009), which may limit the generalizability of these results.

In conclusion, the current study provides a detailed account of the temporal dynamics of cognitive structure and processing over treatment for depression. Results challenge previous conclusions that change in cognitive structure is unique to CBT. Stable cognitive risk factors evidenced a comparable change and causal role across both CBT and pharmacotherapy for depression, suggesting that cognitive organization may be more dynamic than previously believed and that patients may not require targeted treatment to exhibit changes in this risk factor. Patients who exhibit maladaptive cognitive functioning but do not have access to CBT may be assisted by medications administered according to best practices. It is possible, however, that these assays of cognitive function represent a final common pathway; further research is

needed to evaluate whether CBT and pharmacotherapy have their impact upon this outcome by different mechanisms.

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Table 1. *Depression Severity and Cognitive Structure and Processing Descriptives*

	CBT (*n*=54)				PHT (*n*=50)			
	Week				Week			
	0	4	8	16	0	4	8	16
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
BDI-II	30.69 (8.73)	25.97 (11.07)	19.85 (12.69)	11.43 (9.42)	29.10 (8.43)	20.14 (10.57)	18.41 (12.83)	14.57 (12.00)
Ham-D17	16.91 (5.03)	14.62 (5.20)	12.18 (6.19)	8.14 (6.28)	16.42 (5.33)	11.45 (5.87)	9.46 (6.31)	8.19 (6.08)
Psychological Distance Scaling Task								
IP	.68 (.36)	.55 (.31)	.51 (.25)	.43 (.25)	.64 (.31)	.55 (.28)	.47 (.31)	.45 (.27)
IN	.88 (.44)	.93 (.44)	.98 (.40)	1.10 (.44)	.80 (.33)	1.06 (.55)	1.20 (.56)	1.17 (.56)
AP	.97 (.56)	.94 (.55)	.78 (.47)	.64 (.37)	.94 (.45)	.82 (.48)	.78 (.59)	.70 (.52)
AN	.66 (.42)	.68 (.43)	.81 (.55)	.99 (.48)	.68 (.44)	.89 (.49)	.97 (.61)	1.09 (.55)
Redundancy Card Sort Task								
IP	.44 (.21)	.51 (.19)	.51 (.19)	.54 (.18)	.48 (.18)	.52 (.22)	.55 (.25)	.56 (.20)
IN	.36 (.15)	.41 (.15)	.41 (.17)	.39 (.18)	.37 (.16)	.39 (.18)	.43 (.19)	.39 (.20)
AP	.36 (.18)	.40 (.16)	.42 (.17)	.44 (.18)	.39 (.14)	.46 (.22)	.46 (.20)	.48 (.18)
AN	.38 (.16)	.40 (.16)	.39 (.15)	.34 (.16)	.40 (.16)	.42 (.20)	.43 (.18)	.40 (.22)
Self-Referent Encoding Task								
PE	16.04 (7.68)	16.75 (7.93)	19.75 (7.87)	23.03 (8.62)	16.83 (9.57)	20.00 (10.43)	21.02 (10.88)	21.92 (11.44)
P RT	1.75 (1.29)	1.53 (.67)	1.54 (1.02)	1.32 (.48)	1.52 (.48)	1.40 (.48)	1.37 (.65)	1.30 (.64)
P Recall	.04 (.07)	.05 (.08)	.05 (.09)	.05 (.10)	.03 (.06)	.05 (.09)	.05 (.11)	.03 (.08)

NE	21.77 (8.84)	18.88 (10.15)	14.58 (8.64)	9.49 (8.78)	21.50 (7.82)	14.09 (9.57)	12.51 (9.46)	11.62 (9.70)
N RT	1.87 (1.20)	1.60 (.85)	1.62 (1.28)	1.30 (.48)	1.72 (.64)	1.48 (.49)	1.43 (.56)	1.29 (.43)
N Recall	.05 (.06)	.03 (.06)	.02 (.04)	.01 (.03)	.05 (.08)	.04 (.06)	.04 (.08)	.02 (.05)

Note: CBT = Cognitive Behavioural Therapy; PHT = Pharmacotherapy; IP = Interpersonal Positive; IN = Interpersonal Negative; AP = Achievement Positive; AN = Achievement Negative; PE = Positive Word Endorsements; P RT = Positive Word Reaction Time; P Recall = Positive Word Recall; NE = Negative Word Endorsements; N RT = Negative Word Reaction Time; N Recall = Negative Word Recall.

Table 2. *Depression Severity and Cognitive Change During Treatment*

	Time		Time x Treatment Condition	
Scale	*F* (*p*)	partial η^2	*F* (*p*)	partial η^2
BDI-II	101.78 (<.01)	.50	6.80 (<.01)	.06
Ham-D17	74.28 (<.01)	.42	3.67 (.01)	.04
Psychological Distance Scaling Task				
IP	18.02 (<.01)	.15	.43 (.72)	<.01
IN	17.63 (<.01)	.15	4.25 (<.01)	.04
AP	13.97 (<.01)	.13	1.36 (.26)	.01
AN	22.74 (<.01)	.19	1.73 (.17)	.02
Attribute Redundancy Card Task				
IP	14.13 (<.01)	.12	.32 (.79)	<.01
IN	3.20 (.03)	.03	.40 (.76)	<.01
AP	14.11 (<.01)	.12	.32 (.78)	<.01
AN	2.59 (.06)	.03	.75 (.52)	.01
Self-Referent Encoding Task				
PE	22.98 (<.01)	.19	2.72 (.06)	.03
P RT	9.94 (<.01)	.12	.02 (.99)	<.01
P Recall	2.38 (.08)	.02	1.18 (.32)	.01
NE	60.01 (<.01)	.38	5.72 (<.01)	.06
N RT	19.55 (<.01)	.21	.14 (.90)	<.01
N Recall	8.89 (<.01)	.08	.79 (.48)	.01

Note: IP = Interpersonal Positive; IN = Interpersonal Negative; AP = Achievement Positive; AN = Achievement Negative; PE = Positive Word Endorsements; P RT = Positive Word Reaction Time; P Recall = Positive Word Recall; NE = Negative Word Endorsements; N RT = Negative Word Reaction Time; N Recall = Negative Word Recall

Figure 1. *Patient Participation*.