Special Series: Targeted Training of Cognitive Processes for Behavioral and Emotional Disorders

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Cognitive Bias Modification for Interpretation in Major Depression: Effects on Memory and Stress Reactivity

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Abstract

Interpreting ambiguous stimuli in a negative manner is a core bias associated with depression. Investigators have used cognitive bias modification for interpretation (CBM-I) to demonstrate that it is possible to experimentally induce and modify these biases. In this study, we extend previous research by examining whether CBM-I affects not only interpretation but also memory and physiological stress response in individuals diagnosed with major depressive disorder. We found that CBM-I was effective in inducing an interpretive bias. Participants also exhibited memory biases that corresponded to their training condition and demonstrated differential physiological responding in a stress task. These results suggest that interpretation biases in depression can be modified and that this training can lead to corresponding changes in memory and to decreases in stress reactivity. Findings from this study highlight the importance of examining the relations among different cognitive biases in major depressive disorder and the possibility of modifying cognitive biases.

Keywords

cognitive bias modification, training, interpretation, memory, depression

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Cognition plays a critical role in human emotion. According to cognitive theories of emotion, appraisals or interpretations of a situation determine whether an emotion is experienced and which emotion that will be (Ellsworth & Scherer, 2003; Siemer, Mauss, & Gross, 2007). It is important, therefore, that cognition is also a primary mechanism through which emotions can be regulated. For example, cognitive reappraisal, or the reinterpretation of the emotion-eliciting situation, has been shown to be a particularly effective emotion-regulation strategy (Gross & John, 2002). Researchers have also demonstrated that memory functioning is critical for the regulation of negative affect (Joormann, Siemer, & Gotlib, 2007). Cognitive biases in interpretation or memory, specifically a tendency to interpret ambiguous material in a negative manner or to preferentially recall negative events may therefore impair emotion regulation and increase vulnerability to emotional disorders (Joormann, Yoon, & Siemer, 2010).

Indeed, cognitive theories of emotional disorders posit that depressed and anxious individuals, as well as people who are at risk for developing these disorders, exhibit cognitive biases in various aspects of information processing, including interpretation and memory (Mathews & MacLeod, 2005). These theories further propose that cognitive biases are not simply epiphenomenal in these disorders but, instead, play an important role in increasing the risk for the onset, maintenance, and recurrence. Indeed, depressed individuals have been shown to demonstrate increased elaboration of negative material and a tendency to interpret ambiguous material in a mood-congruent manner (e.g., Cowden Hindash & Amir, 2012). In addition, biased memory for negative, relative to positive,

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information is perhaps the most robust finding concerning cognitive biases associated with major depression (Matt, Vazquez, & Campbell, 1992).

Given the importance of cognition for everyday emotion regulation and risk for emotional disorders, the modification of cognitive biases may alter individuals' reactivity to emotion-eliciting events and improve their ability to regulate negative affect. Furthermore, research on how these biases can be changed may yield important insights into processes that underlie the onset and maintenance of disorders and, thus, holds promise for efforts aimed at prevention and treatment. Indeed, researchers have investigated the effects of bias modification on various outcome measures, including symptoms of depression and anxiety, and responses to acute stressors. Some of these studies have focused on manipulating attention by guiding participants to attend to either threatening or emotionally neutral stimuli (see Hallion & Ruscio, 2011, for a recent review). Biases in interpretation and memory, however, may have particularly detrimental effects on individuals' ability to regulate negative mood states and may serve to increase risk for the onset and maintenance of debilitating emotional disorders.

In a seminal study, Grey and Mathews (2000) demonstrated that biased interpretation of emotionally ambiguous homographs can be induced and that participants are often not aware of this modification. In a related study, Mathews and Mackintosh (2000) used ambiguous scenarios to train individuals to make either nonanxious or anxious interpretations of ambiguous situations. In this and in later studies, participants who were trained to interpret ambiguity in a nonanxious manner had an attenuated self-reported anxious reaction to a subsequent stressor (e.g., Wilson, MacLeod, Mathews, & Rutherford, 2006; see also Mackintosh, Mathews, Yiend, Ridgeway, & Cook, 2006) and showed improvements in a subsequently induced negative mood state (Holmes, Lang, & Shah, 2009). Beneficial effects of interpretive training on levels of anxiety have been shown to be stable after a 24-hr delay between training and test (Yiend, Mackintosh, & Mathews, 2005). It therefore is not surprising that researchers have begun to examine the usefulness of cognitive bias modification for interpretation (CBM-I) as an intervention strategy. In a recent study, Bowler et al. (2012) demonstrated in a sample of participants with high levels of social-anxiety symptoms that CBM-I led to symptom reduction, lower trait anxiety, and depression, as well as to improved self-reported attentional control.

Despite these successes when CBM-I has been used in anxiety disorders and in participants with elevated levels of anxiety, research in depression has been mostly lacking. A. D. Williams, Blackwell, Mackenzie, Holmes, and Andrews (2013) found that 1 week of CBM-I reduced the severity of symptoms in a sample of clinically depressed individuals and that these changes were at least partially mediated by changes in interpretation biases. This study, however, did not include a control group, which makes it difficult to attribute the symptom change to the intervention. In a study of depressed adolescents and young adults (14–21 years of age), Micco, Henin, and Hirshfeld-Becker (2014) included a control group in a four-session training. The authors reported that both groups, the active training and the control group, exhibited a reduced interpretation bias at follow-up with no significant between-groups difference. When the authors limited their analysis to participants with negative biases at baseline, however, the intervention group exhibited greater improvements in interpretation bias. Still, no group differences were found in depression or anxiety symptom change.

Only one study thus far has focused on whether CBM-I in a depressed sample affects stress reactivity and recovery. Yiend et al. (2014) reported that a single session of CBM-I was effective in changing interpretive biases in depressed adults. These authors did not, however, find a reduction in self-reported stress responding. This lack of transfer of training to stress responding may be due to the use of a single session of training or to the exclusive reliance on self-reported distress. Thus, it is clear that additional studies that use control groups and CBM-I training protocols that encompass more than a single session are needed in research with depressed adults. Moreover, in no study to date have researchers examined whether CBM-I reduces physiological stress reactivity in depression. The present study was designed in part to test this possibility.

Modification of interpretation biases may be a promising approach for the treatment of depression not only because it affects the interpretation of novel situations and responses to stressors but also because changes in interpretation may affect memory. Hirsch, Clark, and Mathews (2006) and Everaert, Koster, and Derakshan (2012) noted that cognitive biases do not operate in isolation but, rather, influence and interact with one another. If individuals tend to interpret situations in a negative manner, they may also be more likely to remember them in a way that is consistent with this initial interpretation. Thus, memory biases may be due in part to earlier biases in interpretation (Hertel, 2004; Hertel & Brozovich, 2010), although very few studies have investigated this possibility empirically. Among the few studies that have done so is one conducted by Hertel, Brozovich, Joormann, and Gotlib (2008), who examined the association between interpretation and memory in individuals diagnosed with social phobia. When asked to recall details from previously presented ambiguous scenarios, socially anxious participants, compared with nonanxious participants, tended to produce more distortions that reflected their

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initial negative interpretations of the scenarios. This result suggests that memory biases can be produced by biased interpretations and that modification of the initial interpretation of events could prevent subsequent biases in memory. Indeed, in a previous study using CBM-I in a nonclinical sample, Tran, Hertel, and Joormann (2011) reported a relation between interpretation and memory biases. In this study, the authors induced positive- and negative-interpretation biases in a student sample using a single session of CBM training and found effects of this training on subsequent recall. This association between interpretation and memory biases, however, has not been examined in clinically depressed participants.

In the present study, we examined whether two sessions of CBM-I in participants diagnosed with major depressive disorder (MDD) affect not only participants' interpretation of novel scenarios but also their memory for these scenarios. We also examined the effects of CBM-I on physiological responses to an acute stressor. In addition, we included several control groups. We compared participants diagnosed with MDD with a group of healthy control participants. We expected training effects in both groups and a stronger training effect in the MDD group. In addition, to examine whether we could replicate the Tran et al. (2011) findings, we randomly assigned all participants to receive either positive- or negative-interpretation training. Although we expected that the negative training would induce a negative-interpretation bias in the control group, we did not expect any effect of this training in the MDD group, given that MDD participants should exhibit a negative-interpretation bias even before the training. Finally, to examine whether training affects interpretation biases in the MDD group, we recruited a separate group of MDD participants who did not undergo training but participated in the follow-up assessment; this procedure allowed us to compare the effects of a no-training condition with a positive-training and a negative-training condition within the MDD sample.

Participants diagnosed with current MDD and nondisordered control participants were randomly assigned to a positive- or a negative-interpretation-training condition using ambiguous social scenarios as stimuli. We assessed the transfer of this training to the interpretation of subsequently presented novel ambiguous scenarios. We predicted that training would transfer to these novel scenarios; this transfer is indexed by whether participants judge positive or negative interpretations of these scenarios to be more or less similar to the novel scenarios. Thus, compared with participants in the negative-training condition, participants in the positive-training condition were predicted to judge positive interpretations to be more similar to the ambiguous scenarios. We also predicted that the training would be effective in both the MDD and the control participants but that the MDD participants would show greater improvement than would the control participants. Furthermore, to investigate the relation between interpretation and memory biases, we asked participants to recall these novel scenarios, guided by the hypothesis that CBM-I would not only change participants' interpretations of novel scenarios but also induce a training-congruent memory bias. Thus, we predicted that CBM-I would lead to a training-congruent memory bias for the ambiguous scenarios such that participants would be more likely to report memory distortions (or intrusions) that were congruent with their training condition. Again, we predicted these training effects across MDD and control participants but expected the effects to be stronger in the MDD group than in the control group.

Participants were also exposed to an acute stressor while we assessed psychophysiological arousal. We predicted that participants who completed positive-bias training would show reduced physiological arousal to the stressor compared with participants who received negative training. We again expected this effect in both the MDD and control groups and a stronger effect in the MDD group. Finally, to further examine the effects of negative- and positive-interpretation training within the MDD group, we compared MDD participants in the two training conditions with MDD participants in the no-training condition. We expected to find no differences in any of our measures when we compared MDD participants in the negative-training versus the no-training condition; however, we expected that MDD participants in the positive-training condition would exhibit more positive interpretations, better recall of positive material, and lower stress reactivity than would MDD participants in the no-training condition.

Method

Participants

Participants were recruited from a variety of sources. Clinical participants were solicited from two outpatient psychiatry clinics in a university teaching hospital, as well as through advertisements posted in numerous locations within the local community (e.g., Internet bulletin boards, university kiosks, supermarkets). Healthy control participants were recruited from the community through advertisements posted in the same locations. Participants' responses to a telephone interview provided initial selection information. This phone screen established that participants were fluent in English and were between 18 and 60 years of age. Participants were excluded from analysis for severe head trauma, learning disabilities, current psychotic symptoms, bipolar disorder, and alcohol or substance abuse within the past 6 months. This telephone

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interview was also used to identify individuals who were likely to meet criteria for one of the two diagnostic groups; these individuals were invited to come to the laboratory for a more extensive interview. Participants were paid $25 per hour for participation in this study.

Trained interviewers administered the Structured Clinical Interview for *DSM–IV* Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 1995) to these individuals during their first session in the study. The SCID has demonstrated good reliability for the majority of the disorders covered in the interview (J. B. Williams et al., 1992). All interviewers had extensive training in the use of the SCID, as well as previous experience in administering structured clinical interviews with psychiatric patients prior to beginning the current study. Our team of interviewers achieved excellent interrater reliability. The kappa coefficients were .93 for the MDD diagnosis and .92 for the "nonpsychiatric control" diagnosis, that is, the absence of current or lifetime psychiatric diagnoses, according to the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM–IV*; American Psychiatric Association, 1994) criteria.

Participants were included in the depressed group if they met the *DSM–IV* criteria for MDD. The never-disordered control group consisted of individuals with no current diagnosis and no history of any Axis I disorder. Participants also completed the Beck Depression Inventory–II (BDI-II; see the Questionnaires section). Participants were scheduled for a second session of "computer tasks" usually within 2 weeks after the interview.

In total, 76 individuals (48 MDD, 28 control) participated in this study. The MDD participants were randomly assigned to the positive-training (*n* = 16), the negative-training (*n* = 15), or the no-training (*n* = 17) condition. The control participants were randomly assigned to either the positive-training (*n* = 14) or the negative-training (*n* = 14) condition.

Questionnaires

BDI-II. Severity of current depressive symptoms was assessed using this 21-item self-report measure. The BDI-II is a widely used depression scale with good psychometric properties (Beck & Steer, 1993; Beck, Steer, & Garbin, 1988) and correlations with clinician ratings of depression of .62 to .66 (Foa, Riggs, Dancu, & Rothbaum, 1993).

Mood ratings. To assess current mood, we had participants rate multiple mood items before and after each training session by indicating the degree to which the items described how they felt right now. Responses were made on a scale from 1 (*not at all*) to 11 (*extremely*) and were averaged across items to yield positive (*interested, excited, enthusiastic*) and negative (*distressed, upset, nervous*) affect scores.

CBM training

In this training, participants were exposed to ambiguous scenarios and asked to complete word fragments that solve the ambiguity in either a positive or a negative direction. The rationale behind the training is that participants develop implicit expectations that ambiguous situations are more likely to end positively or negatively depending on the training condition. Participants in the positive- and negative-training conditions took part in two training sessions that were scheduled within 1 week. Participants in the no-training condition participated only in the test phase (see later discussion). In each training session, participants were presented with 10 blocks of 13 scenarios each in which they were asked to imagine themselves as the central character. For example, in a scenario titled "Meeting a Friend," participants were asked to picture themselves waiting at an empty bar to meet an old friend. Instructions and scenarios were taken from training studies reported by Mathews and Mackintosh (2000). Each scenario consisted of a title and two to three sentences and ended with a word fragment for participants to complete. Within each of the 10 training blocks, 8 training scenarios, 2 probe scenarios, and 3 filler scenarios were presented. The filler scenarios were identical in both training conditions and, thus, helped to disguise the training condition. For the training scenarios, each word fragment could be completed to produce only one possible solution, which disambiguated the meaning of the scenario according to the assigned training condition. Thus, for the positive-training group, the completed fragment produced a positive outcome for the scenario, whereas for the negative-training group, the completed fragment produced a negative outcome. In the probe scenarios, the word fragment disambiguated the sentence in the same way (either positive or negative) for all participants, regardless of training group. In the filler scenarios, completion of the word fragments produced a neutral meaning. Examples can be found in previous training studies (e.g., Mathews & Mackintosh, 2000).

Prior to training, participants were told that for each trial, they would be shown a brief scenario that would end with an incomplete word fragment. They were instructed to press the spacebar as soon as they were able to solve the word fragment. After the key press, the scenario disappeared from the screen and participants then typed the completed word on the next screen. In the final segment of the trial, participants were presented with a simple comprehension question and responded by pressing "Y" (yes) or "N" (no). This comprehension

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question served to emphasize the valence of each scenario, as well as test participants' understanding of the text. Participants were given the opportunity to complete three practice trials prior to beginning the training to ensure their understanding of the task. The order of the training blocks and the order of the scenarios within the blocks were newly randomized for each participant.

Test phase

In the test phase, participants were presented with 20 novel ambiguous scenarios that were identical in structure to those they had viewed in the training phase. The main difference between the training and test scenarios was the fact that, although there was only one possible solution for the word fragment, the resolved word maintained the ambiguity of the preceding text and did not resolve the scenario in a positive or a negative way. The scenarios were presented in random order. Participants were shown each scenario on the computer screen again and were instructed to press any key as soon as they were able to solve the word fragment. After doing so, the scenario disappeared from the screen, and participants were asked to enter the completed word. Next, to maintain consistency, we presented participants with a comprehension question and asked them to indicate their answers with a "Y" or "N" response. After participants provided their response, they were presented with the next test scenario. Unlike the comprehension questions during the training phase, these questions did not draw attention to the emotional implications of the scenario.

Interpretation test. After finishing a brief filler task, participants completed a computer task in which they were presented with the titles of the previously presented test scenarios. Each title was presented one at a time on the screen in random order. For each scenario title, participants were instructed to rate four sentences according to their similarity to the original scenario with the corresponding title (1: *very different*; 2: *fairly different*; 3: *fairly similar*; 4: *very similar*). In each case, two of these sentences were target sentences—a positive target that matched a positive interpretation of the original scenario (e.g., *You arrange to meet in a bar and your friend arrives late*) and a negative target that matched a negative interpretation (e.g., *You arrange to meet in a bar but your friend doesn't turn up*). The other two sentences were positive and negative foils—sentences with a generally positive or negative meaning that were unrelated to the ambiguous concept in the original scenario. These foil statements were included to assess broader valence effects of the training. The positive-foil sentence assigned a generally positive meaning to the scenario but was not based on any information provided by the original text (e.g., *Your friend wants to meet again but you don't have time*); similarly, the negative-foil sentence assigned a generally negative meaning but was not based on the original text (e.g., *Your friend tells you that she does not want to meet you*).

To assess interpretations of the test scenarios, we presented each of the four sentences (per scenario) one at a time under the scenario title. When each sentence appeared on the screen, participants were instructed to type the number corresponding to their rating of similarity to the meaning of the scenario. Once they entered their similarity rating, they were presented with the next sentence until they had provided ratings for all four sentences corresponding to that scenario title. The order of these sentences was newly randomized for each participant.

Recall task. Finally, participants were asked to recall details from the 20 test scenarios. The titles of the scenarios were presented in random order on the computer screen. When presented with each title, participants were instructed to recall aloud as many details as they could from the corresponding scenario. A key press initiated the next trial. Responses were audiotaped and later transcribed. Two independent raters were trained to code the transcriptions for whether each recalled scenario contained intrusions or new ideas (yes/no) and, if so, the valence of each intrusion (positive, negative, neutral). Once adequate levels of interrater agreement in the number and valence of intrusions were achieved (r = .85) using independent training scenarios, two raters who were blind to the experimental conditions categorized intrusions in each recalled scenario as belonging to one of three groups: negative (e.g., *everyone stares and laughs at you at the bar*), positive (e.g., *your friend arrives right as you walk in the door and is happy to see you*), or neutral (e.g., *you have a seat and wait at the bar*).

Stress task

The stress induction was based on a procedure developed by Waugh, Panage, Mendes, and Gotlib (2010). After completing the test phase, participants sat and rested for 5 min. Participants were then instructed that they might have to give a 5-min speech and would have 2 min to prepare the speech. They were told that their speech would be recorded and judged by evaluators on clarity, coherence, and persuasiveness and that at the end of the 2-min preparation period, the experimenter would flip a coin to determine whether the participants had to give a speech. The experimenter then told participants the speech topic was, "Why are you a good friend?"—a topic used successfully in previous studies to induce

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anticipatory-stress responses (Fredrickson, Mancuso, Branigan & Tugade, 2000; Waugh et al., 2010)—and left them alone to prepare the speech for 2 min. The experimenter then flipped a double-tailed coin to ensure that the participants would not have to give the speech. No participants reported being suspicious about this fixed coin flip. After anticipating giving the speech, participants sat and rested for 5 min. This anticipatory-stress procedure has been shown to induce increases in both heart rate and negative affect that are comparable with stress procedures in which the participants actually give the speech. An additional advantage of this anticipatory-stress procedure that is less true of speech stressors is that anticipatory stress–induced negative affect and heart rate are positively correlated, thereby making it an effective test of whether changes in negative-interpretation biases can influence physiological responses to stress (Waugh et al., 2010).

Self-reported distress. We used average scores on three items to assess self-reported distress during the stress task (*distressed, upset, nervous*). All three items were given three times during the stress task: at baseline before the onset of the stressor (prestressor), after the anticipation phase of the stressor when participants were finished preparing the speech (anticipation), and after a 5-min recovery period when they had been told that they did not have to give the speech (recovery).

Heart rate. Immediately on participants' entering the lab for either their second training session plus test session (training conditions) or just their test session (no-training condition), disposable snap electrodes were attached to the participants using a Lead II configuration. During the stress task, cardiovascular responses were recorded at 1-kHz sampling rate with the electrocardiogram module of an integrated physiological acquisition system (Biopac MP150; Biopac Systems, Goleta, CA) and then high-pass (.5 Hz) and low-pass (40 Hz) filtered. We inspected the electrocardiogram data for artifacts and missing R peaks (on the basis of improbable interbeat intervals) using a physiological analysis software package (ANSLAB; Wilhelm & Peyk, 2005). If a single R peak was missing, an R peak was inserted at a time point halfway in between the two neighboring R peaks. If more than one R peak was missing in a row, those data were not scored. Heart rate (beats per minute) was then calculated from the scored interbeat intervals for each time period (baseline – 5 min; anticipation – 2 min; recovery – 5 min).

Overall procedure

All participants took part in the phone interview and the SCID, which took approximately 2 hr to complete. Within 1 week after the SCID interview, participants in the training conditions took part in the first training session, which was followed by the second training session within 3 days. After the second training session, participants completed a 15-min word-scramble filler task, which was followed by the test phase. During the test phase, participants first read the set of 20 emotionally ambiguous scenarios and then completed another brief filler task, the reverse-digit-span task from the fourth edition of the Wechsler Adult Intelligence Scale (Wechsler, 2008), before performing the interpretation and recall tests, in that order. The test phase was followed by the stress task. All participants (training and no-training conditions) completed the test phase and the stress task. The training sessions lasted approximately 45 to 60 min, the test phase about 30 min, and the stress task 12 min. All study procedures were approved by the institutional review board.

Results

Demographic characteristics and mood ratings

Demographic characteristics and mood ratings throughout the training are presented in Table 1. Participants in the five groups did not differ in gender, age, or education. As expected, there was a main effect of diagnostic group for BDI-II scores, $F(1, 55) = 213.28$, $p < .001$, $\eta^2 = .79$, there was no main effect of training condition, $F(1, 55) < 1$, and no interaction of group and condition, $F(1, 55) < 1$. Approximately half of the MDD participants in each group presented with a comorbid condition, mostly anxiety disorders, $\chi^2(2, N = 48) = 3.86$, $p > .10$. We also compared mood ratings at three time points during the training—prior to the interpretation training (Time 1), after the first training session (Time 2), and after the second training session (Time 3)—using a mixed-design analysis of variance (ANOVA) with group (MDD vs. control) and training condition (positive vs. negative) as the between-subjects factors and time point and valence (positive affect vs. negative affect) as the within-subjects factors. The analysis yielded main effects of time, $F(2, 110) = 20.37$, $p < .001$, $\eta^2 = .27$, of valence, $F(1, 55) = 104.6$, $p < .001$, $\eta^2 = .66$, and of group, $F(1, 55) = 6.95$, $p = .018$, $\eta^2 = .11$, and an interaction of group and valence, $F(1, 55) = 69.15$, $p < .001$, $\eta^2 = .56$. No main or interaction effects involving training condition were found. Participants in both training conditions improved in their negative affect, but MDD participants reported more negative affect throughout the course of the study. In addition, we found a greater decline in negative affect in the MDD group compared with the control group. It is important to note, however, that training condition did not affect mood ratings.

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Table 1. Demographic Characteristics, Mood Ratings, and Self-Reported Distress in Stress Task by Group and Training Condition

	Control (n = 28)		MDD (n = 48)		
Measure	Positive	Negative	Positive	Negative	No training
Gender (male/female)	5/9	6/8	6/10	4/11	5/12
Age	40.93 (11.24)	42.07 (12.77)	38.50 (10.77)	39.40 (12.18)	33.88 (11.25)
College (%)	64	92	57	60	48
Comorbid disorders (%)	0	0	43	53	70
BDI-II	3.07 (3.61)	1.71 (2.61)	32.88 (8.18)	30.93 (12.07)	36.41 (10.77)
NA Time 1	1.12 (0.28)	1.16 (0.31)	1.81 (0.93)	2.02 (0.82)	
NA Time 2	1.14 (0.31)	1.11 (0.28)	1.66 (0.66)	1.65 (0.47)	
NA Time 3	1.02 (0.09)	1.04 (0.12)	1.35 (0.61)	1.64 (0.62)	
PA Time 1	3.57 (0.74)	3.33 (0.89)	1.93 (0.87)	2.20 (0.81)	
PA Time 2	3.11 (1.08)	2.76 (0.88)	1.75 (0.82)	2.00 (0.77)	
PA Time 3	3.07 (0.82)	2.62 (1.01)	1.81 (0.79)	1.67 (0.62)	
Stress task: Self-reported distress					
Baseline	1.28 (0.69)	1.14 (0.31)	1.75 (0.68)	1.93 (0.96)	
Anticipation	2.00 (1.15)	2.19 (0.95)	3.04 (0.94)	3.26 (1.11)	3.41 (1.15)
Recovery	1.19 (0.33)	1.29 (0.55)	1.39 (0.51)	1.71 (0.65)	2.15 (1.19)

Note: Unless otherwise noted, the table presents means for each measure. Standard deviations are shown in parentheses. MDD = participants diagnosed with major depressive disorder; BDI-II = Beck Depression Inventory–II; NA= negative affect; PA = positive affect.

Interpretation training

Means and standard deviations for all main study variables are presented in Table 2. We first compared MDD and control participants in the positive-training versus negative-training conditions. We predicted that the training should affect all participants but that training effects should be larger in the MDD group than in the control group. To examine the effects of CBM-I on participants' interpretations of novel scenarios, we analyzed similarity ratings for the test scenarios by a mixed-model ANOVA with group (MDD vs. control) and training condition (positive vs. negative) as the between-subjects factors and valence of the statements (positive vs. negative) and type of statement (target vs. foil) as within-subjects factors. This analysis yielded a three-way interaction of training condition, valence, and type, $F(1, 52) = 11.19$, $p = .002$, $\eta^2 = .18$. Contrary to expectations, no effect of diagnostic group emerged. Follow-up analyses on this

Table 2. Recognition Ratings, Intrusions, and Heart Rate During Stress Task

	Control		MDD		
Measure	Positive	Negative	Positive	Negative	No training
Recognition					
Foil positive	1.56 (0.41)	1.44 (0.35)	1.97 (0.74)	1.61 (0.65)	1.68 (0.50)
Foil negative	1.34 (0.33)	1.52 (0.33)	1.76 (0.59)	1.85 (0.75)	1.86 (0.59)
Target positive	2.82 (0.38)	2.49 (0.35)	2.99 0.48)	2.50 (0.58)	2.48 (0.60)
Target negative	2.09 (0.46)	2.65 (0.39)	2.59 (0.55)	2.76 (0.58)	2.58 (0.54)
Recall					
Intrusion positive	5.89 (5.97)	2.96 (3.97)	4.21 (4.23)	1.60 (1.96)	2.88 (2.94)
Intrusion negative	4.42 (4.13)	6.32 (4.14)	3.75 (2.25)	8.20 (7.97)	6.29 (6.07)
Intrusion neutral	9.64 (4.88)	10.93 (6.99)	8.21 (4.31)	9.54 (4.78)	7.26 (2.85)
Stress task: Heart rate					
Baseline	68.33 (10.86)	69.28 (7.93)	72.26 (9.06)	69.32 (10.77)	79.74 (11.84)
Anticipation	70.68 (11.64)	73.73 (11.10)	74.77 (8.84)	74.66 (11.20)	80.76 (12.35)
Recovery	68.05 (11.44)	70.58 (8.34)	73.03 (9.82)	69.66 (9.15)	80.30 (12.11)

Note: The table presents means for each measure. Standard deviations are shown in parentheses. MDD = participants diagnosed with major depressive disorder.

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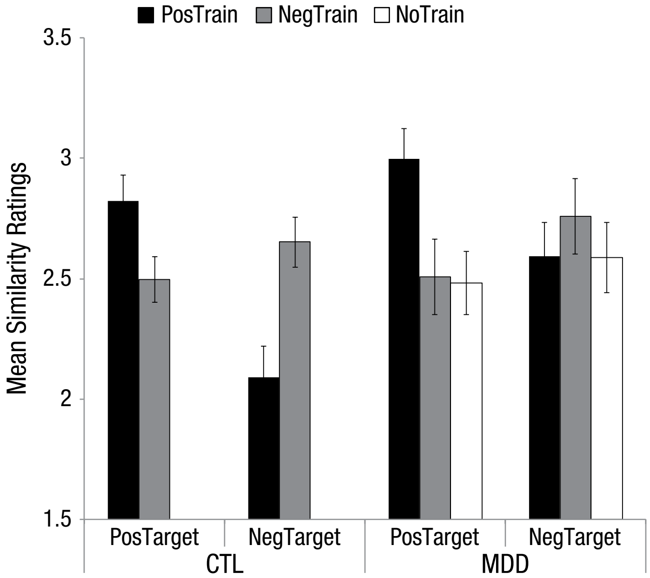

Fig. 1. Results: mean similarity ratings for positive and negative target statements when rating novel test scenarios separated by training group (PosTrain = positive training; NegTrain = negative training; NoTrain = no training) and diagnostic group (CTL = control participants; MDD = participants diagnosed with major depressive disorder). Similarity ratings ranged from 1 (*very different*) to 4 (*very similar*). Error bars represent 1 *SE*. PosTarget = positive target; NegTarget = negative target.

three-way interaction were conducted separately for foil and target statements. Results of the follow-up tests revealed no significant training-condition differences in similarity ratings for either positive foils, $t(54) = 1.64$, $p = .107$, or negative foils, $t(54) = 0.78$, $p = .436$. There were, however, significant training-condition differences for the target statements (see Fig. 1 for mean similarity ratings). Compared with participants in the negative-training condition, participants in the positive-training condition chose higher similarity ratings for positive target statements, $t(54) = 3.39$, $p = .001$, and lower similarity ratings for negative target statements, $t(54) = 2.45$, $p = .018$. Overall, there was no significant main effect of group and no significant interactions with group. Thus, the training was effective in all participants, and the effects did not differ as a function of diagnostic group.

Finally, we conducted ANOVAs to compare MDD participants in the positive- and negative-training conditions with those in the no-training condition. The results of these analyses yielded no training condition differences for negative targets, $F(2, 43) < 1$, for negative foils, $F(2, 43) < 1$, or for positive foils, $F(2, 43) = 1.34$, $p = .274$. MDD participants in the three training conditions did differ significantly, however, in their responses to the positive targets, $F(2, 43) = 4.09$, $p < .024$, $\eta^2 = .16$. Depressed participants in the positive-training condition endorsed higher similarity ratings for positive target statements than did depressed participants in both the negative-training, $t(27) = 2.46$, $p = .021$, and the no-training, $t(30) = 2.64$, $p = .031$, conditions who did not differ in their endorsement of positive statements, $t(29) < 1$. In summary, participants endorsed higher similarity ratings for target statements that corresponded to their training condition. No differences were found between MDD and control participants. Within the sample of MDD participants, those in the negative-training condition did not differ from those in the no-training condition. In contrast, MDD participants in the positive-training condition endorsed higher similarity ratings for positive target statements than did MDD participants in both the negative-training and the no-training conditions.

Recall task

We also examined whether CBM-I affects participants' memory for the test scenarios. In this context, we predicted that CBM-I would result in a corresponding memory bias in the free-recall task and that MDD and control participants would differ in the strength of this training effect. We assessed the number and valence of memory distortions or intrusions (i.e., new details that the participants "recalled" that had never been part of the original scenarios). Similar to the analytic approach reported earlier, we first conducted a mixed-model ANOVA with group (MDD vs. control) and training condition (positive vs. negative) as the between-subjects factors and valence of the intrusion (positive vs. negative vs. neutral) as the within-subjects factor to compare the training conditions on number of intrusions. This analysis yielded a significant interaction of training condition and intrusion valence, $F(2, 110) = 7.90$, $p = .001$, $\eta^2 = .13$; the effect of diagnostic group was not significant. Follow-up tests showed that participants in the two training conditions did not differ in the number of reported neutral intrusions, $t(57) < 1$; there were significant differences between the positive- and negative-training conditions, however, in the number of both positive intrusions, $t(57) = 2.48$, $p = .016$, and negative intrusions, $t(57) = 2.47$, $p = .017$. As illustrated in Figure 2, participants in the positive-training condition recalled more positive intrusions than did participants in the negative-training condition; similarly, participants in the negative-training condition recalled more negative intrusions than did participants in the positive-training condition. These results indicated that participants in each training condition reported more memory intrusions that corresponded to the valence of their training.

Finally, we conducted an ANOVA to compare the positive- and negative-training conditions with the no-training condition within the MDD sample. Although not

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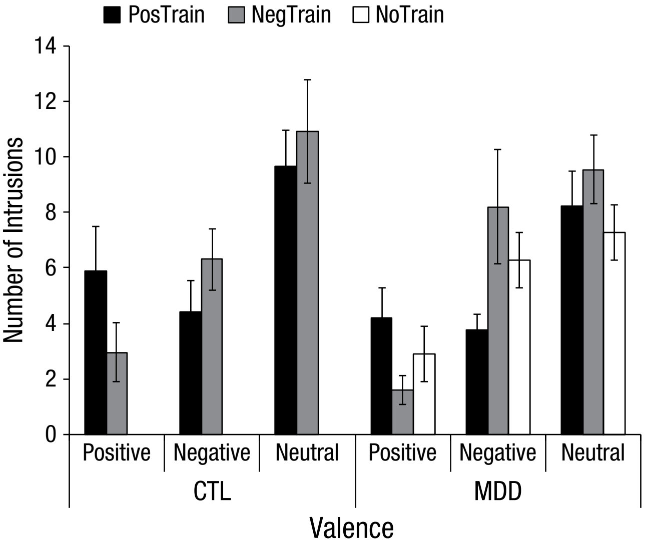

Fig. 2. Results: mean number of positive, negative, and neutral memory intrusions (i.e., material that was not originally presented) made by each training group (PosTrain = positive training; NegTrain = negative training; NoTrain = no training) and diagnostic group (CTL = control participants; MDD = participants diagnosed with major depressive disorder) during the recall task. Error bars represent 1 *SE*.

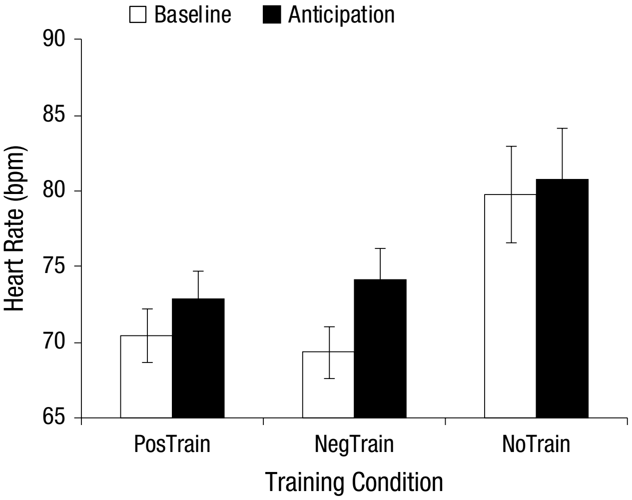

Fig. 3. Results: mean heart rate at baseline and after anticipation in the three training groups (PosTrain = positive training; NegTrain = negative training; NoTrain = no training). Error bars represent 1 *SE*.

reaching conventional levels of statistical significance, there were trends for both positive, $F(2, 45) = 2.60$, $p = .08$, and negative, $F(2, 45) = 2.24$, $p = .11$, intrusions that were in the predicted direction—neutral intrusions: $F(2, 45) = 1.1$, $p = .338$. As illustrated in Figure 2, MDD participants in the positive-training condition reported more positive intrusions than did MDD participants in the negative-training condition, $t(29) = 2.81$, $p = .037$; similarly, MDD participants in the negative-training condition reported more negative intrusions than did MDD participants in the positive-training condition, $t(29) = 2.51$, $p = .040$. MDD participants in both training conditions, however, did not differ significantly from participants in the no-training condition. Further supporting the formulation that interpretation and memory biases are related, significant correlations among number of intrusions and similarity ratings for target statements were obtained across all participants. These correlations were as follows: positive intrusions and positive targets, $r(73) = .41$, $p < .001$; negative intrusions and negative targets, $r(73) = .40$, $p < .001$. There were no significant correlations among intrusions and similarity ratings for target statements when we examined each training condition separately.

Stress task

We examined heart rate and self-reported distress to assess whether the training conditions differentially affected stress reactivity and recovery. We conducted ANOVAs with time (baseline, anticipation, and recovery) as the within-subjects variable and diagnostic group and training condition as the between-subjects variables. The prestressor questionnaire was not given to participants in the no-training condition; therefore, the analyses for self-reported distress focus on only the two training conditions. The ANOVA investigating self-reported distress (see Table 1) yielded a main effect of time, $F(2, 110) = 54.07$, $p < .001$, $\eta^2 = .49$, and a main effect of group, $F(1, 55) = 22.43$, $p < .001$, $\eta^2 = .29$, which were qualified by a significant interaction of group and time, $F(2, 110) = 4.14$, $p = .018$, $\eta^2 = .07$. These results indicated that the stressor was perceived as stressful and that the MDD and control groups differed in their perception of the stressfulness. There was, however, no effect of training on self-reported level of distress. The ANOVA for heart rate yielded a significant main effect of time, $F(2, 116) = 27.80$, $p = .000$, $\eta^2 = .32$, which was qualified by a significant interaction of time and condition, $F(2, 116) = 2.95$, $p = .005$, $\eta^2 = .05$; there was no effect of diagnostic group on heart rate. An inspection of Figure 3 shows that participants in the two training conditions differed significantly in their increase in heart rate from baseline to anticipation: Participants in the negative-training condition exhibited a significantly higher increase in heart rate than did participants in the positive-training condition, $t(55) = 2.18$, $p = .033$. Participants in the negative- and positive-training conditions did not differ in heart rate at recovery, $t(55) < 1$.

Finally, we compared MDD participants in the positive- and negative-training conditions with MDD participants in the no-training condition. This ANOVA yielded a significant interaction of time and condition, $F(1, 43) = 2.78$, $p = .032$, $\eta^2 = .12$. MDD participants in the no-training

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condition did not differ from MDD participants in the positive-training condition with respect to increase in heart rate, $t(29) = 1.08$, $p = .286$, but they exhibited a smaller increase in heart rate than did MDD participants in the negative-training group condition, $t(27) = 2.38$, $p = .025$. These results should be interpreted with caution, however. As Figure 3 shows, the MDD participants in the no-training condition had elevated heart rate at baseline; therefore, the lack of reactivity in participants in this condition may be due to a ceiling effect.

Discussion

The present study was conducted to examine whether CBM-I in participants diagnosed with MDD affects interpretation of novel ambiguous scenarios, memory, and physiological stress responding. The results indicate that MDD and control participants in the positive-training condition demonstrated an interpretation bias that corresponded to their training condition. Specifically, in both diagnostic groups, participants in the positive-training condition were more likely to rate positive than negative target sentences as similar to the test scenario and were also more likely to do so than were participants in the negative-training condition. The study included a sample of MDD participants who did not undergo training. MDD participants in the positive-training condition were significantly more likely to endorse positive interpretations than were MDD participants in this no-training condition; in contrast, MDD participants who were assigned to the negative-training condition did not differ from MDD participants in the no-training condition. It is important to note that we found training effects on memory and stress responding. Specifically, compared with the participants in the negative-training condition, those in the positive-training condition were more likely to report positive memory intrusions and showed a smaller increase in heart rate in response to the stress induction.

The current findings replicate past research that has demonstrated effects of CBM-I (e.g., Mackintosh et al., 2006; Mathews & Mackintosh, 2000; Salemink, van den Hout, & Kindt, 2007; Yiend et al., 2005). Most CBM-I studies, however, have focused on anxiety disorders. This study shows that CBM-I is beneficial in MDD participants, which supports findings from recent studies that have used this training in MDD (Bowler et al., 2012). Like Bowler et al. (2012) and Yiend et al. (2014), we found effects of the training on interpretation biases in MDD. In contrast to the findings reported by Yiend et al., however, our training also had a positive impact on stress reactivity. The discrepant findings obtained in these two studies may be due to either the difference in number of training sessions (two sessions in our study vs. one in the study by Yiend et al.), the use of psychophysiological measures of stress responding, or both. Indeed, in the current study, we found no indication of changes in self-reported stress responding but a significant difference when we examined heart rate. Heart rate and affective responses during stress are correlated with each other only very loosely (Cohen et al., 2000) and only under certain circumstances (Waugh et al., 2010), which suggests that the heart rate changes in this study may have been due to training-induced effects in some process other than negative affect, such as in the perceived effort of the task (Peters et al., 1998). There is a clear need for more studies in which researchers examine stress reactivity using a multimethod approach and add more training sessions to corroborate these findings.

In addition, previous studies have focused only on one cognitive bias, despite researchers' suggestion that cognitive biases interact and influence each other (e.g., Hirsch et al., 2006). Indeed, in the current study, our measures of interpretation and memory bias were significantly correlated across groups. These findings concerning memory bias are consistent with research that has demonstrated that how events are initially interpreted affects how they are subsequently recalled (Hertel & Brozovich, 2010). Given the evidence for memory biases in depression (Matt et al., 1992; Watkins, Mathews, Williamson, & Fuller, 1992) and the potential benefits on emotion regulation and stress reactivity from training positive biases, the investigation of the association between interpretation and memory is a critical area for further exploration.

For example, the tendency to respond to negative events and mood states with rumination is an important risk factor for the onset of depression (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). People who ruminate repetitively think about past events and interpret these events negatively. Indeed, rumination has been shown to strengthen mood-congruent memory biases (Lyubomirsky, Caldwell, & Nolen-Hoeksema, 1998). In contrast, the benefits of reappraisal as a more adaptive emotion-regulation strategy may lie in its resemblance to positive-interpretation training. Our findings suggest that the habitual use of rumination or reappraisal may have important consequences not only for acute emotional responding but also for how the emotion-eliciting event will be remembered and thereby affect emotional well-being in the future.

The present study also replicates previous results by Salemink, Hertel, and Mackintosh (2010), who trained biases to examine whether the recall of prior events could be modified by subsequently acquired biases. Participants in this study exhibited biased recall of their own interpretation of the scenarios but not of the scenarios themselves. This lack of a bias in recall of the scenarios was predicted on the basis that recall intrusions

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arise from imagery processes that operate during initial interpretations (see Hertel et al., 2008; Hirsch, et al., 2006).

Although previous training studies have reported effects of both positive and negative training (Mathews & Mackintosh, 2000; Salemink et al., 2007; Yiend et al., 2005), our findings suggest that positive training had stronger effects than did negative training. MDD participants in the negative-training group did not differ from those in the no-training group in their performance on any of the outcome measures. Indeed, our findings show that compared with control participants, MDD participants show a negative bias from the outset and that whereas training induced a negative bias in control participants, it did not make MDD participants worse.

Findings concerning training effects on stress response in previous studies on CBM-I in depression have been equivocal. The present study is the first to investigate physiological stress responding; our results indicate that training affects physiological arousal in response to an acute stressor. This result has important clinical implications. Depression has been associated with cardiovascular dysregulation (Salomon, Clift, Karlsdóttir, & Rottenberg, 2009) and has been shown to be a risk factor for heart disease (Musselman, Evans, & Nemeroff, 1998). The finding that CBM-I training affects cardiovascular stress responding is promising, but it is clear that these findings require replication. Unfortunately, the fact that participants in the no-training condition were elevated in their heart rate at baseline precluded us from being able to compare the positive- and negative-training conditions with the no-training condition. It is likely that this initial heart rate elevation is due to this being their first visit to the laboratory.

We should note three limitations of this study. First, we did not assess pretraining biases in interpretation or memory. We did, however, include a no-training control condition that allowed us to compare baseline responding with training-induced responding; our results show clear differences between the no-training and the positive-training conditions on all of our measures. We should point out, however, that we included a no-training condition only for the MDD group; we did not recruit a group of control participants who did not undergo training—including this group was not central to the main aim of this study, which was to examine CBM-I in clinical depression. It would be helpful in future work to include both control and MDD groups who do not undergo the training. Second, the training consisted of only two sessions. Two training sessions is an improvement over the many studies in this area that have used a single training session and clearly was sufficient to demonstrate that biases can be modified. The use of a larger number of training sessions would be important in studies on the longer-term clinical impact of these trainings. Indeed, recent studies on CBM-I as an intervention for depression have focused on interventions lasting 10 weeks or more. It is encouraging that the two-session training used in this study yielded significant findings, but future research is required to extend the training time to examine the effects of more prolonged interventions on memory and on stress reactivity.

Finally, we used the training scenarios developed by Mathews and Mackintosh (2000) that describe situations that are most centrally relevant to socially anxious participants. Other researchers have now developed training protocols that are more specific to the concerns of depressed participants (Lester, Mathews, Davison, Burgess, & Yiend, 2011; Yiend et al., 2014), and the use of such stimuli could result in stronger training effects than those documented in this study. Indeed, it is possible that the lack of group differences is due to the use of scenarios that are not depression specific. Future studies are needed to investigate this possibility more explicitly and systematically.

Alternative explanations of our results involve mood and the order of our tasks. Mood affects memory and it is therefore possible that training-related changes in mood contributed to the changes in interpretation and memory that we found in this study. This account does not appear to be viable, however, given that mood did not change as a consequence of training and that mood was not related to measures of memory or interpretation.[1] Second, because we necessarily assessed interpretation bias before recall bias, it is possible that the assessment itself played a role in changes in our dependent measures. Participants in both training conditions were exposed to the same four sentences (two targets and two foils); thus, condition-associated differences in recall cannot be explained by differences in exposure to statements in the interpretation task. In fact, we would have encountered several problems if we had measured recall first. During recall, participants are given more time to elaborate on their memory of the previously presented scenarios; therefore, their subsequent similarity ratings would primarily be assessments of how participants recalled the descriptions during recall, rather than how they interpreted the situation initially. In the design of the current study, we presented the interpretation task as a brief exercise in which participants were asked to quickly indicate similarity ratings, and we allowed less time for elaboration. We believe that the main constraint that test order places on these results involves external validity. It may be that explicit interpretation is necessary to obtain biases in remembering the scenarios. This possibility should be investigated in future research.

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Biases in interpretation and memory affect emotion regulation in various ways. They can influence judgments of the frequency of positive and negative events and of the likelihood that these types of events will occur in the future. Memory biases have also been associated with lowered self-esteem and with increased levels of negative affect and hopelessness (MacLeod & Campbell, 1992). Increased accessibility of negative material and difficulties recalling mood-incongruent material may interfere with the use of effective mood-regulation strategies. These difficulties in effectively managing negative mood may be an important mechanism by which memory biases affect the maintenance and recurrence of depressive episodes (Nolen-Hoeksema, 2000; Nolen-Hoeksema & Larson, 1999). Increased accessibility and recall of positive material, conversely, is related to higher levels of well-being (Charles, Mather, & Carstensen, 2003). A reduction in negative biases in memory and interpretation therefore may improve mood and decrease emotional vulnerability after stressful experiences, which reduces the risk for the onset and recurrence of emotional disorders. Future studies are needed to examine underlying mechanisms and the durability of the training effects. Given the critical role of memory biases in the development and maintenance of emotional disorders, the ability to manipulate interpretation biases and thereby change individuals' memory for events could hold great promise for the prevention and treatment of these disorders and provide greater insight into the functional role of cognitive biases in emotional disorders.

Author Contributions

J. Joormann developed the study concept. All authors contributed to the study design. Testing and data collection were performed by research assistants under the supervision of C. E. Waugh and I. H.Gotlib. J. Joormann and C. E. Waugh performed the data analysis and interpretation. J. Joormann drafted the manuscript, and C. E. Waugh and I. H. Gotlib provided critical revisions. All authors approved the final version of the manuscript for submission.

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Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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Note

1. No significant correlations were found among mood ratings assessed after the training and any of the interpretation or memory measures (i.e., similarity ratings for positive and negative targets and positive, negative, and neutral intrusions) in the two training groups.

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