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Efficacy of Interpretation Bias Modification in Depressed Adolescents and Young Adults

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Abstract

This study evaluated the efficacy of a four-session Cognitive Bias Modification-Interpretation program for 45 depressed adolescents and young adults (14–21 years old; 12 males, 33 females; Beck Depressive Inventory, Second Edition = 14) randomized to an active intervention condition (repeated exposure to positive outcomes of depression-relevant ambiguous scenarios; $n=23$) or a control condition ($n=22$). Both conditions experienced reductions on a Test of Interpretation Bias at post-treatment, with no significant between-group differences. When limited to those with negative bias at baseline, the intervention group showed greater improvement in interpretation bias at mid- and post-treatment. In addition, the intervention group overall had greater improvements in self-reported negative cognitions than the control group at post-intervention and two-week follow-up. However, there were no differences between groups in depression or anxiety symptom change. Potential factors contributing to mixed findings are discussed.

Keywords

Interpretation bias; Cognitive bias modification; Adolescents; Depression

Nearly 6% of adolescents meet criteria for a depressive disorder at any given time (Costello, Erklani, & Angold, 2006), with approximately 20% experiencing at least one lifetime major depressive episode before adulthood (Brent & Birmaher, 2006). The frequency with which depression affects adolescents, as well as the potential for recurrence or chronicity, and the severe morbidity of this condition, underscore the importance of developing efficacious treatments for this population. Recent large, multi-site clinical trials, including the Treatment of Adolescent Depression Study (TADS; Glass, 2004), have demonstrated the efficacy of treatments such as fluoxetine and cognitive-behavioral therapy (CBT) for adolescents with major depressive disorder (MDD). However, even when medication and CBT were combined in TADS, nearly 30% of adolescents did not significantly improve. Thus, novel effective interventions for depressed adolescents are needed.

Cognitive theories suggest that depressed individuals display a cognitive style characterized by negative interpretations of neutral or ambiguous information and selective attention to negative versus positive information (Beck, 1976; Beck & Clark, 1991; Ingram, 1984). Numerous empirical studies have confirmed the presence of these negative biases in depressed adults (Butler & Mathews, 1983; Cane & Gotlib, 1985; Mogg, Bradbury, & Bradley, 2006; Norman, Miller, & Klee, 1983; Nunn, Mathews, & Trower, 1997) and youth

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(Dalglish et al., 1997; Dineen & Hadwin, 2004; Eley et al., 2008; Gencoz, Voelz, Gencoz, Pettit, & Joiner, 2001; Neshat-Doost, Taghavi, Moradi, Yule, & Dalglish, 1998; Reid, Salmon, & Lovibond, 2006; Timbremont, Braet, Bosmans, & Van Vlierberghe, 2008; Whitton, Larson, & Hauser, 2008). Adolescents with symptoms of depression are also prone to selective abstraction, or intent focus on the negative details in a situation to the exclusion of positive or neutral details (Weems, Berman, Silverman, & Saavedra 2001). Further, in a combined community and clinical sample of children and adolescents, there was an association between greater symptoms of depression and higher frequency of thoughts of failure and personal loss (Schniering & Rapee, 2004).

The cognitive distortions associated with depression can be effectively targeted with CBT through the use of thought identification and cognitive restructuring (Lewinsohn, Clarke, Hops, & Andrews, 1990). Adolescents learn about their negative thought patterns and the link between their thoughts and moods, and then practice realistically evaluating their thought patterns and generating positive counter thoughts (Clarke, DeBar, Ludman, Asarnow, and Jaycox, 2002). Cognitive restructuring is a well-established, overt strategy for changing biased thinking patterns that involves in-session training and repeated between-session practice.

Recent studies have suggested that cognitive distortions may also be successfully targeted in a less overt fashion, using a computerized paradigm that trains individuals away from automatic negative interpretations of ambiguity. In the seminal study of this paradigm, Mathews and Mackintosh (2000) presented participants with a series of short social scenarios that remained ambiguous in valence until the last word, which resolved the ambiguity in either a predominantly positive or predominately negative direction. Participants assigned to the negative condition made more negative interpretations of ambiguity post-test and experienced an increase in post-test state anxiety, whereas those assigned to the positive condition made more positive interpretations and experienced a significant decrease in anxiety (Mathews & Mackintosh, 2000). Other studies from this group have replicated the original findings and shown that the induced interpretation biases endure for at least 24 hours (Yiend, Mackintosh, & Mathews, 2005) and persist despite changes in environmental context (Mackintosh, Mathews, Yiend, Ridgeway, & Cook, 2006). A growing literature including non-clinical adults with elevated anxiety and clinical samples of adults with anxiety disorders supports the efficacy of these computerized protocols (termed Cognitive Bias Modification – Interpretation [CBM-I]) in changing interpretation biases and reducing anxiety symptom severity (for a review, see Beard, 2011). A recent meta-analysis of these studies (Hallion & Ruscio, 2011) found that CBM-I has a large effect on interpretation bias change ($g=.81$) and a small effect on anxiety symptom reduction ($g=.13$ post-CBM). Notably, only four studies of clinically anxious samples were included in this meta-analysis, underscoring the need for more research on CBM-I for adults with clinical anxiety disorders.

Studies have also examined the application of CBM-I to depression or depressive symptoms, although paradigms have varied across these studies. Some paradigms have targeted interpretation of ambiguous situations similar to those used for anxiety (Blackwell & Holmes, 2010; Lang, Blackwell, Harmer, Davison, & Holmes, 2012; Tran, Siemer, & Joormann, 2011), while others have successfully trained reappraisal of autobiographical memories (Lang, Moulds, & Holmes, 2009; Schartau, Dalglish, & Dunn, 2009 [study 4]), or have taught participants to focus on concrete aspects of memories to challenge overgeneralization (Watkins, Baeyens, & Read, 2009). Overall, these studies have shown beneficial effects of CBM on interpretation biases and symptoms of depression or self-esteem. Few of these studies have included participants with clinical depression, but those

that have (Blackwell & Holmes, 2010; Lang et al, 2012) have also shown improvements in interpretation bias and depression symptoms.

There have been only a few studies to date of CBM-I with pre-adolescent children, and all have focused on anxiety and used non-clinical or sub-clinical samples. These studies have shown that after one session of CBM-I, non-clinical school-aged children can be trained to interpret anxiety-relevant situations positively or negatively, consistent with condition (Muris, Huijding, Mayer, & Hameetman, 2008; Muris, Huijding, Mayer, Remmerswaal, & Vreden, 2009), with positive training having variable effects on avoidance behavior and no effect on self-reported anxiety (Lester, Field, & Muris, 2011a; 2011b). However, CBM-I may result in symptom reduction for children with higher levels of anxiety. Vassilopoulos, Banerjee, and Prantzalou (2009) presented three sessions of CBM-I to children with elevated social anxiety and found that those receiving positive training showed decreases in interpretation bias, decreases in self-reported social anxiety, and less anxiety about an anticipated social encounter compared to a no-training control group. Effects of CBM-I on cognitive biases and anxiety symptoms may also vary by type of instructions provided to children. Vassilopoulos, Blackwell, Moberly, and Karahaliou (2012) found that instructing non-clinical children (ages 10–12) to focus on the verbal content of ambiguous scenarios (versus to imagine the scenarios) enhanced the effects of four sessions of positive interpretation training on cognitive biases and also led to greater reductions in social anxiety symptoms.

Several recent studies have examined the efficacy of one-session CBM-I with non-clinical adolescents, with promising effects on interpretation bias. Lothmann, Holmes, Chan, and Lau (2011) randomized 82 healthy adolescents (ages 13–17 years) to one session of negative or positive CBM-I (60 scenarios developed for adolescents), examining the effects on subsequent interpretation bias and mood. Results were consistent with condition, with those adolescents in the positive training showing reductions in negative interpretations and increases in positive interpretations (and vice versa for negative training). In addition, those receiving the positive training showed reductions in negative affect. Using a similar paradigm, Lau, Molyneaux, Telman, and Belli (2011) found that in a non-clinical group of 39 adolescents (ages 13–18), post-training interpretations were consistent with condition. In contrast to Lothmann et al. (2011), there were no overall changes in positive or negative affect for either training group, but those with lower self-efficacy who were assigned to negative training showed a significant decrease in positive affect.

Salemink and Wiers (2011) collected complete data on 144 non-clinical adolescents (ages 14–16 years) randomized to one session of CBM-I (socially-relevant scenarios with positive outcomes) or one session of a placebo control (a balance of negative, positive, and neutral outcomes). Those receiving positive training became quicker at identifying positive versus negative interpretations of training scenarios, and at post-training they made fewer negative and more positive interpretations of new ambiguous scenarios (with no changes in the placebo group). CBM-I was effective for adolescents with both high and low trait anxiety. Notably, pre-training negative interpretation bias moderated the effects of CBM-I on post-training interpretations of ambiguity and speed to identify positive versus negative interpretations. Specifically, positive training was particularly efficacious for those adolescents with initial negative interpretation bias. In a sub-sample from this study (Salemink & Wiers, 2012), the researchers examined whether regulatory control (as measured by the classic Stroop task) was associated with interpretation bias and its modification. Those with poor regulatory control (but not high regulatory control) benefited from CBM-I, perhaps because these adolescents had higher levels of interpretation bias to remediate.

In sum, studies of non-clinical adolescents have found that CBM-I effectively modifies interpretation bias, particularly in adolescents with negative interpretation bias at baseline, though effects on negative affect have varied. Studies of clinically affected adolescents with a wider range of symptom severity and degree of interpretation bias are needed to better understand the effects of CBM-I on these variables.

Given the potential efficacy of CBM-I in modifying interpretation biases in adults and non-clinical children and adolescents, and the clear need for research extending this intervention to youth with clinical levels of depression, we developed and tested the efficacy of a four-session CBM-I intervention. The current study is the first to examine the efficacy of CBM-I with a predominantly clinically depressed sample of adolescents and young adults, using developmentally tailored training scenarios relevant to potential loss, rejection, and failure. We hypothesized that, compared to a control group, youth receiving positive interpretation training would show: 1) greater decreases in negative interpretations and increases in positive interpretations of ambiguous scenarios at post-training and two-week follow-up, and 2) greater decreases in scores on measures of depression and anxiety at post-training and follow-up.

Since our CBM-I intervention was intended to target negative interpretation biases, and keeping in mind the association between negative interpretation biases and depression, we also examined whether depressed participants with negative interpretation bias at baseline (as measured by a Test of Interpretation Bias) responded differently to the intervention than the group as a whole. Compared to analyses of the group as a whole, we expected that effect sizes for CBM-I would be stronger for those with baseline negative interpretation bias on measures of interpretation bias, depression, and anxiety at post-training and follow-up.

Methods

Participants

Depressed adolescents and young adults, ages 14–21 years, were recruited using a variety of methods, including fliers posted in outpatient psychiatry clinics at the hospital where the study was conducted, direct referrals from clinicians in the hospital system, and advertisements in the community (including an ad in the local free paper, fliers posted on bulletin boards, and postings on the internet). Potential participants (and their parents, if they were younger than 18 years old) completed a phone screen to establish eligibility for the study. Inclusion criteria included a score of 14 or above on the Beck Depression Inventory, 2nd Edition (BDI-II; indicative of at least mild symptoms of depression), and a working command of the English language. Participants were not required to meet criteria for Major Depressive Disorder (MDD) in order to participate (see rates of MDD, below). Exclusion criteria were: 1) current manic episode, acute suicidality, or history of psychosis, 2) previous diagnosis of pervasive developmental disorder, mental retardation, or dyslexia (because of the amount of reading involved in the study), 3) new psychiatric medication or dose changes within two weeks prior to starting the study, or 4) changes in psychotherapy within two weeks prior to participation.

We phone-screened 76 potential participants; 5 were found ineligible on the phone screen, and 71 were invited to participate. Twenty-three of those invited to participate did not follow through with making an appointment or showing up for their initial study visit. Of those eligible for participation, we enrolled 48 youth in the controlled trial (mean age = 18.19 ± 1.94 years; 13 males, 35 females), including one participant who had just turned 22 years old. Three of the enrolled participants were subsequently found to be ineligible: two participants had a BDI-II score less than 11 by the first visit, and one participant met criteria for an acute manic episode. Twenty-three participants (7 males, 16 females, mean age =

17.70 $\pm$ 1.94 years, mean grade = 12.09 $\pm$ 1.99) were randomized to the active intervention condition, and 22 (5 males, 17 females, mean age = 18.86 $\pm$ 1.81 years, mean grade = 13.19 $\pm$ 1.69) were assigned to the control condition. Three participants (two intervention, one control) dropped out after the first visit, although their first session data are included in the analyses. Thus, 42 participants completed all four sessions.

All participants were evaluated for DSM-IV MDD using a structured clinical interview (see Measures, below). Rates of current (past month) MDD did not differ significantly between groups. Within the intervention condition (n=23), 15 met full criteria for current MDD, seven met sub-threshold criteria (i.e., at least three symptoms), and one did not currently have MDD; functional impairment ranged from mild (27%) to moderate (55%) to severe (18%). All intervention condition participants had at least one past episode of full MDD. Within the control condition (n=22), 13 met for full current MDD, eight for sub-threshold, and one had no MDD. Thirty-eight percent had mild functional impairment, 33% were moderate, and 29% were severe; baseline functional impairment did not differ between the control and intervention groups ($\chi^2=1.98$, $p=.372$). All but two participants met criteria for at least one past episode of full MDD. Most of the participants had received some form of treatment for their depression, with no significant differences between the intervention and control groups in type of treatment: 26% and 24% received inpatient hospitalization, respectively; 43% and 38% psychotherapy plus medication; 9% and 10% medication only; 13% and 14% therapy only; and, 9% and 14% no prior treatment.

We also assessed for DSM-IV dysthymia, social phobia, and mania. Rates of past and current dysthymia in the whole sample were 36% and 20%, respectively, with no differences between conditions. Fifty-six percent met criteria for past and 41% for current social phobia, again with no significant differences between conditions. Three in the intervention condition and two in the control condition met criteria for a full manic episode in the past.

CBM-I Protocol

Participants were told that the study was evaluating an experimental computer program developed to reduce negative feelings. Scenarios used in the protocol were developed by the investigators for use with adolescents and young adults. At each session (lasting 30 minutes on average), adolescents assigned to the active intervention condition were exposed to 100 three-line scenarios (randomly drawn from a pool of 200 and presented in random order); 76 of the scenarios were relevant to potential loss, rejection, or failure and ambiguous until the final word, which forced a positive interpretation. The final word was presented as a word fragment (with one missing letter), after which participants were required to type the missing letter of the word on the keyboard to ensure they were attending to the scenario and encoding the intended interpretation valence. The computer indicated if they correctly identified the word. The scenario was then followed by a yes/no comprehension question. An example of a positive training scenario is: *You have to give an oral presentation in history class this morning. You stand up in front of your class with your notes in your hand. Partway through, people think your presentation is good.*

The remaining 24 scenarios were neutral filler scenarios, intended to mask the “obviousness” of the paradigm. A sample filler scenario is: *You and your family are attending your cousin’s third birthday party. After eating cake, it is time for her to open her presents. Your family is giving her a present wrapped in paper that is yellow.*

The adolescents in the control group completed the same procedure, except that these adolescents were exposed to 100 neutral filler scenarios, also randomly selected from a pool of 200. Before the first session, all participants were presented with five example scenarios, unrelated to the training, in order to practice the task.

Measures

Diagnostic assessment

Kiddie-Schedule of Affective Disorders and Schizophrenia-Epidemiologic Version (K-SADS-E; Orvaschel, 1994), or the Structured Clinical Interview for DSM-IV (SCID-IV; First, Spitzer, Gibbon, & Williams, 1995): We administered the mood and social phobia modules of the K-SADS-E (if under 18 years old) or SCID-IV (if 18–21 years old) to the adolescent and his/her parent (when applicable). The K-SADS-E is a widely used, semi-structured psychiatric diagnostic interview with established psychometric properties. It was designed for use in clinical and epidemiologic research in order to obtain a past and current history of psychiatric disorders in children and adolescents ages 6–17. Adolescents and their parents were interviewed separately; if either the adolescent or his/her parent endorsed a mood disorder or social phobia at a clinically significant level, the diagnosis was assigned. The SCID-IV is a reliable instrument developed to standardize the information gathering process necessary for making past and current differential diagnoses.

For both interviews, a diagnosis was assigned if the full DSM-IV criteria were met. A diagnosis was considered “subclinical” if more than half (but less than all) of the symptom criteria were met. The first author (JM), a licensed clinical psychologist, administered the SCID/KSADS at all time points. Before beginning this study, she completed an extensive, lab-sponsored training program in the administration of these clinical interviews, which involved observing interviews performed by experienced clinicians and rating these interviews until agreement on all diagnoses was achieved. Once achieving this benchmark, she began independently administering diagnostic interviews.

Self-report measures of depression and anxiety

Beck Depression Inventory, 2nd Edition (BDI-II; Beck, Steer, & Brown, 1996): The BDI-II is a psychometrically sound (Beck et al., 1996), 21-item self-report measure of depressive symptoms. Each item consists of four statements, with the participant endorsing which statement is most similar to his/her experience over the past two weeks. Items are scored on a scale from 0–3, with higher ratings corresponding to more severe symptoms. Internal consistency is excellent (Cronbach’s $\alpha = .92$), and one-week test-retest reliability is high ($r = .93$; Beck et al., 1996).

State-Trait Anxiety Index, Trait Scale (STAI-T; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983): The STAI-T contains 20 statements, and the participant rates each statement on a four-point scale (“almost never” to “almost always”) according to how often the statement describes him/her; we modified the time range to include the week leading up to participation in the study. The STAI-T has strong internal consistency ($\alpha = .89$) and concurrent validity ($r = .71-.85$; Bieling, Antony, & Swinson, 1998), and good reliability (Spielberger et al., 1983).

Cognitive measures

CANTAB Affective Go/No-Go Test (AGN; Fray, Robbins, & Sahakian, 1996): The AGN assesses information processing biases for positive and negative stimuli and takes 10 minutes to administer. The test consists of several blocks, each of which presents a series of words from two different affective categories: Positive (e.g., “joyful”) and Negative (e.g., “hopeless”). For each block, the subject is given a target category, and is asked to press a button when they see a word matching this category while ignoring words from the other category (distracters). Response time to hit the press pad when the target is presented is calculated in milliseconds. We calculated a “latency difference score,” which was response time for accurate hits on negative targets minus response time for accurate hits on positive

targets. Thus, a negative latency difference score indicates faster response times for negative words (i.e., a negative bias). We also analyzed the frequency of errors made during the task. Commission errors occurred when the participant hit the button when they saw a distracter instead of a target word. Omission errors occurred when the participant failed to hit the button when they saw a target word. CANTAB psychometric data for children and adolescents are described in detail in Luciana (2003).

Dysfunctional Attitudes Scale, Form A (DAS; Weissman & Beck, 1978): The DAS is a 40-item self-report measure of depressogenic beliefs. The scale has two factors: Perfectionism and Need for Social Approval (Imber et al., 1990). Internal consistency and concurrent validity have been found to be acceptable (Blatt, Quinlan, Pilkonis, & Shea, 1995; Imber et al., 1990). In a sample of depressed adolescents, internal consistency was strong ($\alpha = .93$), and concurrent validity was adequate ($r = .49$ with self-report measure of depression; Rogers et al., 2009).

Test of Interpretation Bias (TIB): The TIB is an adaptation of the recognition task developed by Mathews and Mackintosh (2000), modified by the investigators of the present study for use with depressed adolescents. The TIB is the main outcome measure of the study and consists of 10 scenarios, similar to scenarios used in the CBM-I program (see above) except that the last word of all of the scenarios (presented as a word fragment) remains ambiguous in valence. An example ambiguous scenario is: “*You are on your way to meet a friend at the movie theater. You are supposed to meet him near the ticket booth. When you arrive, your friend is not waiting.*”

After each scenario, participants identify the missing letter in the last word to ensure that they attended to the scenario. They are then presented with four statements and asked to rate on a scale from 1 (not at all similar) to 4 (very similar) how similar the statement would be to their own interpretation of the scenario. Two target statements are presented, one with the positive interpretation and one with the negative interpretation. Two “foil” sentences (positive and negative), less relevant to the scenario, are also presented to examine the degree to which the induced biases generalize beyond the main aspect of the scenarios. The sentence types are presented in random order. For example:

How similar is each statement below to “The Movies” scenario?

1. *When you arrive, your friend is running late for the movie.* [Positive Target]
2. *When you arrive, your friend has stood you up.* [Negative Target]
3. *When you arrive, you realize you have money for popcorn.* [Positive Foil]
4. *When you arrive, you realize that the movie is sold out.* [Negative Foil]

Thirty scenarios were developed by the first author for the TIB. Depressed participants received ten different TIB test scenarios at visits one, two, four, and follow-up; the 30 scenarios were presented in random order for visits one, two, and four. The purpose of this was to minimize method variance that may exist if participants were presented with the scenarios in the same order, with items 1–10 making up Form A, items 11–20 making up Form B, etc. At follow-up, ten scenarios were selected at random from those already seen by each participant.

Total scores for the negative target, positive target, negative foil, and positive foil scales on the TIB ranged from 10–40. We calculated the TIB bias ratio by dividing the total positive target score by the total negative target score, with lower ratios (i.e., below 1.0) indicative of a more negative interpretation bias. A foil ratio score was similarly calculated.

We assessed the reliability and validity of our developmentally adapted TIB, using a sample of 24 healthy comparison (HC) participants (mean age=18.95 $\pm$ 1.97; 7 males, 17 females), who did not have a history of mood disorder (as assessed by the KSADS-E/SCID-IV), and had a current BDI-II score less than 14. There were no significant demographic differences between healthy comparison and depressed participants. To examine discriminant validity of the TIB, we compared TIB bias ratio scores (positive interpretation score divided by negative interpretation score) across groups; depressed participants, at baseline, had significantly more negative bias ratios than HC participants (0.90 and 1.45, $t=6.57$, $p=.000$). This was also true for the foil ratio scores (0.99 and 1.36, $t=5.56$, $p=.000$). To examine convergent validity, we calculated the correlation between the DAS and the TIB bias ratio for the combined group ($r(67) = -0.65$, $p=.000$), showing that more negative thinking style on the DAS is associated with a more negative interpretation bias on the TIB. There was also a significant correlation between the TIB foil ratio score and the DAS ($r(67) = -0.49$, $p=.000$). Convergent validity was also supported by strong correlations with another measure of negative cognition, the Children's Automatic Thought Scale (Schniering & Rapee, 2002): Personal Failure scale: $r(67) = -0.56$ ($p=.000$) and Social Threat scale: $r(67) = -0.47$ ($p=.000$).

We examined internal consistency of each of the four scores on the TIB: positive and negative target scores, and positive and negative foil scores. Internal consistency was acceptable, with Cronbach's α of 0.78 (positive target), 0.81 (negative target), 0.74 (positive foil), and 0.65 (negative foil). Because the 10 scenarios comprising the TIB were different across participants at each time point, inter-item correlations were not calculated.

Procedure

All study procedures were approved by the hospital Institutional Review Board. Participants and their parents (when applicable) reviewed and signed informed consent and assent forms. After signing consent, participants completed the KSADS/SCID, followed by the baseline self-report measures, including the baseline Test of Interpretation Bias. Cognitive bias and symptom measures were repeated at all time points during the study (pre, mid, post, and follow-up), except that the KSADS/SCID and DAS were not administered at mid-treatment, and the AGN was administered only at pre- and post-intervention. Diagnostic interviews after baseline assessed for interim symptoms of mood disorders and social phobia.

Adolescents completed the interpretation bias modification program on four occasions over the course of approximately two weeks (mean = 15.5 $\pm$ 6.36 days), as administered on a laptop computer using Inquisit software programmed for the purposes of this study; all study sessions were conducted at our clinical research facility. Research assistants set up the computer at each session, allowing the diagnostic interviewer to remain blind to participant condition. The first CBM-I session was conducted immediately after the pre-treatment assessment was complete. The post-treatment assessment occurred right after the completion of the fourth CBM-I session. Thirty-eight participants (19/23 intervention group, 19/22 control group) then completed the two-week follow-up assessment, with measures administered over the phone. There were no statistically significant differences in baseline demographics, TIB bias ratio, or symptom scores between those who completed the two-week follow-up and those who did not. Adolescents and their parents were debriefed about the study procedures and their study condition at the end of the follow-up period.

Participants who completed all four CBM-I sessions were reimbursed \$100 for their time.

Data Analyses

STATA 10 (StataCorp, 2007) was used to conduct all statistical analyses. To examine baseline differences between groups, t-tests were conducted for continuous measures and chi-square analyses for categorical measures. Pearson correlation analyses were conducted

to examine the relationship between all measures at baseline. Analyses were two-tailed with $\alpha < .05$. We used mixed-effect regression models with random intercepts, unstructured covariance, and restricted estimated maximum likelihood (REML) to analyze differences between the active intervention and control groups in rate of change in TIB, DAS, BDI-II, AGN, STAI-T, and number of MDD symptoms over the course of the study. Specifically, slope of change was compared between the two groups, with a positive slope reflecting improvement on the TIB (i.e., reduction in negative bias) and negative slope reflecting improvement on the remaining measures.

We estimated that there would be a large between-groups effect size, based on previous CBM-I studies using clinical samples; on their measure of interpretation bias (Scrambled Sentences test), we calculated that Lang et al. (2012) had a between-groups effect size of $d = .82$, while Amir and Taylor (2012) found a between-groups effect size of $d = .92$ for change in negative interpretations. With $\alpha = 0.05$ and power $(1 - \beta) = .80$, a sample size of 21 participants per group was needed to detect a between-groups effect size of $d = .90$.

Results

Baseline Differences

There were no significant differences between intervention and control conditions in sex ($\chi^2 = 0.34$, $p = .559$), grade ($t(43) = 1.94$, $p = .059$), ethnicity (74% and 68% Caucasian, 17% and 14% multi-racial, 4% and 9% Asian-American, 0% and 9% African-American, and 4% and 0% Latino; $\chi^2 = 3.58$, $p = .466$), or parental marital status (68% and 59% married, 22% and 23% separated/divorced, 5% and 12% widowed, and 5% and 6% never married; $\chi^2 = 0.62$, $p = .893$). Participants in the intervention group were significantly younger than those in the control groups ($t(43) = 2.09$, $p = .043$); however, preliminary analyses showed no association between age and the outcome measures over time, so age was not included as a covariate in the regression analyses. Correlations between cognitive and symptom measures at baseline are described in Table I.

There were no significant between-group differences at baseline for any of the outcome measures except for the TIB bias ratio (0.98 intervention group, 0.82 control group, $t(43) = -2.06$, $p = .046$); these differences were accounted for within the mixed-effect regression models. When restricting the sample to those with negative baseline interpretation bias ($n = 26$), again there were no significant differences between groups on any of the demographic variables, although differences in age approached significance and mirrored those found in the sample overall, ($t(24) = 1.94$, $p = .064$). There were also no baseline differences on any of the outcome measures.

Treatment Outcomes of CBM-I (Table II)

Main outcome: TIB bias ratio scores—We examined differences between the intervention and control groups in change on TIB bias ratio scores (positive target score/negative target score) over time. Keeping in mind that a positive β indicates reduction in interpretation bias, results showed a main effect for time at post-treatment ($\beta = 0.214$, $p = .016$), with both groups showing improvement in bias scores, but not follow-up ($\beta = 0.08$, $p = .367$). There were no significant group by time interaction effects at any time point, indicating that the two groups did not differ in their response to CBM-I over time on the TIB bias ratio.

Across both conditions, 26 participants had a negative interpretation bias at baseline (i.e., TIB bias ratio < 1.0), 9/23 in the intervention group and 17/22 in the control group. As shown in Figure 1, when the sample was limited to those with baseline negative bias, there

was a main effect for time at post-treatment ($\beta=0.212$, $p=.011$) as well as a significant group by time interaction at mid-treatment ($\beta=0.330$, $p=.024$) and, at trend, at post-treatment ($\beta=0.263$, $p=.071$). The intervention group showed greater improvements in their interpretation bias at these time points. The group by time interaction was no longer significant at follow-up ($\beta=0.17$, $p=.270$). There were medium to large between-groups effect sizes for participants with negative baseline bias at post-treatment ($d=0.77$) and follow-up ($d=0.66$), while in the sample as a whole, effect sizes were negligible ($d=-0.14$ and 0.15).

We also analyzed change in the TIB foil ratio scores over time and found no significant main or interaction effects; this was also the case when the sample was restricted to those with negative interpretation bias at baseline.

Secondary cognitive outcomes: DAS and AGN—For these measures, a negative β indicates an improvement in cognitive bias. As displayed in Figure 2, there was a group by time interaction effect at post-treatment ($\beta= -15.37$, $p=.045$) and follow-up ($\beta= -26.29$, $p=.001$) for the DAS, with those in the intervention group experiencing greater reductions in dysfunctional cognitions compared to those in the control group (between-groups $d=.60$ at post and $d=1.02$ at follow-up). There were no main effects. When the sample was restricted to those with negative interpretation bias on the TIB at baseline, these interaction effects on the DAS were attenuated with only a trend group by time interaction at follow-up ($\beta= -17.33$, $p=.089$). However, the pattern of results was similar to that in the whole sample, with the control group showing no change in the DAS over time (162.37 ± 25.44 at pre, 160.94 ± 24.73 at post, and 159.93 ± 23.09 at follow-up; within-group $d=0.06$ at post and $d=.10$ at follow-up) and the intervention group showing almost a 20-point improvement by follow-up (161.71 ± 29.26 at pre, 153.64 ± 40.61 at post, and 142.14 ± 41.89 at follow-up; within-group $d=0.25$ at post and $d=.59$ at follow-up).

Change in latency difference scores (reaction time for negative trials minus reaction time for positive trials) on the Affective Go/No-Go from pre-treatment to post-treatment was examined; results showed a main effect (at trend) for time ($\beta= 18.68$, $p=.056$) in the positive direction and no group by time interaction effect. Results were nearly identical when the sample was restricted to those with baseline negative bias. There was a significant group by time interaction for AGN commission errors during positive trials ($\beta=-2.22$, $p=.037$), with the intervention group having greater reduction in these errors at post-treatment (intervention group: pre= 4.65 ± 3.64 , post= 1.63 ± 1.71 , within-group $d=1.06$, between-groups $d=0.88$; control group: pre= 3.29 ± 2.12 , post= 2.55 ± 2.54 , within-group $d=0.33$). In other words, the intervention group was less distracted by negative stimuli when attending to positive stimuli (i.e., they had fewer instances of hitting the button for negative words when they were supposed to hit for positive words). There were no significant effects for AGN commission errors during negative trials (hitting the button for positive instead of negative words). There were main effects for time for AGN omission errors (i.e., failing to hit the button when a target word appeared) during both positive ($\beta=-2.56$, $p=.004$) and negative trials (at trend, $\beta=-1.53$, $p=.060$), but no interaction effects, meaning that both groups improved equally from pre- to post-treatment. When the sample was restricted to those with baseline negative bias, there were no significant group $\times$ time interaction effects for any of the AGN errors.

Secondary symptom outcomes: BDI-II, STAI-T, and symptoms of MDD—Again, for these measures, a negative β indicates a reduction in symptoms. Mixed-effect regression analyses showed that both groups significantly improved on the BDI-II at mid-treatment ($\beta= -5.82$, $p=.002$), post-treatment ($\beta=-5.73$, $p=.002$), and follow-up ($\beta=-7.35$, $p=.000$), but there were no differences in rate of change between groups. The same pattern of findings

was observed when the sample was restricted to those with negative interpretation bias at baseline. Similarly, both groups significantly improved on symptoms of anxiety (STAI-T), with a main effect for time at post-treatment ($\beta = -4.14$, $p = .039$), and follow-up ($\beta = -7.86$, $p = .000$), but no differences in improvement between groups; again, the same pattern of findings was found when only including participants with baseline negative bias.

Symptoms of DSM-IV MDD were measured by the SCID-IV/KSADS-E. Similar to findings on the BDI-II, regression analyses showed that both groups experienced reductions in number of depression symptoms at post-treatment ($\beta = -1.04$, $p = .040$) and follow-up ($\beta = -1.84$, $p = .000$), but there were no group by time interaction effects. A main effect for time was also found for those with negative baseline interpretation bias, but again no group by time interaction effect.

Discussion

The present study is the first to evaluate the efficacy of interpretation bias modification in a sample of adolescents and young adults with symptoms of depression, 96% of whom also had a lifetime history of major depressive disorder. Using the TIB as the main outcome measure, we found no significant differences between the active intervention and control groups in interpretation bias change; both groups showed reductions in negative bias at post-intervention, with small to medium within-group effect sizes. However, when the sample was restricted to adolescents with baseline negative interpretation bias, the intervention group showed greater improvement in interpretation bias at mid-treatment and post-treatment (at trend), though effects diminished at follow-up. Within-group effect sizes for the intervention group were large at each time point, and between-group effects were medium to large. As anticipated, effect sizes for the intervention condition were stronger when the sample was limited to those with baseline negative bias compared to the group as a whole. Notably, our findings are consistent with those of Salemink and Wiers (2011) who found that effects of one session of positive CBM-I on post-training interpretation bias were enhanced for adolescents with negative interpretation bias at baseline.

However, there were no effects of training on symptoms of depression and anxiety, with all adolescents showing improvements on the BDI-II, STAI-T, and number of depression symptoms over time. Between-groups effect sizes were negligible to small. The same pattern of results was found when the sample was restricted to those with negative baseline bias. These findings are in contrast to CBM studies of other clinical samples, which largely found reductions in anxiety symptoms or disorders (Amir & Taylor, 2012; Beard, Weisberg, & Amir, 2011; Hayes, Hirsch, Krebs, & Mathews, 2010; see also Lang et al., 2012, which used a modified CBM-I paradigm for depression), but similar to a few other studies (mainly using non-clinical child and adolescent samples) that found changes in interpretation bias but lack of symptom improvement (Lau et al., 2011; Lester et al., 2011b; Salemink, van den Hout, & Kindt, 2007; Salemink & Wiers, 2011). It is possible that effects of classic CBM-I on symptoms of anxiety are more immediate than effects on symptoms of depression, and a longer follow-up period may be necessary to observe differences between groups on symptom measures. Studies with a larger sample and repeated assessments across a sufficient follow-up period can also help us understand whether changes in interpretation bias precede changes in depression symptoms. Indeed, while we could not directly evaluate this hypothesis, it may be that those who respond to CBM-I with significant reductions in interpretation bias may then experience a subsequent reduction in depression, although larger studies with the power for finer-grained analyses are needed to evaluate this hypothesis.

Regardless of baseline bias, adolescents in the intervention condition showed significantly greater reduction in general depressogenic cognitions, as measured by the DAS, than those in the control condition at post-treatment and two-week follow-up, suggesting that the effects of CBM-I extend to perfectionistic or rigid thinking and need for social approval. Our finding of a medium to large effect size of CBM-I on the DAS at post-intervention ($d=.60$) and follow-up ($d=1.02$) compares favorably to that of CBT for adolescent depression. Indeed, the TADS study found a small between-group effect size for improvements on the DAS-Perfectionism scale in the CBT+ medication group compared to the placebo group ($d=.25$), and those in the CBT alone group actually improved less on this scale than those in the placebo group (Jacobs, Silva, Reinecke, Curry, Ginsburg, & Kratochvil, 2009). In addition, regardless of baseline bias, those in our intervention group also made fewer commission errors on the Affective Go/No Go Task at post-treatment compared to controls (i.e., were less distracted by negative words when attending to positive words), with a large between-groups effect.

Our results suggest that while CBM-I appears to reduce self-reported dysfunctional thinking in depressed adolescents and young adults, the effects of the intervention on interpretation of ambiguous situations may be specific to those with initial negative interpretation bias. We had reason to think that adolescents with more balanced interpretations of ambiguity might benefit from CBM-I, becoming even more positive in their interpretations, given the number of studies showing positive training effects in non-clinical samples (e.g., (Mathews & Mackintosh, 2000)). However, our findings suggest that negative interpretation bias must be present in order to be remediated, a finding that bears replication with other depressed samples. By contrast, there may have been more room for improvement for those without initial bias on cognitive measures that were not specific to interpretation of ambiguity, with the effects of repeated exposure to positive resolutions of depression-relevant scenarios generalizing to measures of more global depressogenic thinking (the DAS and portions of the AGN).

Indeed, interpretation bias does not appear to be universally present in depressed adolescents; in our study, 26/45 (58%) had a negative bias ratio on the TIB, leaving a sizeable minority without a negative bias. There are a number of factors that may contribute to development of interpretation biases in some adolescents; these factors have been more thoroughly studied in anxious youth (see Field & Lester, 2010) with need for further research in youth who are vulnerable to depression. Potential risk factors for negative interpretation bias include family variables, such as family history of depression (e.g., Dearing & Gotlib, 2009) and parental transmission of bias, and individual variables such as executive functioning and attention control, interpersonal stressors, and mood severity. Interpretation bias does appear to be highly correlated with negative mood, although the direction of this relationship is unclear (i.e., does depression precede interpretation bias, or does interpretation bias precede depression?). In our sample, baseline TIB and BDI-II were correlated at $r(43)=-.44$ ($p<.01$; $r(67)=-.63$, $p<.0001$, in the combined depressed and healthy control sample). More work needs to be done, however, to determine the relationship between state negative affect and cognitive biases (Everaert, Koster, & Derakshan, 2012). One study (Standage, Ashwin, & Fox, 2010) found that while a brief, modified CBM-I changed both mood and interpretation bias as expected, a musical mood induction altered only mood and not interpretation bias, suggesting that changes in mood state do not lead to changes in interpretation bias. However, this study was conducted with a small non-clinical sample and did not examine the effects of concurrent CBM-I plus mood induction. Future studies should examine whether negative mood induction prior to training helps to strengthen the effects of CBM-I in depressed individuals, particularly given the effects of mood congruency on learning.

Factors specific to the design of this study may have contributed to our mixed findings on measures of interpretation bias and depression symptoms. First, it is possible that the effects of the positive training condition were diluted by the fact that 24% of the scenarios at each session were filler scenarios; the intention was to mask the obviousness of the paradigm, but the result is some overlap between the two conditions in material presented. Future studies should consider examining the effects of a “purer” positive training condition without filler scenarios. Further, unlike control conditions used in many previous CBM-I studies, participants in our control group were not exposed to negative interpretations of ambiguous scenarios, which may have reduced the between-group differences in interpretation bias change. Second, it is unclear if four sessions of CBM-I are sufficient for remediation of interpretation biases and reduction in symptoms, or enough to sustain improvements past the post-treatment time point. Although we opted to administer four sessions of CBM-I over the course of approximately two weeks, the number of sessions has varied widely across clinical trials from one (Hayes et al., 2010) to eight (Beard et al., 2011) to 12 (Amir & Taylor, 2012). There has been no agreed upon “dose” of this intervention, though in their meta-analysis, Hallion and Ruscio (2011) found a trend for multiple-session CBM protocols to have a larger effect on symptom measures. Thus, future studies are needed to examine the effects of number of sessions and session frequency and length on response to CBM-I.

Our study is limited by a smaller sample size, which prevented us from examining whether certain clinical or demographic characteristics predict treatment response. Specifically, it may be that our sample overall was too severely depressed to benefit from four sessions of CBM-I; indeed, nearly a quarter of the sample had previously been hospitalized for depression and five met criteria for Bipolar I Disorder. Further, as mentioned above, only 26 of the participants had negative interpretation bias at baseline, and these were by chance unevenly distributed across the intervention and control conditions. This may have affected our ability to detect smaller effects on cognitive and symptom measures for this important subsample. We were also limited by a truncated clinical interview, which kept us from being able to evaluate all comorbid disorders that may have also affected treatment outcome. Larger studies can examine the effects of these and other clinical characteristics on who benefits from CBM-I. Finally, our follow-up TIB was comprised of ten scenarios that were previously seen by participants; as with any repeated measure, responses at follow-up may have been influenced by memory of prior responses.

Despite these limitations, our study has a number of strengths. This is one of the first studies of CBM targeting biased interpretation of ambiguity in depressed individuals, and the very first of depressed adolescents. We used a predominantly clinical sample that was thoroughly evaluated for mood disorders via structured diagnostic interview. Unlike many previous CBM studies, we included a brief follow-up period to examine duration of treatment effects. We developed depression-relevant scenarios for the training program and Test of Interpretation Bias that were developmentally tailored for adolescents and young adults, and we confirmed the validity and reliability of the TIB using a healthy sample of adolescents.

The promise that CBM-I has shown in reducing anxiety and negative cognitions in adults underscores the importance of extending this intervention to younger populations. Further, continuing to develop new, individually tailored treatment strategies to augment existing interventions for adolescent depression, such as CBT, may improve rates of successful outcomes for this population. Though CBT has been shown to be an efficacious treatment for adolescent depression, successful implementation may be thwarted by the unavailability of an experienced CBT therapist, unwillingness on the part of the adolescent to participate during CBT sessions, or lack of motivation to complete cognitive restructuring assignments between sessions. If future studies find that changes in cognitive bias precede reductions in depression, clinicians may consider incorporating CBM-I into the treatment plan for

depressed youth, particularly those found to have negative interpretation bias at intake. Some adolescents may also be more likely to adhere to computerized interventions that can be delivered via the Internet. Future studies may examine the efficacy of an Internet-based CBM-I for depressed adolescents with negative interpretation bias who can complete the program at home.

In summary, this study demonstrated the potential for CBM-I to modify self-reported negative cognitions in depressed adolescents and young adults. For those with baseline negative interpretation bias, CBM-I may also lead to more positive and less negative interpretations of ambiguity, at least in the short term. Further studies are needed, however, to determine if changes in interpretation bias lead to reductions in depression, as the present study did not find an effect of CBM-I on symptom measures. These findings lay the groundwork for future studies to determine which adolescents benefit most from CBM-I, and the paradigm characteristics (e.g., number of sessions, ratio of positive scenarios) that will most likely lead to clinically significant improvements in interpretation bias and depression.

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Figure 1.
Change in Test of Interpretation Bias Ratio for participants with baseline negative bias (<1.0).

Note. Error bars represent standard errors. † $p < .10$, * $p < .05$

Figure 2.
Change in Dysfunctional Attitudes Scale (DAS) total score.
Note. Error bars represent standard errors. * $p < .05$, *** $p = .001$

Table 1
Correlations between Baseline Measures of Interpretation Bias, Depression, and Anxiety (n=45)

	1.	2.	3.	4.	5.	6.
1. TIB Bias Ratio	---					
2. DAS ^a	-0.43**	---				
3. AGN Latency Difference	0.14	0.07	---			
4. BDI-II	-0.44**	0.12	-0.10	---		
5. STAI-T	-0.47**	0.31 [†]	-0.11	0.79***	---	
6. MDD Symptoms	-0.31*	-0.05	-0.05	0.69***	0.59***	---

Note. AGN = CANTAB Affective Go/No-Go Test; BDI-II = Beck Depression Inventory, 2nd Edition; DAS = Dysfunctional Attitudes Scale; STAI-T = State-Trait Anxiety Inventory, Trait Scale; TIB = Test of Interpretation Bias.

^aN=37
[†]p<.10,
*p<.05,
**p<.01,
***p<.001

Table II

Means, Standard Deviations, and Effect Sizes for Outcome Measures

Measure	Intervention				Control			
	Pre	Mid	Post	FU	Pre	Mid	Post	FU
TIB Bias Ratio								
Mean	0.98	1.22	1.14	1.10	0.82	0.87	1.03	0.90
SD	0.30	0.49	0.35	0.26	0.25	0.26	0.49	0.29
Within-group <i>d</i>	---	0.61	0.50	0.44	---	0.20	0.56	0.31
Between-groups <i>d</i>	---	0.56	-0.14	0.15				
TIB Bias Ratio^a								
Mean	0.68	1.06	1.15	0.96	0.75	0.80	0.96	0.89
SD	0.10	0.26	0.40	0.13	0.16	0.21	0.48	0.31
Within-group <i>d</i>	---	2.11	1.77	2.63	---	0.28	0.61	0.59
Between-groups <i>d</i>	---	1.74	0.77	0.66				
DAS^b								
Mean	155.74	---	144.18	130.22	154.53	---	60.94	159.93
SD	30.00		33.11	35.00	30.01		25.52	23.47
Within-group <i>d</i>	---		0.38	0.81	---		-0.24	-0.20
Between-groups <i>d</i>	---		0.60	1.02				
AGN Latency Diff								
Mean	-1.68	---	0.37	---	-14.50	---	4.16	---
SD	39.07		36.69		26.09		25.17	
Within-group <i>d</i>	---		0.06		---		0.75	
Between-groups <i>d</i>	---		-0.52					
BDI-II								
Mean	27.59	23.52	21.17	20.47	28.00	22.85	22.62	21.55
SD	10.64	10.87	14.81	11.65	10.86	13.97	13.30	10.80
Within-group <i>d</i>	---	0.39	0.51	0.66	---	0.42	0.46	0.61
Between-groups <i>d</i>	---	-0.09	0.08	0.06				
STAI-T								
Mean	58.83	55.43	52.05	50.16	58.55	55.24	54.48	50.74

Measure	Intervention				Control		
	Pre	Mid	Post	FU	Pre	Mid	Post FU
SD	9.25	10.05	15.87	11.35	8.52	10.70	10.75 11.21
Within-group <i>d</i>	---	0.36	0.54	0.87	---	0.35	0.43 0.81
Between-groups <i>d</i>	---	0.01	0.24	0.08			
MDD Sx							
Mean	5.59	---	4.45	3.47	5.45	---	4.43 3.76
SD	2.00		2.34	2.26	2.05		2.44 2.18
Within-group <i>d</i>	---		0.54	1.02	---		0.47 0.82
Between-groups <i>d</i>	---		0.05	0.20			

Note.

^aOnly included participants who had a negative interpretation bias ratio at baseline (n=26).

^bDAS was completed by 37/45 participants.

BDI-II = Beck Depression Inventory, 2nd Edition; DAS = Dysfunctional Attitudes Scale; FU = two-week follow-up; MDD Sx = symptoms of major depressive disorder; STAI-T = State-Trait Anxiety Inventory, Trait Scale; TIB = Test of Interpretation Bias.