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Depression has been widely associated with a cognitive deficit leading to the negative interpretation of ambiguous information. Recently, cognitive bias modification (CBM) procedures have shown that such negative biases are causally related to emotional vulnerability. However, research using CBM has been notably lacking in depression. This is the first double blind randomised controlled study investigating the effect of cognitive bias modification-errors (CBM-errors), on depression and its influence on mood and resilience to stress. CBM-errors is a new form of cognitive bias modification for interpretation, which targets the full range of cognitive errors as well as interpretation biases. Forty clinically depressed participants were randomly allocated to a positive training or neutral text reading control group. Participants trained to make positive interpretations subsequently interpreted novel ambiguous information in a positive manner compared to controls. The results suggest that a positive cognitive bias can be induced in clinically depressed individuals using a simple computerised intervention. There was little evidence of corresponding benefits in terms of mood or response to stress, suggesting that multiple sessions are likely to be needed to confer symptom related change. A systematic investigation of the optimum number and timing of multiple sessions is now called for.

Keywords (separated by '-'): Cognitive bias modification - Depression - Randomised controlled trial
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Modifying Interpretation in a Clinically Depressed Sample Using ‘Cognitive Bias Modification-Errors’: A Double Blind Randomised Controlled Trial

Jenny Yiend · Jong-Sun Lee · Sinem Tekes · Louise Atkins · Andrew Mathews · Manouk Vrinten · Christian Ferragamo · Sukhwinder Shergill

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Abstract Depression has been widely associated with a cognitive deficit leading to the negative interpretation of ambiguous information. Recently, cognitive bias modification (CBM) procedures have shown that such negative biases are causally related to emotional vulnerability. However, research using CBM has been notably lacking in depression. This is the first double blind randomised controlled study investigating the effect of cognitive bias modification-errors (CBM-errors), on depression and its influence on mood and resilience to stress. CBM-errors is a new form of cognitive bias modification for interpretation, which targets the full range of cognitive errors as well as interpretation biases. Forty clinically depressed participants were randomly allocated to a positive training or neutral text reading control group. Participants trained to make positive interpretations subsequently interpreted novel ambiguous information in a positive manner compared to controls. The results suggest that a positive cognitive bias can be induced in clinically depressed individuals using a simple computerised intervention. There was little evidence of corresponding benefits in terms of mood or response to stress, suggesting that multiple sessions are likely to be needed to confer symptom related change. A systematic investigation of the optimum number and timing of multiple sessions is now called for.

Keywords Cognitive bias modification · Depression · Randomised controlled trial

Introduction

Cognitive theories of depression postulate that depressed individuals have a tendency to interpret ambiguous information in a negative manner (e.g. Beck 1967). Such biases pervade cognitive processing and prevent a realistic appraisal of everyday events, leading to the maintenance of psychopathology (e.g. Yiend and Mackintosh 2004). Despite decades of research into the causes and optimal treatments for clinical depression a chronic shortage of resources precludes readily available treatment. There is an overwhelming “urgency of addressing depression as a public health priority” (Moussavi et al. 2007) and the need for accessible, cost-effective treatments is paramount (Layard 2005). Further compounding the situation, recent research suggests that the prognosis of depression as seen in primary care settings is worse than previously thought (Yiend et al. 2009).

An experimental technique, cognitive bias modification for Interpretation (CBM-I) offers a potentially cost effective and widely accessible solution. Experimental manipulations of cognitive biases have confirmed their causal role in sustaining clinical disorders (Mathews and MacLeod 2005), and interest now focuses on the adaptation of these techniques for potential treatment. CBM-I studies have shown that processing biases can be induced through repeated processing of emotionally ambiguous information that encourages either negative or benign interpretations. This subsequently leads to congruent biases in the interpretation of new material (Mathews and Mackintosh 2000). Potential interventions based on this technique use only non negative or positive inductions to normalise pre-existing negative biases in patients or those with vulnerability to psychological disorders.

Cognitive bias modification methods offer many potential advantages over existing therapist-delivered psychological
interventions. They are a more convenient, flexible mode of
treatment, not requiring meetings with a therapist. They
offer the potential for delivery using modern technolo-
gies (e.g. internet or mobile phone) and require minimal
supervision. They could therefore become highly cost
effective and widely accessible. CBM methods are also less
demanding and more acceptable to patients than traditional
therapies. This is because personal thoughts and beliefs are
not directly interrogated and there is no need for social
interaction or stigmatising visits to outpatient clinics. Simi-
larly patient insight is not required because CBM seeks to
target the underlying maintaining cognitive bias directly and
therefore patient engagement is likely to be easier. In sum,
CBM methods offer a high gain, low cost treatment option
because they can circumvent many of the practical and
psychological requirements that disadvantage competing
psychological interventions.

The success of CBM methods targeting attentional bias
(CBM-A) in anxiety disorders is well established (Haka-
mata et al. 2010; Beard et al. 2012). For instance, a meta
analysis (Beard et al. 2012) reported large effect sizes for
attentional bias modification in samples with high levels of
social anxiety, GAD, phobias and worry. However other
research suggests that CBM-I has significantly larger effect
sizes than CBM-A (Hallion and Ruscio 2011). There is
little research specifically investigating the use of CBM-I
techniques in depression (MacLeod 2012). In their recent
meta analysis of CBM studies Hallion and Ruscio (2011)
found only three studies on clinical depression and all used
attentional bias modification (CBM-A) rather than CBM-I
(Baert et al. 2010; Koster et al. 2010; Wells and Beevers
2010). This is slightly surprising given that the evidence
base for naturally occurring biases in depression is con-
siderably stronger for biased interpretative processes (e.g.
Cowden Hindash and Amir 2012; Wisco et al. 2010) than it
is for biased attentional effects (see recent meta-analysis of
Peckham et al. 2010). Nevertheless, beneficial emotional
effects of CBM-A were demonstrated in a sample of mild
110 to moderately depressed students (Wells and Beevers 2010)
111 and shown to reduce recurrence risk in patients with
112 remitted depression (Browning et al. 2012). However
113 findings have been somewhat inconsistent when using
114 CBM-A with moderate to severe depression. Some studies
115 have observed an increase in depressive symptoms and
116 others have failed to effectively change, or sustain change
117 in, attentional bias (Baert et al. 2010; Haefelf et al. 2012).

Only two other studies to date, not included in the above
meta analysis, have investigated CBM-I in a clinically
depressed sample. Blackwell and Holmes (2010) con-
ducted a single case series investigating the impact of
112 week of daily sessions of CBM-I. Four out of seven
113 people demonstrated improvements in cognitive bias or
114 mood immediately after the sessions and this was largely
115 maintained at 2-week follow up. Although promising,
single case series are not designed to allow wider gener-
alisation of results. The second study compared the impact
of 1 week of daily sessions of positive CBM in thirteen
depressed participants, to a matched depressed control
group who were exposed to positive and negative informa-
tion equally (Lang et al. 2012). Significant improve-
ments on a cognitive bias measure, the Scrambled
117 Sentences task (Wenzlaff 1988, 1993), and depressive and
118 intrusive symptoms were reported immediately after posi-
tive CBM, with improvements dropping to trend level by 2-
week follow-up.

Although promising, the findings of Lang et al. (2012)
leave several questions unanswered. Most importantly no
measure of biased cognition was given at baseline. Re-
searchers in the field now recognise the importance of
assessing the mechanism one is seeking to change, before
attempting to change it. There is considerable variance in
the level of naturally occurring biased cognition in any
sample and without baseline assessment it is impossible to
rule out group differences apparently relating to training,
which are in fact a result of failed randomisation. This is
especially true with small sample sizes where randomisa-
tion frequently fails unless some method of minimisation,
balancing prognostic factors, is used. It is clear then that
there remains a gap in the literature with regard to CBM-I
for clinical depression. The current study sought to con-
tribute to filling this gap by conducting a single session
double blind randomised controlled trial using a clinically
depressed sample and a new version of CBM-I, called
CBM-errors (Lester et al. 2011). CBM-errors is designed to
target the entire range of cognitive errors first described by
Beck et al. (1979).

Cognitive bias modification-errors offers several advan-
tages over alternative CBM-I methods. First, the content was
generated from a dedicated exercise to accumulate real world
clinical exemplars from the content of therapy sessions
(Lester et al. 2011). It therefore has stronger face validity and
end user relevance than researcher generated content. Sec-
ond it is likely that other CBM versions have omitted
important types of cognitive error categories, which are
nevertheless ubiquitous in clinical settings. CBM-errors
targets the full range of inferential biases identified by Beck
et al. (1979) and therefore includes categories of inference
not previously incorporated within CBM-I content (most
notably personalization, see Table 1). Finally, many ver-
sions of CBM-I are designed for a specific disorder such as
social anxiety and are therefore not ideally positioned for use
in depression. By developing a version of CBM which tar-
gets cognitive errors rather than a specific disorder, one can
bypass traditional diagnostic labels and instead work
towards a method which targets underlying functional maintaining mechanisms of potential transdiagnostic appli-
cability (Harvey et al. 2004).

In CBM-errors, training scenarios are used to provide practice in the benign resolution of thinking errors believed by many clinicians (e.g. Beck et al. 1979) to contribute to maintaining emotional disorders. The randomised controlled trial (RCT) is widely accepted as the gold standard research method for establishing efficacy of putative new interventions, giving utmost priority to minimising any source of potential bias. In this sense it is a ‘proof of principle’, rather than an attempt to establish ‘real world’ usefulness (effectiveness). CBM-errors has previously been shown to promote positive inferences, reduce vulnerability to stress and improve self perception of performance in a sample of healthy volunteers showing elevated levels of negative affect and cognition (Lester et al. 2011). This intervention aims to reduce the cognitive errors (Beck et al. 1979) most commonly targeted during therapy (Iliardi and Craighead 1999) as underlying mechanisms that sustain a range of disorders (Johnson et al. 1992), including depression.

To the standard CBM-errors reported by Lester et al. (2011) we added a component designed to prompt positive future-directed cognition. It has been suggested that depression is characterised by a deficit in processing positive information rather than an excess of negative cognitions, especially when projecting into the future (Stöber 2000). The reduced ability to think positively about the future arises from a difficulty in accessing mental representations of those experiences (MacLeod and 

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Salaminioti 2001), which may result in the belief that such events are less likely to occur. Therefore, we reasoned that encouraging positive prospective cognition as part of the CBM-errors intervention could be especially beneficial for clinical depression.

Methods

Participants

Participants were recruited through a combination of advertisement in King’s College University campuses, online depression support and self-help websites, and GP surgeries within local boroughs. Advertisements asked for ‘people who suffer from depression to take part in a study examining whether changing the way we think about the future has an impact on our thinking style and mood’. Telephone screening was conducted to establish eligibility. Inclusion criteria required participants to meet screening criteria for Major Depressive Disorder (current episode) on the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al. 1998; administered by phone) or score above 15 on the BDI-II (administered by email). Participants were also required to be fluent English-speaking and between the ages of 18 and 70. Exclusion criteria were: receipt of current psychotherapy, changes to medication within the last 2 months, significant Axis I or Axis II comorbidity, previous head injury involving loss of consciousness for more than 3 min, current major physical illness (e.g. heart disease, stroke). Of 182 potential participants responding to advertisement, 111 were not eligible. Of these, 49 were ineligible due to significant comorbidities (37 bipolar, 7 OCD and 5 drug/alcohol abuse); 11 due to medication changes; 22 due to receiving current psychotherapy; 21 due to not meeting screening criteria for MDD and 8 due to major physical illness and/or previous head injury. Of the remaining 71 eligible, a further 31 subsequently declined to participate.

The 40 eligible, consenting participants were aged between 18 and 70, mean = 43.12, SD = 12.2. A CONSORT diagram is shown in Fig. 1.

Baseline Measures

Credibility and Expectancy Questionnaire (CEQ)

One question (‘how successful do you think this session will be in reducing your symptoms?’) was extracted from the CEQ (Devilly and Borkovec 2000) with a scale ranging from 1 (‘not at all useful’) to 9 (‘very useful’). The question was asked as part of the sociodemographic questions to assess participants’ expectations of the session.

MINI Clinical Interview (M.I.N.I; Sheehan et al. 1998)

The M.I.N.I is a short semi-structured diagnostic clinical interview, designed to establish both DSM-IV and ICD-10 diagnoses and to be valid for use by non-clinicians after a brief period of training. The interviewers were given a 1 day training with a psychiatrist, which included a seminar, role-playing and practicing administration of the interview with actors as well as patients attending psychiatric assessment. The M.I.N.I has high internal reliability and test–retest reliability (Sheehan et al. 1998). The Major Depressive Disorder module was used to ascertain the proportion of the sample meeting criteria for current Major Depressive Episode at the time of testing.

Mood Measures

The BDI-II (Beck et al. 1996) and the Major Depression Inventory (MDI; Bech et al. 2001) were used to assess the severity of depressive symptoms. Positive and negative affect was measured using the trait version of the Positive and Negative Affect Schedule (PANAS-T; Watson et al. 1988). Visual analogue scales (VAS; Aitken 1969) measured state “sad” or “anxious” mood on two separate 10-cm scales. Mood is measured as a proportion between 0, “not at all” to 1, “extremely”.

Scrambled Sentences Task (SST; Wenzlaff 1988, 1993)

The baseline measure of biased interpretation was the SST with cognitive load. It consisted of 20 scrambled sentences of six words each which, when reordered, permitted either a positive or negative sentence formation. Although the SST may not be a ‘process pure’ measure of interpretation, it was chosen as a reliable task, related to interpretation, which has an established sensitivity to individual differences in depression. For example, the negativity bias on the SST is a known predictor of depressive symptoms (Rude et al. 2003). Following a practice, participants were instructed to use five out of the six words in each list to create a grammatically correct sentence (e.g. from ‘winner am born I loser a’, ‘I am a born winner’ or ‘I am a born loser’). Participants were required to remember a six-digit number while performing the task.

Stressor Task

A video task was used to assess baseline resilience to stress. Two mildly stressful video clips of life-threatening accidents (approximately 1 min each) were taken from a real life documentary. Participants saw clip 1 at baseline and clip 2 at test, with order of presentation counterbalanced across participants, within each group. Clips were...
taken from those used in previous studies (Hoppitt et al. 2010a, b). Two 10 cm visual analogue scales (Aitken 1969) were used before and after the video, with adjectives “sad” or “anxious”, as described above. An index of mood change was calculated by subtracting ‘after’ from ‘before’ values.

**Intervention**

**Active Condition**

CBM-error training used 72 items from Lester et al. (2011) divided into four blocks of 18 items each, with an optional rest between blocks and included approximately equal numbers of each type of error. Blocks 1 and 2 were non-negative, whereas 3 and 4 were overtly positive (see Mathews et al. 2007; Lester et al. 2011). Table 1 gives the range of errors targeted and provides examples of both source and modification materials.

Item content covered seven categories: academic, family, mood and health, relationships, social activities, hobbies and work. In order to maximise the personal relevance of the intervention all participants were asked to indicate at screening which one of these categories was least relevant to them. For those subsequently assigned to the active condition, randomisation included automatic allocation to a personalised version of the intervention programme, that omitted all items in a participant’s least relevant category. In addition, a picture related to the topic of each passage was added to every trial, after debriefing comments from pilot work suggested that this would assist participants to imagine themselves in the relevant situation.

Participants were presented with 72, three-line scenarios appearing one sentence at a time that was followed by a positive word fragment, which resolved the ambiguity of the descriptions (for full description of training format see Yiend et al. 2005). A question forcing positive response (requiring yes/no response) appeared, which was reinforced by providing feedback to question (correct/incorrect). See Fig. 2 for an intervention trial example.

Frame 3 of Fig. 2 highlights how we attempted to control participants’ engagement in training items by providing a fixed 5 s imagery period on each trial, together with a future directed sentence stem (whose content was uniquely related to each trial). This was designed to constrain and direct participants’ engagement with processing the positive meaning of ambiguous training passages. This new addition to our previous CBM-errors intervention was also designed to prompt positive future-directed cognition and comprised the instruction ‘Now imagine the situation that you have just read and what happened next…’ followed by a suggested positive continuation sentence and a fixed 5 s pause to allow processing of the positive continuation. The total duration of training was approximately 45 min.
The control condition followed an identical trial design and procedure to the intervention, including all imagery components, pictures, and imagination stem and future thinking, as shown in Fig. 2. The only difference was the content of the reading items which were unambiguous and emotionally neutral (e.g. ‘You turn the kettle on and wait for the water to boil. You get a teabag out of the tin, which you put into a mug, and pour the boiling water onto the teabag. Next, you add the m_ _k (milk). Have you made a cup of tea?’).

**Primary Outcome**

**Similarity Ratings Test (SRT; Mathews and Mackintosh 2000)**

Our chosen primary outcome measure was the SRT due to its widespread previous use in interpretation bias modification studies. It is usually given once only due to the surprise element inherent in the task. The present version consisted of 10 novel ambiguous test items taken from Lester et al. (2011) involving potential cognitive errors. The task followed the same format as that described in detail previously (Mathews and Mackintosh 2000; Yiend et al. 2005), but in brief this comprised two parts: the presentation of novel ambiguous items and the recognition test. Ambiguous items were similar in form to the training items, but novel in content and each had a designated ‘title’. Below the title, three sentences described an emotionally ambiguous social situation, ending in a word fragment completion followed by a question which—unlike the training items—maintained the ambiguity of the preceding text. Participants were thus able to apply their own spontaneous interpretation to the meaning of these test passages. For example:

**The wedding reception**

Your friend asks you to give a speech at her wedding reception. You prepare some remarks and when the time comes, get to your feet. As you speak, you notice some people in the audience start to l_ _gh (laugh). ‘Did you stand up to speak?’ (factual question, correct answer ‘Yes’).

Ten such items were shown consecutively. The second part of the SRT task, the recognition test, followed immediately and involved the presentation of corresponding title-sentence pairs. Participants rated each sentence on a Likert scale to indicate its similarity to the previous passage (1 = ‘very different’, 4 = ‘very similar’). Each title appeared four times, alongside four different types of sentence: two target sentences matched the positive and negative meanings of the previous passage respectively (these probed participants’ spontaneous interpretation of the ambiguous passage) and two foil sentences did not match the passage directly, but were positively and negatively valenced (these measured response bias and assessed any valence priming effects of training). In the example given above, the following sentences were rated:

**The wedding reception**

As you speak, people in the audience find your efforts laughable. (negative target)

As you speak, people in the audience laugh appreciatively. (positive target)

As you speak, some people in the audience start to yawn. (negative foil)
As you speak, people in the audience applaud your comments. (positive foil)

Secondary Outcomes

Two additional, parallel versions of the Scrambled Sentences Task and video stressor task, were used as secondary outcomes. Versions were counterbalanced across participants within each Group.

Follow Up Measures

Automatic Thoughts Questionnaire-Revised (ATQ-R; Hollon and Kendall 1980)

The ATQ-R was chosen as measure of biased cognition suitable for use at follow up. It is a self report instrument which assesses the frequency of negative cognitions related to the self. It contains 40 items, 10 positive (e.g. “I am proud of myself”) and 30 negative (e.g. “I'm worthless”) rated on a 5-point (1 = not at all, 5 = all the time) indicating frequency of occurrence over the past week.

Other follow up measures assessed mood and symptoms using the BDI-II, PANAS and MDI measures which are described above.

Procedure

Participants were randomly assigned to either the experimental (N = 19) or control arm (N = 21) of the study using a procedure of randomisation with minimisation on sociodemographic factors and screening instrument (MDI, BDI) scores (Pocock and Simon 1975). A blinded researcher, outside the research team, used a randomisation computer programme to automatically allocate participants to pre-specified conditions, which included task counterbalancing. Participants were blind to their condition of assignment. They were told that: We are testing two procedures to see whether either is effective in reducing depressed mood. You will be assigned to one of them. Similar procedures have sometimes been helpful for non-depressed volunteers, but neither has yet been shown effective in clinical trials. This rationale was used by the team and in all written documentation associated with the study, following ethical approval. All programmes and materials were arbitrarily coded, with relevant randomisation codes being communicated to the team prior to each session. The intervention/control procedure was administered by one researcher in the team, while two independent researchers shared equally the administration of pre and post measures. Using these procedures all members of the research team, as well as participants themselves, were blinded to the assigned condition, and remained so until after the final follow up questionnaire had been returned.

Participants attended a single session conducted between February and April 2012 at the Institute of Psychiatry, London. After consent procedures, sociodemographic questions included level of education, imagination type; ‘is your imagination primarily auditory/visual (i.e. image-based) or verbal?’, expectation as measured by the CEQ and diagnostic interview (including age of onset). Thereafter participants completed baseline measures: BDI-II, MDI, PANAS-T in a fixed random order, followed by the SST and stressor task given in counterbalanced order across participants. Participants then received their allocated condition. Both were presented on a 15-in. laptop screen using E prime version 2.0 and lasted approximately 45 min. Thereafter participants completed a 5 min emotionally neutral and unrelated filler task, involving reading neutral text and answering questions. This was administered to allow dissipation of any short-term mood effects induced by the intervention or control. Finally outcome measures were completed: the SRT followed by VAS, SST and video stress task in counterbalanced order. Participants were informed that debriefing and payment would be given after the 4-week follow-up. The duration of the entire session was approximately 2 h.

The mean duration from testing to follow up was 28.97 days (SD = 8.07, range = 20–65). Thirty four of 40 (85 %) participants returned the following paper based measures by post: BDI-II, MDI, PANAS-T, ATQ-R. Participants also completed a feedback form including questions regarding the aims of the study and how much they liked/thought the session helped them, rated on a scale ranging from 1 to 7 (1 = not at all/really disliked, 7 = extremely/really liked). The full debrief and unblinding procedure took place once data analyses were completed.

All procedures and measures were approved by the King’s College London Psychiatry, Nursing and Midwifery Research Ethics committee and participants were given £20 for their participation.

Results

Analytical Approach

Data was analysed using the IBM Statistical Package of Social Sciences (SPSS) version 20.0. Prior to analysis, all data were screened for missing values and outliers. Variables were checked for the assumptions of parametric testing prior to applying statistical tests. Normality was assessed using Kolmogorov–Smirnov tests, visual inspection of histograms and boxplots. Skewness and kurtosis...
values were scrutinised for each dependent variable. Le- 
vene’s Test was used to assess and, if necessary, adjust for 
homogeneity of variance in pairwise comparisons.

509 Participants

The M.I.N.I (Sheehan et al. 1998) diagnostic interview 
revealed that across the whole sample 38 out of 40 (95 %) 
met full diagnostic criteria for current episode MDD at the 
time of testing. The two not meeting full diagnostic criteria 
were excluded from all analyses. A further two participants 
were observed by researchers during the session to be 
greatly distracted and not engaging correctly with tasks to 
the extent that the validity of their data was comprom- 
ised. An a priori decision was therefore made to exclude 
them from all analyses.2 The final sample therefore com- 
pared 36 participants, 17 and 19 in CBM-errors and control 
groups respectively. As shown in Table 2, these groups 
were comparable at baseline on all measures. Importantly, 
groups were matched at baseline on interpretation bias as 
measured by the Scrambled Sentences Task (see Table 2). 
Moreover, scores indicated the presence of a clear negative 
bias (more sentences resolved in the negative direction than 
positive in both groups), as would be expected in a clin- 
cally depressed sample. Overall mean BDI-II score was 
30.06 (SD = 7.44, range = 17–45.50), which indicated a 
severe level of depressive symptoms (Beck et al. 1996). 
Screening data showed that one participant had multiple 
sclerosis and hypoglycaemia.

State Mood

State mood was measured prior to any of the outcome 
measures to ensure group differences could not be con- 
sidered a secondary consequence of any immediate mood 
inducing effects of the active intervention. Groups were 
comparable in state sadness, t(33) = .77, p = .448 
(Experimental M = .32, SD = .22, Control M = .37, 
SD = .20) and anxiety t(33) = .90, p = .373 (Exp- 
imental M = .25, SD = .17, Control M = .32, SD = .22).

Primary Outcome: Similarity Rating Test

Mean recognition ratings from the Similarity Rating Test 
were calculated for each participant across the four dif- 
ferent conditions: non-error target, error target, positive foil 
and negative foil. These means were entered into a mixed-

model ANOVA with Group (Experimental, Control) as a 
between-participants factor, and Sentence Type (Target, 
Foil) and Sentence Valence (error/negative, non-error/ 
positive) as a within-participants factor.

The analysis revealed large main effects of Sentence Type 
F(1,31) = 47.97, p = .0005, ηp² = .61, (target M = 2.3, 
SE = .07, foil M = 1.7, SE = .07) and Sentence Valence 
F(1,31) = 60.70, p = .0005, ηp² = .66 (error/negative 
M = 1.7, SE = .05, non-error/positive M = 2.3, SE = .08). 
There was a significant interaction between Group, Sentence 
Type and Sentence Valence F(1,31) = 6.54, p = .016, ηp² = 
.17 (Intervention group: non error target M = 2.74, SE = 
.14, error target M = 1.90, SE = .11, non error foil 
M = 1.96, SE = .15, error foil M = 1.54, SE = .09. Con- 
trol: non error target M = 2.48, SE = .12, error target 
M = 2.06, SE = .10, non error foil M = 1.93, SE = .13, 
error foil M = 1.35, SE = .07).

A mixed model ANOVA (Group × Sentence Valence) 
was conducted separately for each level of Sentence Type, 
targets (which reflect interpretation bias) and foils (which 
reflect response bias). The analysis revealed a significant 
interaction Group × Sentence Valence interaction for targets, F(1, 31) = 4.21, p = .049, ηp² = .12, but not foils, F(1, 31) = 0.87, 
p = .358 (means given above).

Figure 3 shows that the interaction on target items reflected 
significantly higher ratings for non error over error interpre- 
tations in the intervention group compared to controls. Further 
follow up t-tests revealed a non significant trend for the 
intervention groups to endorse non error interpretations more 
strongly than did controls, t(31) = 1.36, p = .092, inter- 
vention group: M = 2.74, SD = .70 versus control group: 
M = 2.48, SD = .39.

As shown in Fig. 3(a), the presence of the significant 
cross over interaction Group × Sentence Valence for tar- 
gets alone, supported by the higher order Group × Sen- 
tence Type × Sentence Valence interaction indicated a 
significant group difference on our primary outcome 
measure. This interaction was clearly carried (irrespective of 
follow up tests) by the intervention group showing a sig- 
nificantly stronger bias (steeper gradient) than controls in 
favour of non error compared to error interpretations.

Secondary Outcome Measures

Scrambled Sentences Task.5

Scoring of this task followed procedures described in 
previous publications (e.g. Rude et al. 2003) supplemented 
by personal communication with authors. Total negativity

\[ \text{2FL01} \]

\[ \text{2FL02} \]

\[ \text{2FL03} \]

\[ \text{3FL01} \]

\[ \text{4FL01} \]

\[ \text{Subsequent analyses performed at the request of an anonymous reviewer and reinstating both participants did not alter the pattern of the results reported on any measure.} \]

\[ \text{One participant had missing data on this measure.} \]

\[ \text{Three participants had missing data on this measure.} \]

\[ \text{Three participants had missing data on this measure.} \]
and positivity scores were obtained by calculating the proportion of sentences corresponding to each valence and dividing by the total number of completed sentences (maximum possible = 20). Each participant thus obtained a score that was a proportion of 1 (Rude et al. 2003). Only sentences that were exact expected matches of the positive or negative unscrambled sentence were counted. Consequently, and in line with previous studies, a number of ‘errors’ and ‘invalid’ responses were also recorded, for example where sentences were grammatically incorrect, used fewer than 5 words or otherwise did not match the one of the two possible designated sentences. As a result positivity and negativity proportions are not simply direct inverses of each other, but may reflect different directional biases. 

Table 2 Mean participant characteristics or counts by group with standard deviations in parentheses

<table>
<thead>
<tr>
<th>Group</th>
<th>Statistical Test</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>(n = 17)</td>
<td>(n = 19)</td>
<td></td>
</tr>
<tr>
<td><strong>Sociodemographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>42 (12.5)</td>
<td>43 (13.0)</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Education (university or above)</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Age of onset</td>
<td>22.7 (13.4)</td>
<td>22.2 (10.6)</td>
</tr>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI-II</td>
<td>30.8 (7.8)</td>
<td>29.7 (7.3)</td>
</tr>
<tr>
<td>MDI</td>
<td>32.9 (7.0)</td>
<td>32.3 (5.5)</td>
</tr>
<tr>
<td>PANAS-positive</td>
<td>18.8 (6.4)</td>
<td>20.8 (6.0)</td>
</tr>
<tr>
<td>PANAS-negative</td>
<td>28.8 (7.2)</td>
<td>26.4 (8.2)</td>
</tr>
<tr>
<td>VAS—sad</td>
<td>0.5 (0.3)</td>
<td>0.5 (0.2)</td>
</tr>
<tr>
<td>VAS—anxious</td>
<td>0.4 (0.2)</td>
<td>0.4 (0.2)</td>
</tr>
<tr>
<td><strong>Baseline measures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SST</td>
<td>Positive</td>
<td>.24 (.11)</td>
</tr>
<tr>
<td>Vulnerability to stress</td>
<td>Negative</td>
<td>.51 (.19)</td>
</tr>
<tr>
<td>VAS sad change</td>
<td>0.00 (0.11)</td>
<td>0.00 (0.10)</td>
</tr>
<tr>
<td>VAS anxious change</td>
<td>0.04 (0.13)</td>
<td>0.02 (0.13)</td>
</tr>
<tr>
<td><strong>Auditory/visual imagination</strong></td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Expectation of change (CEQ)</td>
<td>4.9 (2.0)</td>
<td>3.9 (1.5)</td>
</tr>
<tr>
<td>Do you think the session helped you?</td>
<td>2.9 (1.5)</td>
<td>2.8 (1.9)</td>
</tr>
<tr>
<td>How much did you like session?</td>
<td>3.7 (1.8)</td>
<td>3.1 (1.2)</td>
</tr>
<tr>
<td><strong>Likeability of session</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Similarity Rating for different directions of a targets and b foils by group (Experimental, Control), as measured at test (error bars ± 1 standard error)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a)</td>
<td>(b)</td>
<td></td>
</tr>
<tr>
<td>Non error Target</td>
<td>Error Target</td>
<td>F = 4.21, p &lt; .05</td>
</tr>
<tr>
<td>Non error Foil</td>
<td>Error Foil</td>
<td>Intervention</td>
</tr>
</tbody>
</table>

Fig. 3 Alternative, less stringent scoring procedures, as reported in some papers, did not result in significant changes to the pattern of results.

References

Cogn Ther Res
A mixed model ANOVA was conducted on these SST proportion scores, for the negativity and positivity measures separately, with one within-participants factor, Time (pre-, post-intervention) and one between-participants factor, Group (experimental, control). For positivity scores the Group × Time interaction revealed a non significant trend, $F(1,31) = 2.82, p = 0.103, \eta^2_g = 0.08$, as did negativity scores, $F(1,31) = 3.17, p = 0.085, \eta^2_g = 0.09$.\footnote{Combining both types of score to give a single bias score for analysis resulted in a Group × Time, $F(1,31) = 3.06, p = 0.09$.}

Inspection of the condition means for both types of score (see Table 3), suggested that in both cases the direction of trends was in line with hypotheses, showing an increase in the proportion of positive sentences, and a reduction in negative, from baseline to test in the intervention group only. Hypothesis-driven follow-up t-tests confirmed this, showing no significant changes from baseline to test in controls (all $t < 1$, $p > 0.3$), but a significant increase in positive, $t(14) = -2.06, p = 0.029$, and near significant decrease in negative sentences, $t(14) = 1.68, p = 0.057$, across time in the intervention group.

We suspected the lack of outright significance in these analysies was due to the compromised power resulting from the loss of data on this measure in our already reduced final sample (3 additional participants did not complete this measure as required at the two time points). We therefore conducted the above analyses on the full sample ($n = 36$) after imputing means for the relevant missing data. This indeed showed clearly significant effects on negativity bias scores, including a significant Group × Time interaction, $F(1,38) = 4.92, p = 0.033$, supporting a significant reduction in negative bias score in the intervention group, $t(18) = 2.33, p = 0.016$, but not the control group, $t(20) = -0.84, p = 0.206$. However, as imputation of means is a controversial practice, we present these findings purely as context for the preceding analyses.

### Stress Vulnerability

State mood change in response to the stressful video clips was calculated by subtracting the post viewing score from the pre viewing score separately for VAS sad and VAS anxious scales. Higher scores thus reflected an increase in negative mood. This provided two change index scores for each adjective, one at baseline and the other at the test. Group (experimental, control) × Time (baseline, test) ANOVAs were conducted for each adjective separately. For VAS-sad there was a trend main effect of time, $F(1,32) = 3.16, p = 0.085, \eta^2_g = .09$, suggesting that the video elicited less sadness at test than at baseline. The interaction between

<table>
<thead>
<tr>
<th>Experimental</th>
<th>Positive</th>
<th>Negative</th>
<th>Control</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>.24 (.11)</td>
<td>.51 (.19)</td>
<td>.34 (.20)</td>
<td>.44 (.23)</td>
<td>.37 (.24)</td>
<td>.44 (.25)</td>
</tr>
</tbody>
</table>

Table 3 Mean proportion of positive and negative sentences on the scrambled sentences task at baseline and test (standard deviations in parentheses)

The reliable change index (RCI) was calculated following the method of Jacobson and Truax (1991). RCI is obtained by multiplying the standard error of difference between two sets of test scores (here 3.65, taken from normative data on the BDI-II) by 1.96 (z-value for $p < .05$ significance level), which gave a value of 7.15. Thus any change in BDI-II score of 7.16 or above would be unlikely to occur in absence of actual change.

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\footnote{Authors’ note: Figures and tables are placeholders and will be included in the final version of the manuscript.}

7FL01

8FL01
Discussion

The present study investigated a single session of computerised CBM-errors in a clinically depressed sample using a rigorous double blind randomised controlled methodology. Participants who were assigned to CBM-errors, perceived novel ambiguous situations (designed to invite cognitive errors) in a more positive, error-free manner, than did matched controls who received an unambiguous, neutral reading programme. This confirms the hypothesized potential for CBM-errors to reduce cognitive errors in individuals currently suffering from depression. Non significant trends suggested potential benefits on a related measure of biased cognition, the scrambled sentences task. There were no significant group differences on resilience to stress or on follow up measures of mood, symptoms and self reported cognition.

There is a growing literature evidencing cognitive bias modification (CBM) techniques as potential low cost, theoretically driven interventions for a range of clinical disorders, including anxiety and depression. Of the two main versions of CBM, that which targets attentional biases (CBM-A) and that which targets interpretation biases (CBM-I), the former has arguably generated the widest application. However, in clinical depression CBM-A has not, to date, proven promising (Hallion and Ruscio 2011).

Two studies using CBM-I for clinical depression have yielded better results but have either used single case methods (Blackwell and Holmes 2011) or have not examined whether comparison groups were matched for pre-existing interpretation biases at baseline (Lang et al. 2012). Therefore the main aim of the present study was to show that CBM-I can successfully reduce negative interpretation bias in clinical depression when groups were carefully matched on a range of measures (including pre-existing interpretation bias) and a strict double blind randomised controlled methodology is used. To this extent the aims of the present work were fulfilled. Effect sizes on the primary outcome for cognitive change (the similarity rating task) were large (non-error targets $\eta^2 = .62$, means 2.74 vs. 2.48) and comparable to those found using this technique in a subclinical sample (Lester et al. 2011: 2.92 vs. 2.38), confirming the reliability and translational potential of CBM-errors.

On our secondary measure of cognitive change, the scrambled sentences task, a near significant trend provided tentative evidence that participants receiving the intervention showed an increase in the proportion of positive, and decrease in the proportion of negative, sentences generated, at test compared to baseline, relative to controls who did not show this pattern of change over time. It is likely that our study was underpowered to see clear results on this measure, due to missing data. Indeed a sample size calculation for the negativity bias measure, based on variance estimates from the present data (where observed effect size $f = 0.31$) showed that 80% power to detect significance (assuming alpha set at 0.05) would be achieved by a sample size of 16 per group. This measure has been shown to be a significant predictor of depressive symptoms (Rude et al. 2003) and thus the ability of any intervention to induce change on this measure has encouraging implications for the likely consequences for depressive symptomatology.

Notably, by 4 weeks, there was no longer any evidence of enduring cognitive change from this single session intervention, according to self report responses on the Automatic Thoughts Questionnaire. This is perhaps not surprising, and could be attributed to a number of different factors, but the time course of decay of cognitive effects will continue to be an essential parameter to map out in future work, as will the potential benefits and optimum timing of ‘top-up’ sessions. It is important that early studies, such as this one, include follow up assessments in order to estimate feasibility parameters including response rates, selection of most appropriate outcomes and testing of data collection methods (Lancaster et al. 2004). It is also unclear the extent to which the positive findings here.

In other respects the data presented here leave many unanswered questions. Perhaps the most surprising result was the lack of evidence for group differences in stress resilience, given the precedent of previous single session CBM-I studies that have demonstrated this (e.g. Mackintosh et al. 2006; Wilson et al. 2006). There are several possible explanations. One is that observing effects on emotional reactivity could depend on the comparison conditions used.

Studies using similar stress tasks report that participants trained to make threatening interpretations display significant elevations of state anxiety following a stressor, whereas those in benign conditions do not show pronounced changes (Wilson et al. 2006; Lester et al. 2011). Therefore, as noted by Mackintosh et al. (2006), it is possible that positive training compared to neutral control in the current study was insufficiently powerful to elicit any differential stress effects.

Another possible explanation is that the anxiety related content of the stressor task was insufficiently matched to the predominantly dysphoric concerns of our sample. However, mitigating against this explanation, the same stressor task proved sensitive to differences among the mildly depressed sample of the second study reported by Lester et al. (2011). Conversely, a study measuring CBM effects which did use videos content matched to the dysphoric concerns of the sample (depicting scenes of bereavement and bullying) found no significant differences between positively and negatively trained groups (Lang et al. 2011).
et al. 2009). It is therefore unlikely that content alone can explain the lack of findings here.

An equally likely explanation is that our stress task was simply insufficiently intense to elicit meaningful mood change. Practical constraints dictated that only one very short (1 min) video clip could be used, resulting in smaller than expected mood change scores during the course of viewing, which is likely to have compromised sensitivity. Thus one clear recommendation for future research is to optimise stressor tasks during piloting to avoid ceiling or floor effects, both of which appear to have compromised stress resilience findings in the literature to date.

Notwithstanding the above limitations, this study is distinctive as the first randomised controlled trial of the version of CBM-I, known as CBM-errors. CBM-errors was specifically designed to target and reduce the interpretations reflecting the full range of cognitive errors originally identified by Beck et al. (1979: arbitrary inference, selective abstraction, minimization, dichotomous thinking, overgeneralisation, personalization, catastrophising/magnification) and typically seen and worked within routine clinical practice. Situations inviting possible cognitive errors were generated in earlier work using exemplars taken directly from clinicians and patients (Lester et al. 2011). Thus the content of the material used in CBM-errors has inherent face validity. The present work should be considered a starting point for the further development of CBM-errors as a putative intervention for clinical depression. In this context, the present study is 'proof of principle', establishing that this particular technique can effectively reduce cognitive errors in clinically depressed patients. Any 'real' benefits to patients in terms of mood, resilience or longer term cognition have yet to be fully tested. We did not anticipate significant change in trait mood or symptoms in a clinical sample after only one short intervention session, which was not presented to patients as a treatment per se. Nevertheless we took the opportunity to measure trait mood and symptoms at test and 4 week follow up, as a useful referent point for future work and because this is recommended in pilot and feasibility studies such as this (Lancaster et al. 2004). It is likely that experimentally induced improvement in maladaptive cognitive mechanisms would require multiple sessions of implementation to accrue lasting experiential benefits observable to depressed patients, as might be expected with any other psychologically driven therapy.

While most CBM experts would agree with the need for multiple sessions to effect symptom change, as yet there has been no attempt to systematically investigate how many and of what duration would be optimum. To date studies have somewhat arbitrarily chosen the number, timing and length of sessions, without any clear evidence base. These have typically ranged from a session a day over eight consecutive days (Salemink et al. 2009) to four sessions over a 2 week period (Mathews et al. 2007). Related to this is the question of the likely decay of induced cognitive effects, its timecourse and thus the optimum approach to 'top up', should that be needed. In addition, optimising and improving the strength of transfer effects of CBM techniques will become an increasingly important issue, as translational work continues. Other evidence suggests that behavioural interventions can be more effective at instigating belief change than purely cognitive ones (van McManus et al. 2011) which raises another possible direction for future CBM research. As with face to face cognitive therapies, one way of improving efficacy and transfer may be to add supplementary behavioural reinforcement. We would advocate, as one of the next priorities for the CBM field, a systematic approach to investigating these questions (number timing and length of sessions; need for 'top up'; improving effect sizes and transfer) and establishing an appropriate evidence base for the further implementation of translational studies.

The literature also shows that there are often important individual differences in treatment response (e.g. van Doorn et al. 2012). This is likely to be the case with CBM techniques and future work needs to pay closer attention to this. Indications from our post hoc analyses were in line with previous research suggesting CBM interventions yield most benefit for those with milder depression levels (Baert et al. 2010). In our sample a near significant trend suggested the same. The cognitive deficits associated with depression are well known (e.g. Watkins and Brown 2002) and although one attraction of CBM is its relatively low cognitive demands compared to traditional psychological therapies, it may nevertheless be proportionately more difficult to engage those with more severe depression. Thus one might usefully focus on simplifying and shortening the cognitive demands of text based CBM while seeking to maintain the key mechanism of bias manipulation. One way to do this would be reducing item length to one sentence; indeed pilot work in our laboratory suggests this is feasible. Another way might be the use of auditory presentation as some are already exploring (Holmes and Mathews 2005, 2010). Our participants, severely depressed but not receiving treatment, represent a wider population of individuals for whom a more accessible, cost-effective, intervention such as CBM could be enormously beneficial.

In summary, this study reports the first double blind randomised controlled trial investigating the effect of CBM-errors in a clinical sample. Our data suggest that a positive cognitive bias can be induced in clinically depressed individuals using a simple computerised intervention. That there was little evidence of corresponding benefits in terms of mood or response to stress suggests that multiple sessions are likely to be needed to confer...
symptom related change. This in turn raises the important
question of how many sessions, over what timescale and
for what duration will be optimal? To date, the field has
approached this aspect, of translating a basic experimental
manipulation into a clinical intervention, in a rather ad-hoc
fashion. A systematic investigation of these questions is
now called for.

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