From cognitive targets to symptom reduction: overview of attention and interpretation bias modification research

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ABSTRACT

Cognitive bias modification (CBM) is a class of mechanised psychological interventions designed to target specific aberrant cognitive processes considered key in the aetiology and/or maintenance of specific psychiatric disorders. In this review, we outline a multistage translational process that allows tracking progress in CBM research. This process involves four steps: (1) the identification of reliable cognitive targets and establishing their association with specific disorders; (2) clinical translations designed to rectify the identified cognitive targets; (3) verification of effective target engagement and (4) testing of clinical utility in randomised controlled trials. Through the prism of this multistage process, we review progress in clinical CBM research in two cognitive domains: attention and interpretation; in six psychiatric conditions: anxiety disorders, major depressive disorder, post-traumatic stress disorder, addictive disorders, eating disorders and obsessive–compulsive disorder. The review highlights achievement as well as shortcomings of the CBM approach en route to becoming a recognised evidence-supported therapy for these disorders.

INTRODUCTION

Cognitive bias modification (CBM) is a class of interventions targeting aberrant cognitive processes considered key in the aetiology and maintenance of different psychopathologies. CBM focuses on underlying mechanistic dysfunctions, rather than on symptoms used as basis for diagnostic categories. Reliable CBM procedures depend on a multistage translational process involving (1) identification of reliable treatment targets (ie, biassed cognitive functions related to a specific disorder); (2) clinical translation to rectify the identified bias; (3) effective target engagement (ie, the devised translation effectively modifies the identified bias); and (4) testing of clinical utility in randomised controlled trials (RCTs).[1]

The most advanced CBM procedures focus on attention and interpretation biases. Attention bias modification (ABM) typically uses spatial cues or gaze-contingent reinforcement to train patients to allocate attention to neutral or positive over negative stimuli.[2] Cognitive bias modification of interpretation (CBM-I) trains participants to disambiguate information in a neutral or positive manner over a negative manner.[3] See figures 1–3 for examples of trials in ABM and CBM-I tasks. Here, using the prism of the multistage translational process described previously, we review progress in ABM and CBM-I research across various psychopathologies. We address target identification, target engagement and symptom reduction while specifically focusing on clinical populations and formal RCTs.

ANXIETY DISORDERS

Attentional biases in processing threat-related information have been assigned a prominent role in the aetiology and maintenance of anxiety disorders.[3] Experimental work established that the attentional system of anxious individuals is indeed distinctively sensitive to threat-related stimuli, favouring attention allocation to threat over neutral stimuli.[4] Extant evidence establish threat-related attention biases in anxiety as viable therapeutic targets in adults. In contrast, studies in youth are scanter, and meta-analyses suggest small effect sizes and conflicting results. Hypervigilance towards threat was found in reaction time (RT)-based studies,[5] whereas threat avoidance emerged in eye-tracking studies.[6]

Successful modification of attention biases in anxious individuals using ABM procedures has been demonstrated in numerous RCTs with meta-analyses indicating greater reductions of threat-related bias from pretreatment to post-treatment in ABM compared with control conditions.[7] Anxiety reduction following ABM has been observed in 8 out of the 10 reported meta-analyses summarising this field,[8] indicating small-to-medium clinical effect sizes. A recent network meta-analysis of ABM trials also reported significant symptom reduction in ABM compared with waitlist and shame conditions, excluding post-traumatic stress disorder (PTSD).[9]

Patients' age has emerged as a potential mediator of ABM efficacy, suggesting an inverted U-shaped effect with greater symptom reduction evident in adolescents and young adults relative to young children and older adults.[7] A pooled patient-level meta-analysis has also shown that higher baseline bias predicts greater bias reduction from pretreatment to post-treatment, subsequently predicting greater anxiety relief following ABM.[7] Finally, stronger effects of ABM were noted when delivered in controlled lab settings rather than remotely at home.[7 10]

Threat hypersensitivity in anxiety also manifests in interpretation biases. Relative to non-anxious individuals, anxious adult patients are prone to interpret ambiguous information as threatening.[11] Similarly, anxiety disorder content-congruent interpretation biases are evident in clinically anxious youth, with patients with social anxiety, separation anxiety or

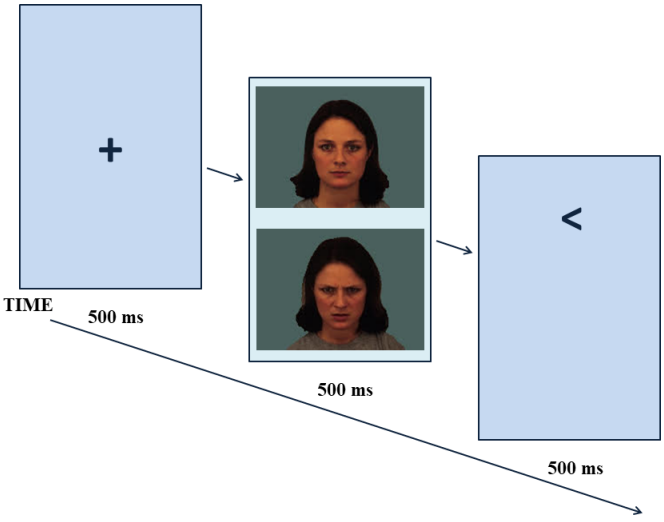

Figure 1 In each trial of the probe detection task, the most commonly used RT-based form of ABM, a fixation cross is followed by two stimuli of various valences, which are then replaced with a visual probe (eg, an arrow pointing left or right) at the location of one of the stimuli. Patients are asked to discriminate the probe's type as quickly and accurately as possible. For example, when aiming to rectify an attentional bias towards threat, target arrows will be placed at the location of the neutral face location with higher frequency than in the threat face location. With repeated trials (and training sessions), patients gradually learn the predictive value of neutral faces in relation to target location and thus shift their attention to these locations as this facilitates task performance. Repeated training is thought to rectify the bias and consequently reduce symptoms. Treatment protocols range from 1 to 24 sessions, presenting 100–400 trials per session. The most commonly applied protocols involve eight biweekly sessions with 160 trials per session. Face stimuli were taken from the Karolinska Directed Emotional Faces stimulus set. ABM, attention bias modification; RT, reaction time.

simple phobia exhibiting an interpretation bias specifically for subtype-specific items.[12] Together, these findings render interpretation biases as another viable target for intervention.

Clinical RCTs of CBM-I are more scarce. However, meta-analyses of extant RCTs suggest that CBM-I significantly reduces the targeted biases and outperforms waitlist or sham training in anxiety reduction.[9 13]

In summary, CBM shows promising clinical potential for the treatment of anxiety disorders. Most RCTs of ABM indicate effective bias modification and reduction in anxiety symptoms, placing it at the forefront of CBM interventions on the verge of acceptance as evidence-supported therapy. However, recent findings suggesting that traditional control conditions may also serve to reduce anxiety,[14] and concerns regarding the reliability of some bias measurements[15] warrant additional research on the mechanisms underlying ABM treatment response. Indeed, preliminary studies and RCTs suggest that applying eye-tracking technology may offer more reliable and robust ABM protocols for anxiety.[16] Though results from CBM-I in anxiety disorders are promising, larger and more definitive RCTs in clinical patients are still required to determine its clinical utility.

DEPRESSION

Echoing the depressed mood and anhedonia of depression, two types of attention biases have been noted in depressed patients: (1) prioritising attention to negative over neutral and positive stimuli and (2) lacking an attentional bias in favour of positive over neutral or negative stimuli. Meta-analyses of RT-based studies[17] and eye-tracking studies[4] support the existence of both biases in depressed compared with non-depressed individuals, indicating small and moderate-to-large effect sizes for RT and eye-tracking studies, respectively, rendering both types of biases viable targets for intervention.

The number of clinical RCTs in depression is small. Modification of attentional biases has been successful in most RCTs training depressed individuals to attend away from negative and/or towards positive stimuli,[18 19] with a meta-analysis suggesting small-to-medium effect sizes.[20] While the clinical efficacy of ABM in depression has been questioned in an older meta-analysis, including both clinical and subclinical RCTs,[21] more recent clinical RCTs have shown significant symptom reductions after ABM compared with control training.[18] However, such clinical efficacy was not found for web-based ABM.[19] Moderators' analyses suggest that ABM may be better suited for patients in their first depressive episode than for patients with recurrent episodes.[22]

A similar 'double bias' has been also observed in relation to interpretation biases in depression. Specifically, a meta-analysis indicates both negative and a lack of a positive interpretation biases in depressed patients compared with healthy controls, both of medium effect size.[23]

Conclusions about the effect sizes of CBM-I on bias in depressed patients cannot be drawn due to a small number of RCTs and meta-analyses that conflate CBM interventions and/or psychopathologies.[20] However, extant clinical RCTs in depression indicate both

Figure 2 In each trial of gaze-contingent therapy, a second-generation ABM protocol using eye-tracking technology, participants view a matrix of mixed valance stimuli and are reinforced with music when looking at the targeted stimuli. For example, if the aim is to increase attention to neutral over disgusted faces with the intention to rectify a bias observed in patients with SAD, music will play as long as the patient is fixating on one of the neutral faces and will stop when fixating on one of the disgusted faces. With repeated trials of this protocol, attention is gradually shifted away from threat and symptoms reside. Face stimuli were taken from the Karolinska Directed Emotional Faces stimulus set. ABM, attention bias modification; SAD, social anxiety disorder.

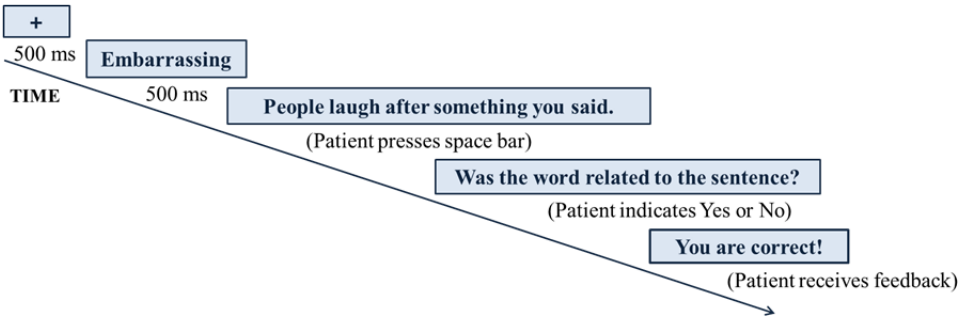

Figure 3 In each trial of the word–sentence association paradigm, one of the most common CBM-I tasks, patients are presented with a fixation cross followed by a word representing either a benign or a negative interpretation to an ambiguous situation presented in the following screen. Patients are then asked if the word and situation presented were related. Positive feedback is provided for responses that accept benign interpretation or reject negative interpretations. With repeated trials, it is expected that patients will make more benign or positive interpretation, rectifying an interpretative bias and reducing symptoms. CBM-I, cognitive bias modification of interpretation.

decrease in negative bias and increase in positive bias after CBM-I compared with control training and waitlist conditions when modifying negative-valenced interpretations[24] but less favourable results when modifying hostile interpretations.[25] A network meta-analysis examining the clinical potential of CBM-I found it to significantly reduce both primary and comorbid depression compared with waitlist.[9]

Application of imagery rather than verbal stimuli in CBM-I appear to increase training effects on negative interpretation bias and symptoms.[26] Also, unlike in anxiety, RCTs of CBM-I in depression suggest clinical potential for remote delivery without compromising efficacy.[26]

In summary, both ABM and CBM-I appear to engage their targeted biases and reduce symptoms in depression. However, the small number of formal RCTs precludes definitive conclusions about the clinical utility of CBM in depression.

POST-TRAUMATIC STRESS DISORDER

Cognitive models of PTSD assign an important role for cognitive biases in vulnerability to, and maintenance of, the disorder, including threat-related and trauma-related attention and interpretation biases.[27] However, empirical studies of attention bias in PTSD have produced inconsistent findings. Some studies report bias towards threat,[28] others away from threat,[29] and some find no evidence for bias.[30] Given these inconsistencies, it was suggested that PTSD may be characterised by hyper-fluctuation of threat-related attention. A new index, attention bias variability (ABV), estimates fluctuation between bias towards and away from threat.[30] ABV is consistently elevated in patients with PTSD relative to other anxiety disorders and healthy controls,[30] making it a viable target for modification in this disorder. Eye-tracking studies of attention bias in PTSD suggest an additional target, with patients consistently displaying greater sustained attention on threat stimuli relative to control populations.[31]

Eye-tracking-based RCTs of ABM in PTSD are yet to be published. In contrast, four RT-based RCTs of ABM as a standalone treatment have been conducted. These clinical RCTs have compared ABM away from threat and attention control training (ACT) aimed at reducing ABV. ACT, originally designed as a placebo–control version of ABM, does not shift attention towards a specific valenced direction, but rather is thought to enhance control over one's attention in an emotional setting.[32] One RCT found ABM and ACT to be equally effective in reducing PTSD symptoms,[33] whereas three more recent RCTs have favoured ACT over ABM.[32 34] Specifically, two independent RCTs of veterans with PTSD indicate that ACT significantly reduced ABV and post-traumatic symptoms, with reduction of ABV partially mediating symptom reduction.[32] An additional RCT compared ACT with a bias-contingent attention bias modification (BC-ABM), in which civilian patient's attention was trained according to their pretreatment bias.[34] Results showed that while both protocols led to clinical improvement, ACT was superior to BC-ABM. Research of ABM in PTSD is in its early days, as is research on its potential moderators. Extant evidence suggests promise for ACT along with a need for more decisive RCTs.

Research on interpretation biases suggest that individuals with PTSD tend to endorse threat-related and trauma-related interpretations for ambiguous information. For example, compared with veterans without PTSD, veterans with PTSD were more likely to choose combat-related words in sentence-completion tasks,[35] and civilians with PTSD were more likely to disambiguate words in a threatening manner.[36] To the best of our knowledge, only one clinical RCT to date examined CBM-I in PTSD. Using an appraisal-based CBM, this RCT found no differences between active and control conditions.[37]

In summary, more research is needed within the field of CBM for PTSD. ACT, targeting ABV reduction, has shown preliminary promise of clinical efficacy. Eye-tracking studies suggest enhanced dwelling on threat and offer a solid target for interventions based on eye-tracking technology. CBM-I for PTSD is currently an uncharted territory calling for further research.

ADDICTIVE DISORDERS

ABM in the context of addictions was designed to change a hypothesised selective attention to abused substances or to cues predicting their use. Such cues are thought to automatically capture attention and weaken control over impulses, thereby supporting a cycle of addiction.[38] Reviews concerning alcohol-related and cigarette-related attentional biases in alcoholics and smokers indicate mixed evidence of bias.[39] In contrast, compared with non-users, cocaine addicts appear to allocate more attention to their drug-related cues.[40]

Some RCTs indicate that ABM can successfully modify attention towards alcohol and smoking-related stimuli.[41] However, a review of 18 studies of various addictions found unreliable evidence of pretraining to post-training reduction in attention bias.[42] Thus, despite initial promise, the empirical evidence supporting ABM's target viability, target engagement and effectiveness for addictions has been mixed. In alcohol dependence, evidence of effectiveness appears to be restricted to its application as an add-on to regular treatment for relapse prevention with small effect sizes.[43] Given

the obstacles ABM is facing in addiction, research on moderators of treatment outcome may be premature.

The tendency to endorse substance-related interpretations for ambiguous information is far less researched. Early studies found evidence for alcohol-relevant interpretation bias in alcohol-dependent patients, with a positive correlation between bias and harmful drinking.[44] Negative bias was also associated with more cravings and less confidence in the ability to resist substance use among inpatients.[45] To our knowledge, no clinical RCTs of CBM-I in addiction have been conducted.

In summary, evidence of substance-related attention bias in alcoholism and smoking appears less consistent than in other drug addictions. The clinical efficacy of ABM in drug addiction is evident in multisession protocols, and efficacy in alcoholism is evident in relapse prevention when applied as an adjuvant to other established treatments. For CBM-I to have clinical relevance in addictions, future research must examine clinical samples in extended protocols.

EATING DISORDERS (EDS)

Cognitive models of EDs suggest that symptomatic preoccupation with food and disliked body parts could manifest in aberrant attention and interpretation of ED-related information.[46] For instance, attentional threat avoidance of food stimuli is thought to reflect avoidance of the threat such stimuli pose to restrictive food intake. A meta-analysis indicates greater bias away from food stimuli in ED relative to healthy controls.[47] In contrast, body-related stimuli appear to capture greater attention in patients with ED relative to controls, with patients overly attending to overweight-related stimuli and to images of regions of their body they consider unattractive.[48]

To our knowledge, no clinical RCTs examining ABM with food stimuli for ED have been conducted. A meta-analysis of non-clinical studies aimed at improving eating habits found ABM to be effective in reducing attentional avoidance of food stimuli and corresponding eating behavior when compared with control conditions.[49] A review of the efficacy of ABM for appearance-related stimuli among healthy, subclinical and clinical populations suggests large effects of ABM on attention, but with no reliable reduction in ED symptoms.[50] This latter results pattern suggests that attention biases might not play a causal role in body-related ED symptom expression.

Interpretation biases in ED have also gained support, with patients with ED more likely to attribute negative body interpretations to ambiguous sentences and scenarios, compared with healthy individuals.[51] A review of CBM-I for appearance-related interpretation bias among healthy, subclinical and clinical populations suggests moderate-to-large reduction in bias, and smaller and less consistent effects on ED symptoms.[50]

In summary, CBM protocols for EDs use either food or body/appearance-related stimuli. While both have been targeted in ABM, only appearance-related stimuli have been applied in CBM-I. Results indicate successful ED bias modification through both ABM and CBM-I, but further examination of clinical efficacy in RCTs is still necessary.

OBSESSIVE–COMPULSIVE DISORDER (OCD)

Extant research on threat-related attention biases in clinical OCD reveals conflicting findings, with some studies reporting bias towards threat[52] and others failing to demonstrate this bias.[53] These mixed findings were attributed to potentially overlooking massive heterogeneity in OCD where biassed attention may manifest only when assessed via idiosyncratic stimuli.

Most ABM studies in OCD have used analogue proof-of-concept samples rather than clinically diagnosed patients, generally showing effective bias modification but no reliable reduction in OCD symptoms.[54] The scant work on ABM in clinical OCD precludes definitive conclusions about its clinical utility.

Research in both clinical and subclinical samples consistently implicates interpretation biases in OCD.[55] The only clinical RCT to examine patients with OCD did find that interpretations changed in response to CBM-I training, with patients also demonstrating less OCD symptoms relative to a control group.[56] Still, more research is needed to determine the clinical efficacy of CBM-I for OCD.

In summary, while ABM and CBM-I both demonstrate target engagement in reducing respective biases, clear evidence on clinical efficacy in OCD is still lacking.

CONCLUSION

Here we provide an overview of attention and interpretation bias modification protocols as an evidence-supported intervention for various psychopathologies. CBM protocols show promise in a variety of clinical domains. However, progress along the translational road towards reliable treatment establishment varies between pathologies. The clinical efficacy of ABM has been extensively supported in RCTs for anxiety disorders but requires more research in all other diagnostic domains. In contrast, CBM-I has shown considerable promise for eating and anxiety disorders, whereas evidence in other disorders is limited. Importantly, many reviews and meta-analyses, on which much of the information provided here relies, conflate different types of CBM (eg, ABM and CBM-I) and/or compiled psychopathologies when reporting combined clinical and target engagement effects, making it difficult to ascertain conclusions for specific disorders and specific CBM interventions. It is crucial for future experimental and meta-analytical work to refrain from mixing apples and oranges in CBM studies, and from providing misguiding interpretations as reflecting the state-of-the-art.

The advantages of CBM over traditional clinical treatment warrant efforts to further develop evidence-supported CBM. CBM interventions are shorter and more cost-effective than traditional treatments and may be used as a first-line intervention to deliver early and available treatment, reducing costs and freeing resources of traditional therapy for those who need it. CBM is mechanised and can be delivered remotely with minimal costs, meeting the growing need to increase accessibility in both in routine and under circumstances in which in-person treatment is limited. To date, most CBM research has indicated reduced efficacy with remote delivery, but preliminary evidence suggests bias reduction among adolescents with heightened anxiety and depression symptoms and among patients with OCD.[57] Therefore, novel approaches to this issue are a priority. Finally, we strongly recommend application of the science-driven multistage translational process taken by CBM researchers towards the establishment of reliable and effective CBM procedures. This approach, while sometimes tedious and highly invested, is still producing one of the most productive, creative and rigorous progress in clinical psychological science.

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