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Cognitive Remediation and Bias Modification Strategies in Mood and Anxiety Disorders

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Abstract

Purpose of review—Cognitive impairments and biases, which are prevalent in patients with mood and anxiety disorders, can affect quality of life and functioning. Traditional treatments are only insufficiently addressing these impairments and biases. We review the cognitive impairments and biases present in these disorders as well as treatments targeting these domains.

Recent findings—Interventions aimed at improving cognitive impairments and biases may help improve cognitive deficits and overall functioning in patients with mood and anxiety disorders. Direct comparisons of treatments for cognitive impairments or biases versus more traditional psychosocial interventions have produced diverse results.

Summary—Overall, treatments for cognitive impairments and cognitive biases warrant additional study in clinical trials. Future research should explore cognitive remediation and cognitive bias modification adjunctive to psychosocial treatments to optimize patient outcomes in mood and anxiety disorders.

Keywords

cognitive remediation; cognitive bias modification; mood disorders; anxiety disorders

Introduction

With a nationwide lifetime prevalence of 20.8% and 28.8% [1], respectively, mood and anxiety disorders exert a detrimental impact on individuals' quality of life and overall functioning. Mood disorders include both major depressive disorder (MDD) and bipolar disorder (BD), characterized by periods of hypomania or mania and most often depression[2]. Anxiety disorders include generalized anxiety disorder (GAD), marked by excessive and chronic worry, social anxiety disorder (SAD), defined by extreme fear in social situations, and panic disorder (PD), characterized by recurring panic attacks[2]. Common to mood and anxiety disorders are impaired/biased cognitive processes that affect illness course and treatment outcomes. For many patients, traditional pharmacotherapy and/or psychotherapy are not sufficient for addressing the cognitive symptoms present in these disorders.

Cognitive symptoms in mood and anxiety disorders can broadly be divided in two groups: (1) cognitive impairments and (2) cognitive biases. Cognitive impairment refers to deficits in cognitive performance with respect to processing information of neutral valence in the domains of attention, memory, and executive functioning, among other areas[3-6]. Data suggests that, in mood and anxiety disorder patients, cognitive functioning tends to be below that of healthy individuals[3, 7, 5, 4, 8]. Treatments targeting cognitive impairments are typically referred to as cognitive rehabilitation, cognitive remediation, or functional remediation.

Cognitive biases, which, for the purpose of this review, include attentional and interpretational biases, refer to the tendency among individuals with mood and anxiety disorders to preferentially process negative and threat-related information[9-12]. Treatments

targeting cognitive biases are most commonly referred to as attentional or cognitive bias modification.

In this review, we discuss abnormalities within cognitive processes in mood and anxiety disorders as well as treatment approaches targeting cognitive impairments and biases that have been developed to help individuals with these disorders.

Mood Disorders

Cognitive Impairments

Cognitive impairments within MDD and BD samples have been found in the domains of attention/processing speed, memory, and executive functioning (i.e. planning or problem solving)[3, 7, 5, 13-15], among other areas. Cognitive deficits are present for many patients with mood disorders across all stages of the illness (e.g., during acute episodes and periods of euthymia) and only partially result from psychiatric medications[16, 17, 7]. Thus, medication does not fully account for cognitive impairments in MDD and BD. Findings from clinical trials in MDD and BD suggest that the severity of cognitive impairments is associated with mood symptom severity[18-21] and that cognitive deficits contribute to low quality of life and reduced psychosocial functioning [22-24]. Recent studies have examined the frequency of cognitive impairments in mood disorders. Gualtieri and Morgan[8] compared MDD and BD patients to healthy control patients on neurocognitive assessments of memory, reaction time, psychomotor speed, cognitive flexibility, and attention. While only 4% of control participants scored below a standard value on at least 2 cognitive areas, 21% of MDD and 30% of BD patients scored below this value. In a study of 267 primary care patients with depression, Conradi et al.[25] found cognitive impairments to be present 85%-94% of the time during acute episodes and 39%-44% of the time during remitted periods. Within BD, between 30%-60% of euthymic patients demonstrate cognitive deficits[4, 3, 7, 26, 5, 27]. In a systematic review, Cullen et al.[20] examined the prevalence of cognitive impairments in euthymic BD. Their findings indicate that cognitive impairments affect a large proportion of euthymic BD patients with prevalence ranges recorded for attention/working memory (9.6%-51.9%), executive functioning (5.3%- 57.7%), reaction time (23.3%-44.2%), visual memory (11.5%-32.9%), and verbal memory (8.2%-42.1%)[20].

In mood disorders, attention deficits have been well-documented with patients showing difficulties on tests of sustained attention, information processing, and attentional switching[28-30]. Within a bipolar sample, patients score below healthy control subjects on attention/information processing speed measures such as the continuous performance task (CPT), the Digit Symbol Substitution Test (DSST), and the Trailmaking Test Part A[31, 32, 3, 7].

Impairments in explicit memory and working memory are common to MDD and BD. Explicit, or declarative, memory refers to conscious, long-term recall of information while working memory refers to the short-term storage of information[33, 34]. In the domain of explicit memory, MDD and BD patients demonstrate difficulties on tests of verbal episodic memory (e.g., the California Verbal Learning test, the Weschler Memory Scale-Revised, the Auditory Verbal Learning Test)[35, 36, 17]. Nonverbal memory has also been found to be

impaired in MDD and BD; both acutely ill and euthymic patients have demonstrated impairments on the Rey-Osterrieth complex figure test[37-39].

On working memory assessments, MDD and BD patients have been shown to exhibit deficits in the backward digit span test, n-back task, the working memory battery of the Cambridge Neuropsychological Battery, the Trailmaking Test Part A, and the DSST. Of note, procedural, or implicit, memory remains largely unimpaired in MDD and BD[16, 40, 41, 21].

Executive functioning centers on the ability to flexibly adjust behaviors/actions, engage in strategic planning, and complete goal-oriented tasks[42]. MDD and BD patients show deficits in several measures of executive functioning/reasoning and problem solving relative to healthy control subjects including deficits on the Wisconsin Card Sorting Test, the Stroop test, the Digits Backwards, the Trail-making Test Part B, the California Verbal Learning Test, and the tower of London task[3, 32, 43-47].

Treatments for Cognitive Impairments

Cognitive remediation treatments typically involve structured training (either computerized or via paper-and-pencil materials) in particular cognitive domains. For example, Meusel et al.[48] demonstrated that, among mood disorder patients who completed a ten-week, computer-assisted cognitive remediation program, improvements were evidenced in a backward digit span task and in 2-back accuracy. Improvements on the 2-back were associated with increases in superior temporal, lateral and medial prefrontal, and lateral parietal region activation as shown by functional magnetic resonance imaging while improvements in recollection were associated with increases in left hippocampus activation[48]. Choi and Medalia[49]found that adult psychiatric outpatients, including patients with MDD and BD, who completed 26 hours of cognitive training demonstrated post-treatment improvements in employment readiness and attention. Of note, those who did not attend sessions regularly or who took longer than 4 months to complete the training sessions did not demonstrate any cognitive improvements. These findings suggest that the efficacy of cognitive remediation treatments may hinge on treatment adherence and attendance. Preiss et al.[50] randomly assigned MDD or BD depressed patients to a cognitive training intervention or standard care alone. Cognitive training was provided through CogniFit, a validated online cognitive training program that includes neurocognitive tests of memory, attention, and executive functioning. At the end of the study, the intervention group demonstrated significantly reduced depressive symptomatology, fewer self-reports of cognitive failures, and fewer challenges in coping with daily life. The control group only demonstrated improvements in working memory and reported cognitive failures[50]. Deckersbach et al.[51] examined 14-sessions of functional remediation for improving psychosocial functioning in a bipolar sample. Functional remediation sessions focused on attention and memory training as well as training for time management, organization, and planning. Patients were trained on implementing compensatory strategies in daily life to improve their work and overall functioning. At three-month follow up, patients demonstrated improved occupational and psychosocial functioning as well as reduced depressive symptoms. Further, gains in executive functioning were associated with

occupational functioning improvements[51]. Similarly, Torrent et al.[26] randomly assigned bipolar outpatients to functional remediation, psychoeducation, or treatment as usual (TAU). Functional remediation consisted of 21, 90-minute weekly sessions that addressed neurocognitive areas such as memory, executive functioning, and attention. Memory, attention, problem solving, and other cognitive exercises were aimed at improved functional outcomes. Significant functional improvements were evidenced at the end of the study within the functional remediation group relative to TAU. Though functioning improved more in the functional remediation group than in the psychoeducation group, this difference was not statistically significant[26].

Cognitive Biases

Research has documented cognitive biases for emotional stimuli in both MDD and BD[9, 52, 53]. Individuals with MDD often selectively attend to schema-congruent information over schema-incongruent information[9]. Depressed individuals also exhibit stronger recall for depression-relevant stimuli over neutral stimuli and negative stimuli over positive stimuli[54-56]. Recently, Platt et al.[57] found a significant association between negative attention biases on a dot-probe task and greater depressive symptomatology among community adolescents. In a meta-analysis, Peckham et al.[58] found evidence of attentional biases to negative stimuli in depressed samples relative to non-depressed samples.

Attentional biases for emotional stimuli are also common to BD. Leyman et al.[53] found that BD patients with current depression had more difficulty in turning their attention away from both angry and happy faces relative to control participants. Specific affective characteristics may influence attentional biases in BD; for example, Peckham et al.[59] found that dampening of positive affect was associated with significantly less attention for positively valenced faces on a dot-probe task. Peckham et al.[59] suggest that bipolar individuals may avoid positive stimuli as a tactic for regulating their positive affect. In another study, bipolar patients with mild depression exhibited an attentional bias away from positive emotional words (e.g., an implicit bias) as well as dysfunctional attitudes (e.g., an explicit bias as measured by the Dysfunctional Attitude Scale). Both euthymic and mildly depressed bipolar patients showed higher levels of neuroticism relative to control participants[60].

In both MDD and BD, patients demonstrate a bias towards extreme attributional styles, or a tendency to explain the causes of events in black-and-white terms; this bias towards negative attributions is associated with a worsened illness course in both disorders[61]. Attributional style is in turn linked to social cognition, which describes an individual's way of understanding and responding to others' actions and intentions across various social situations[62]. Lahera et al.[62] found that, relative to control participants, bipolar patients demonstrated a social-cognitive bias; specifically, bipolar patients exhibited a stronger tendency to assign intentions to ambiguous scenarios.

Treatments for Cognitive Biases

Overall, treatment programs for cognitive biases in emotional disorders strive to change individuals' tendency to focus on negative information in the environment[63, 64]. Cognitive

bias modification (CBM) aims to modify automatic attentional and interpretative biases present in patients with emotional disorders through cognitive training exercises[12]. Studies have primarily focused on two types of CBM: interpretive bias modification (CBM-I) and attention bias modification (ABM or CBM-A). Recent meta-analyses that have examined the effect of CBM-A and CBM-I on depression and anxiety found, overall, rather small effects of CBM interventions on depression outcomes when examined separate from[65] and together with anxiety outcomes[66]. Hallion and Ruscio[66] found a medium effect of CBM on biases that was greater for interpretation biases (CBM-I) than for attention biases (CBM-A).

For example, Williams et al.[67] found that a 7-session, combined CBM-I and internet-based cognitive behavioral therapy (CBT) program modified interpretation biases among patients in a major depressive episode[67]. The CBM-I component consisted of training paragraphs that concluded with positive outcomes. After each training paragraph, participants were asked to rate how vividly they were able to imagine the described scenario[68]. Study results indicated that the combined intervention led to significant reductions on measures of anxiety, repeated negative thoughts, and disability. Further, 65% of participants demonstrated clinically significant change following the combined intervention while 27% demonstrated a change following CBM-I alone[67]. Reductions in clinical symptoms were partially mediated by the change in interpretation bias[67]. This study did not incorporate an active control group and is thus limited in its generalizability[69]. In a more recent study that incorporated a control group, Joormann et al.[69] found that CBM-I impacted physiological response to acute stressors – specifically, depressed participants who had been trained to interpret ambiguous situations positively (positive training) demonstrated a smaller increase in heart rate following a stress induction than did those who had been trained to interpret ambiguous situations negatively (negative training). Further, CBM-I modified participants' memory for the test situations. Individuals who received positive training exhibited more positive memory distortions (e.g., details that had not been included in the test situation) while those who received negative training exhibited more negative memory distortions.

To date, few studies have explored CBM-I in BD. Micco et al.[70] examined a four-session CBM-I program in depressed individuals aged 14-21, five of whom met criteria for bipolar I disorder. Participants were randomized to the intervention (e.g., continuous exposure to positive outcomes of depression-related ambiguous situations) or to a control group (e.g., continuous exposure to neutral situations). Upon examining only those individuals who demonstrated negative bias at baseline, Micco et al.[70] found larger improvements in interpretation bias and self-reported negative thoughts at post-treatment in the intervention group relative to the control group. Given that most research on CBM-I has been conducted in samples of anxious individuals[12, 64], future research should continue to explore CBM-I in mood disorders, particularly in a bipolar sample.

ABM was developed by Macleod et al.[71] to reduce attentional bias, or engagement/disengagement from particular emotional stimuli. Yang et al.[72] randomized 45 adolescents with major depression to an active ABM intervention, which was a variation of the dot probe task, or placebo ABM training. The active ABM group received neutral ABM exercises (e.g., shifting attention from sad words to neutral words) and positive ABM exercises (e.g.,

shifting attention to positive words) while the placebo, or sham, ABM group completed the same exercises with equal shifting to sad and neutral words. Relative to the placebo ABM group, the active ABM group showed larger improvements in clinician-rated depressive symptoms and larger reductions in attentional bias scores. Larger decreases in self-reported depressive and anxiety scores were noted in the active ABM group relative to the placebo group[72]. In a prior study of ABM among depressed college students, Yang et al.[73] noted improvements in depressive symptoms post-training and at 3-month-follow-up with participants receiving ABM remaining asymptomatic at post-treatment.

Recently, a trial conducted by Almeida et al.[74] has explored CBM for reducing the one-year onset of a depressive episode among adults aged 45 and older with subsyndromal depression. The intervention program incorporates both CBM-A and CBM-I treatments. Preliminary findings among a sample of study participants suggest that the CBM program is effective in reducing depressive symptom severity[75].

Anxiety disorders

Cognitive Impairments

Several studies have examined neuropsychological deficits in generalized anxiety disorder (GAD) and, among those studies, some have provided support for cognitive deficits in GAD[4]. Memory deficits have been found in GAD patients in prior trials with participants performing worse on a modified Sternberg memory task[76] and on other tests of working memory[77]. More recently, Yang et al.[78] found decreased N270 amplitude, an event-related potential component thought to be associated with cognitive functioning, in the left hemisphere of GAD patients while they completed a dual-featured delayed matching task. Within older adults, some research suggests that executive functioning may mediate the outcomes of CBT treatments[79]. Mohlman and Gorman[79] found that, in GAD adults aged 60 or older receiving CBT treatment, those with low executive functioning scores from pre- to post-treatment did not respond as well to CBT. Those who demonstrated improvements in executive functioning from pre- to post-treatment, as well as those who had intact executive functioning at baseline, responded well to CBT.

Similar to GAD, varied data exists on neuropsychological functioning within social anxiety disorder (SAD) with some research suggesting neuropsychological deficits to be absent in this disorder[4, 80]. Sutterby and Bedwell[80] examined individuals with SAD on nine functioning areas (e.g., verbal learning, verbal delayed memory, visual immediate memory, visual-spatial processing, verbal working memory, visual working memory, executive functioning, and attention) relative to healthy control subjects. They found no differences between the two groups within each cognitive area. Some research has suggested poor performance within neurocognitive domains in SAD participants[81]. O'Toole et al.[81] administered a neuropsychological test battery to SAD participants and healthy controls. They found that SAD participants exhibited worse performance than healthy control subjects in visuospatial construction, visuospatial memory, word fluency, processing speed, and verbal learning with differences in visuospatial construction reaching significance. Low executive functioning in SAD patients has also been associated with severity of SAD symptoms[82].

In panic disorder (PD), studies have demonstrated deficits in spatial learning, verbal learning, visuoconstruction, and memory (e.g., episodic, visual) with some studies also showing deficits in executive functioning[4, 83-85]. A recent systematic review did not support the presence of cognitive functioning deficits in PD though there was marginal evidence of short-term memory deficits among PD individuals[86]; these findings reflected those of Gladsjo et al.[87] who found no group differences between PD subjects and healthy controls on visuospatial, learning, memory, psychomotor speed, and attention tasks.

There is varying data on the presence of cognitive deficits among these anxiety disorders[80, 88]; thus, it is difficult to assess prevalence and severity of impairments in SAD and PD. In the Gualtieri and Morgan[8] study discussed prior, frequency of cognitive impairments was examined in GAD patients relative to healthy control subjects across five neurocognitive domains. Study findings indicated that 19% of GAD patients scored below a standard value.

Treatments for Cognitive Impairments

Several studies have suggested that working memory training can reduce anxiety and produce improvements in cognitive functions among individuals with anxiety disorders. Sari et al.[89] examined the effects of working memory training on attentional control in subjects with high trait anxiety randomly assigned to an eight-day, two-week adaptive training group or a nonadaptive control group involving a dual n-back task that required participants to note whether there was a match for auditory or visual information in the current trial and a number *n* trials prior in the series. The adaptive nature of the experimental intervention meant that the difficulty of the intervention could increase to 4-back level. The non-adaptive/control program involved only a 1-back level. Attentional control was measured at pre- and post-treatment through a Flanker task and an AntiSaccade task. The Flanker task involves distracter and target arrows pointing in different directions. The test requires the participant to ignore the distracter arrows and report the direction of the target arrow. In the AntiSaccade task, subjects are instructed to saccade towards or away from a peripheral target that appears on the screen. Resting state electroencephalography (EEG) was used as a measure of trait attentional control. Participants in the adaptive training condition demonstrated improvements in attentional control on the Flanker task and in attentional control indices on resting state EEG; training improvements were associated with reduced trait anxiety post-treatment[89]. One study compared a working memory intervention incorporating verbal and visuospatial training versus a group CBT intervention in adolescents aged 11-14 with high anxiety and low attentional control. Overall, both groups showed improvements in anxiety symptoms, increased inhibitory control, and reduced attentional biases to threat at post-treatment with the working memory group demonstrating superior performance to the CBT group on working memory tasks[90]. The authors cite these findings as evidence that working memory training has similar advantages to traditional CBT[90]. By contrast, Wanmaker et al.[91] found that an adaptive working memory training was not beneficial in improving anxiety, depressive, and ruminative symptoms in anxious and depressed patients. The intervention was also not found to be beneficial in improving working memory capacity in study participants. It should be noted that this study had a high drop-out rate of 20.11% from pre- to post-treatment.

In two separate pilot studies, Mohlman et al.[92] examined traditional CBT (study 1) and enhanced CBT (eCBT; study 2) for treating GAD in adults aged 60-74. Both studies incorporated weekly sessions with eCBT involving supplemental learning and memory training aimed at increasing memory for lessons learned during CBT, enhancing homework compliance, and promoting the use of lessons learned during CBT. eCBT led to significant improvements in ratings of GAD severity and self-reported anxiety relative to wait-list control. Further, relative to wait-list control, eCBT produced larger effect sizes than traditional CBT[92].

Cognitive Biases

Common to anxiety disorders are attentional biases towards negative environmental stimuli; in particular, anxious individuals tend to selectively attend to, perceive, and encode information associated with threat stimuli[93, 11]. This bias also operates through an interference effect in which individuals have trouble focusing on the desired task while experiencing anxiety[93]. Studies demonstrate some variability surrounding the direction of the bias; specifically, patients may demonstrate a bias towards or away from a threatening stimulus[94, 95]. However, most studies suggest that anxious individuals exhibit an orientation towards the threat-relevant stimulus[95]. Bar-Haim et al.[96] conducted a meta-analysis of 172 studies of threat-related attentional biases in anxious and nonanxious individuals. Threat-related attentional biases were examined through paradigms such as the dot-probe and emotional Stroop tasks. The dot-probe task involves the simultaneous, brief presentation of a threat and a neutral word or image. The stimuli are subsequently removed with a dot probe replacing one of the stimuli. Participants are asked to determine the location of the dot probe as quickly as possible. In order to modify attentional focus, more dot probes are placed at the location of the desired bias (e.g., at the location of the non-threatening, neutral stimulus). In the emotional Stroop task, participants' response times are noted as they name the colors of neutral versus threat-related words or images[96, 4, 97]. Overall, Bar-Haim found an attention bias towards threat stimuli within anxious patients under different paradigms and across diverse populations (e.g., different anxiety disorders, ages) [96].

Other cognitive biases present in anxiety disorders include interpretation biases. Within anxiety disorders, there is a trend to interpret neutral environmental cues as negative[12]. A common paradigm used to assess interpretation biases in the study of anxiety disorders involves presenting the participant with an ambiguous situation and asking them to rank different interpretations of the ambiguous situation in order of most to least likely. Individuals with SAD tend to rate ambiguous social interactions as more negative than non-anxious individuals with several studies demonstrating a correlation between interpretation biases and social anxiety[98, 99]. Further, socially anxious individuals tend to perceive anxiety-relevant, negative explanations of ambiguous situations as highly likely relative to more neutral explanations[98, 100]. Similarly, individuals with GAD tend to interpret ambiguous sentences as threatening[101]. In a task involving selection of a meaning for homophones with neutral and threat meanings, GAD participants more frequently select the threatening interpretation[102]. Patients with PD also exhibit threat biases in response to

ambiguous information; this is commonly displayed as a tendency to interpret harmless bodily sensations as catastrophic[103].

Treatments for Cognitive Biases

CBM for individuals with anxiety disorders centers on adjusting the cognitive biases that lead to vulnerability for anxiety[12]. Much of the research on CBM in anxiety disorders has focused on both CBM-A and CBM-I treatment programs (for a review, see Beard[12]). CBM-I has demonstrated efficacy in reducing social anxiety, depression, and trait anxiety symptoms while also contributing to improved attentional control, attentional biases, and interpretation biases[104, 105, 66]. As described above, Hallion and Ruscio[66] suggest that CBM may be more beneficial for anxious individuals than for depressed individuals as their meta-analysis revealed that CBM significantly improved anxiety but not depression.

ABM in anxiety aims to reduce implicit attentional biases through computer-based cognitive training exercises[106]. ABM has demonstrated some efficacy in training attention within anxious populations. Amir et al.[107] provided support for ABM in SAD, finding that adults who received eight sessions of ABM over 4 weeks had significantly reduced social anxiety symptoms and demonstrated retention at 4-month follow-up. Further, at post-treatment, 50% of participants in the ABM group did not meet criteria for SAD. Heeren et al.[108] conducted a meta-analysis of ABM for SAD. They found that ABM led to a significant reduction in attentional bias to threat, emotion reactivity to a speech task, and SAD symptoms at post-training and at follow-up. ABM has also demonstrated efficacy in pediatric samples; Shechner et al.[109] found that children receiving ABM in conjunction with CBT demonstrated significant decreases in parent-rated and self-rated anxiety symptoms relative to those receiving a placebo ABM plus CBT treatment or CBT treatment alone. However, all randomized treatment groups demonstrated attentional shifts (e.g., moving away from threat-oriented attentional focus) over the course of the study. Similar findings were demonstrated by Eldar et al.[110] who found anxiety reductions in symptom number and severity among children randomly assigned to ABM treatment.

Other treatment approaches have focused on approach avoidance tasks (AAT), which are based on the notion that stimuli in the environment lead to an automatic response of approach or avoidance[111, 4]. In one study of AAT aimed to increase approach for positive cues, Taylor and Amir[111] had participants pull a joystick towards themselves (approach) or to the right (control) upon exposure to faces expressing positive or neutral emotions. Following training, participants engaged in a relationship-building task with a partner. Participants trained to approach stimuli demonstrated increased social approach behaviors during the social task and received more positive reactions from their partner than did control participants[111].

Conclusions

Overall, data from pilot and randomized trials of interventions aimed at improving cognitive impairments and biases suggest that such treatments can help improve psychosocial and cognitive functioning among patients with mood and anxiety disorders[26, 72, 73, 107, 90, 50, 48, 49]. Of note, direct comparisons of treatments for cognitive impairments or biases

versus CBT or other therapy-based treatments have produced diverse results in mood and anxiety disorders. Among studies examining treatments for cognitive impairments, one trial found greater, though non-significant, improvements in functioning among individuals receiving functional remediation compared to those receiving psychoeducation[26] while another found similar improvements in clinical symptoms among adolescents receiving CBT versus those receiving working memory training[90]. Studies of cognitive remediation in mood disorders have demonstrated improvements in occupational, psychosocial, and interpersonal functioning domains[51, 26, 50, 49]. Future studies of cognitive remediation in anxiety disorders should explore the effect of remediation treatments on daily functioning[90]. Given data suggesting the efficacy of cognitive remediation on improvements in clinical symptoms and functioning in mood disorders, future clinical trials should continue to explore cognitive remediation for all patients with mood and/or anxiety disorders, even for those not currently experiencing cognitive deficits. Indeed, Sari et al.[89] suggest that working memory training may not only improve cognitive deficits in anxiety disorders but also reduce an at-risk individual's vulnerability for developing an anxiety disorder.

For trials exploring treatments for cognitive biases, one study found no difference between CBM and CBT with both interventions significantly reducing clinical symptoms and improving attentional control[104]. Another study found CBT to be more effective in reducing anxiety and CBM to be more effective in improving automatic threat associations[112]. Given that individuals with an anxiety disorder may exhibit a bias towards or away from a threat-relevant stimulus, findings from a recent study of ABM in patients with spider fear lend support to the notion that bias modification treatments may be most effective if tailored to an individual patient's baseline bias orientation[113]. Interventions combining cognitive remediation or bias modification strategies with CBT may be most effective[92, 109, 67]. Thus, future clinical trials in mood and anxiety disorders should continue to explore cognitive strategies adjunctive to psychosocial treatments to enable optimal improvements in treatment outcomes.

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