Cognitive Behavioral Therapy for Anxiety Disorders in Youth: Efficacy, Moderators, and New Advances in Predicting Outcomes

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Abstract

Purpose of Review This review integrates recent systematic reviews and meta-analyses on the efficacy of cognitive behavioral therapy (CBT) for the treatment of anxiety disorders in children and adolescents. To inform personalized approaches to intervention, we also review recent research on moderators and predictors of outcomes.

Recent Findings Meta-analyses provide strong support for the efficacy of CBT for youth anxiety disorders, including with preschool-aged children using appropriate modifications. Furthermore, there is evidence that CBT is an effective adjunct treatment to psychopharmacological interventions, and the combination of treatments may be most effective for some youth. There is limited evidence of consistent demographic and clinical moderators of outcomes. Recent work in neuroscience has highlighted novel predictors of treatment outcomes that, with replication, may aid in more personalized approaches to youth anxiety treatment.

Summary CBT is efficacious for treating anxiety disorders in youth and lowering recurrence rates. CBT can also be an efficacious adjunct treatment for psychopharmacological interventions. Neuroimaging and psychophysiological measures of threat and motivational processing have shown initial promise in predicting symptom change with CBT, with potential implications for precision medicine.

Keywords Cognitive behavioral therapy · Anxiety disorders · Children · Adolescents · Efficacy · Neuroscience

Introduction

Anxiety disorders are mental health disorders characterized by marked fear or anxiety, avoidance of feared stimuli, and significant distress or impairment [1, 2]. Examples of anxiety disorders in youth include conditions such as separation anxiety disorder, panic disorder, agoraphobia, social anxiety disorder, specific phobia, and generalized anxiety disorder [1, 2]. Anxiety disorders tend to onset in childhood or adolescence, with separation anxiety emerging earliest in development and social anxiety disorder, panic disorder, and generalized anxiety disorder becoming more prevalent in late childhood and adolescence [3]. The lifetime prevalence of any anxiety disorder in children and adolescents is approximately 15–32% [3, 4], and these disorders are associated with a range of negative outcomes across development, including disruptions in daily life, academic and social functional impairment, and persistence of symptoms into adulthood [5].

Cognitive behavioral therapy (CBT) is considered a gold standard and efficacious treatment for anxiety disorders in youth and adults [6, 7, 8•]. CBT generally consists of 12 to 18 1-h sessions and focuses on identifying and changing problematic thinking and behavioral patterns that maintain the youth’s presenting symptomatology [9, 10]. CBT clinicians introduce and provide opportunities to practice skills in session and then assign homework for further refinement and generalization of these skills outside of session [10]. Cognitive skills help anxious youth develop awareness of maladaptive thought patterns maintaining anxiety and, in some cases, change them to more realistic or helpful alternative thoughts [9, 10]. Behaviorally, CBT for anxiety usually
Involves repeated, gradual exposure to feared stimuli to reduce avoidance and promote new learning [9, 10].

In the present article, we briefly review recent meta-analytic work examining the efficacy of CBT for anxiety disorders in children and adolescents. Importantly, not all youth respond to CBT despite the intervention’s efficacy [6, 7, 8•, 11]. Accordingly, understanding of moderators and predictors of individual differences in treatment outcomes is needed to personalize treatment and improve outcomes. We first summarize research on clinical characteristics, such as primary diagnosis and symptom severity, and demographic moderators of CBT outcomes, followed by a review of new advances in neural predictors of treatment outcomes. We highlight recent work using neuroscience methods to predict CBT response to potentially improve prediction of outcomes and ultimately inform more personalized approaches to intervention.

**Efficacy of CBT for Anxiety Disorders in Children and Adolescents**

Decades of research supports CBT as an efficacious intervention for treating internalizing disorders in children and adolescents. For example, one recent meta-analysis of 76 studies and 106 CBT treatment groups examining outcomes in the treatment of anxiety, depression, posttraumatic stress disorder, and obsessive–compulsive disorder in youth found that 77.1% of participants at posttreatment and 81.9% at follow-up (ranging from 1 to 89 months) showed significant improvements in target symptom measures compared to pretreatment (considerable heterogeneity between studies; \( I^2 = 80.8–83.8\% \)) [12]. Another study conducted several meta-analyses to examine the effects of CBT for youth anxiety disorders [13]. An analysis of 39 studies (\( N = 2697 \)) that examined remission of a primary anxiety disorder diagnosis at posttreatment found that youth in CBT had a remission rate of 49.4% compared to 17.8% for those in waitlist or no treatment conditions (moderate heterogeneity; \( I^2 = 52\% \)) [13]. Additionally, an analysis of the 28 studies (\( N = 2075 \)) that examined remission of all anxiety disorder diagnoses at posttreatment found that youth in CBT had a remission rate of 46.8% compared to 19.1% for those in waitlist or no treatment conditions (moderate heterogeneity; \( I^2 = 60\% \)) [13].

CBT is efficacious for anxiety beginning even in early childhood using appropriate modifications. A meta-analysis of 41 studies of children aged 3 to 8 years old (\( N = 1965 \)) found that anxiety symptoms significantly decreased from pre- to posttreatment with CBT (SMD = −1.34; moderate heterogeneity, \( \tau^2 = 0.37 \)) [8•] . Anxiety symptoms also decreased when comparing pretreatment to follow-up in 19 studies (\( N = 1423 \)), regardless of length of follow-up (SMD = −1.40; moderate heterogeneity, \( \tau^2 = 0.35 \)) [8•].

In addition to reducing current symptoms in youth, CBT appears to be associated with relatively low relapse rates for youth anxiety disorders. For example, a recent meta-analysis (total \( N = 535 \)) indicated that approximately 8% of youth treated with CBT for anxiety experienced a recurrence at follow-up (average follow-up period being 11.06 months) posttreatment, ranging from 1 to 60 months; 2 studies of youth with autism spectrum disorder not included in this analysis; considerable heterogeneity, \( I^2 = 81.6\% \)) [14•]. Of note, relapse rates were not related to duration of follow-up or to the presence of a comorbid attention-deficit hyperactivity disorder or depressive disorder diagnosis [14•].

Traditional in-person delivery of CBT may not always be available to youth in need of evidence-based services. For example, the COVID-19 pandemic limited access to in-person care, increasing demand for telehealth CBT services. Outside of the context of the pandemic, many youth live in areas with limited access to providers trained in CBT. Fortunately, there is evidence to support the efficacy of technology-delivered CBT when traditional in-person CBT may not be available [6, 15]. For example, a recent meta-analysis of 711 participants found that, compared to control conditions (i.e., treatment as usual, waitlist, or psychological placebo), youth in technology-delivered CBT had higher remission rates for their primary anxiety disorder diagnosis (37.9% versus 10.2%; \( OR = 4.73; k = 9 \); no significant heterogeneity, \( I^2 = 0\)%) and all anxiety disorder diagnoses (19.5% versus 5.3%; \( OR = 3.32; k = 8 \); no significant heterogeneity, \( I^2 = 0\)%) at posttreatment [15]. Another meta-analysis found that technology-delivered CBT performed similarly to active treatment control (i.e., in-person CBT or treatment as usual; \( g = 0.04; N = 203 \); no significant heterogeneity, \( I^2 = 0\)%) and outperformed passive control conditions (i.e., waitlist/no treatment, or information only; trim and fill adjusted \( g = 0.44 \); unadjusted \( N = 822 \); moderate unadjusted heterogeneity, \( I^2 = 52.6\% \)) in reducing anxiety symptoms for adolescent and young adult participants (aged 12–25 years) at posttreatment [6]. There was also no significant difference between technology-delivered CBT and active treatment controls at long-term follow-up (ranging from 6 to 12 months posttreatment) in the 2 included studies on anxiety (\( g = 0.08; N = 140 \); moderate heterogeneity, \( I^2 = 50.6\% \)) [6]. However, for younger participants (i.e., between 3 and 8 years old), in-person individual (SMD = −0.85) and group (SMD = −0.89) delivery of CBT had stronger effects on symptom reduction compared to internet-delivered CBT (SMD = −0.45) [8•]. Given the variety of the ways in which CBT can be delivered via technology (e.g., telehealth with an individual provider, telehealth with a group), research is needed on moderators of technology-delivered CBT and predictors of outcomes to enhance treatment for youth with limited access to in-person CBT, particularly for younger children with anxiety disorders.
Efficacy of Combination Treatment

Selective serotonin reuptake inhibitors (SSRIs) are an efficacious and commonly used psychopharmacological intervention for treating pediatric anxiety disorders [16–18]. Compared to placebo, meta-analyses have found that SSRIs alone are more effective at reducing anxiety symptoms (Log OR = 1.57, N = 734, acceptable heterogeneity, Cochran’s Q = 10.56, p = 0.06 [7]; SMD = −0.65 to −0.61, N = 96–675, moderate to substantial heterogeneity, I² = 55.1–73.4% [19]) and enhancing treatment response (relative risk = 1.96; N = 396; I² = 0%) and remission (relative risk = 2.04; N = 95) [19]. Importantly, the combination of SSRI and CBT may be associated with greater improvement beyond either SSRI or CBT treatment alone [20••, 21, 22]. One of the largest randomized clinical trials compared treatment outcomes for 488 youth with a primary diagnosis of separation anxiety disorder, generalized anxiety disorder, or social phobia [22]. Youth were assigned to the SSRI sertraline, CBT, combination SSRI and CBT, or placebo. The study found that 80.7% of youth in combined treatment showed significant improvement by week 12 as measured by the Clinical Global Improvement-Improvement scale [23] compared to 59.7% in CBT alone, 54.9% in SSRI alone, and 23.7% in the placebo condition [22]. Additionally, meta-analyses found that combination SSRI and CBT treatment significantly reduced anxiety symptoms (SMD = −0.69 to −0.46) and increased treatment response (relative risk = 1.35–1.47) and remission (relative risk = 1.51) compared to SSRI (N = 273) or CBT treatment (N = 279) alone [19]. Despite the benefits of SSRIs, it is worth noting that some patients may not tolerate SSRIs well, and CBT may be particularly well-suited for these youth. A recent meta-analysis of 18 studies (N = 2631) found that SSRIs for anxiety in youth were compared to placebo (no significant heterogeneity, I² = 0%) [24].

Predictors and Moderators of Treatment Outcomes

Despite the efficacy of CBT, questions remain about why it is less effective for some youth than others. Research on factors that moderate treatment outcomes or predict who is most likely to respond is critical to matching children and adolescents to treatments or combinations of treatments that will meet their needs. Despite a relatively large literature in this area, however, few consistent moderators have emerged. For example, little evidence suggests that age or gender moderates the effects of treatment on anxiety outcomes. A recent meta-analysis (N = 766) compared CBT and non-CBT psychological therapies to active and passive controls and found that age and gender were not significant moderators of treatment effects on anxiety symptom severity in adolescents [25]. Another meta-analysis (N = 535) found that relapse rates were higher among younger samples, but gender did not differentially predict relapse rates in youth [14•]. Research examining relapse rates based on race and ethnicity is more mixed; one meta-analysis found a positive association between percent of racial/ethnic minority participants in a sample and relapse rates [14•], while another did not find evidence that ethnicity moderated treatment outcome [25].

Although various clinical characteristics can inform case conceptualization, it remains unclear if they are robustly linked with treatment outcome. For example, recent meta-analyses have found limited evidence that primary diagnosis moderates the effect of treatment on symptoms measured at posttreatment [25] or at the first follow-up (average follow-up period being 11.06 months posttreatment) [14•]. However, children and adolescents with a primary diagnosis of social anxiety disorder were significantly less likely to recover following CBT (35% recovery rate) compared to those with any other primary anxiety disorder diagnosis (54% recovery rate) (N = 635; no significant heterogeneity, I² = 0%) [26]. Another meta-analysis (N = 1169) found that youth with higher pretreatment symptoms were less likely to have a positive CBT outcome, indicated by a lower probability of response, remission, and/or a high symptom rating (substantial heterogeneity, I² = 62%) [27]. Although some studies have found effects of comorbid depression on poorer outcomes in youth [28], two meta-analyses failed to find significant effects in predicting treatment outcomes (N = 680; considerable heterogeneity, I² = 81%) [27] or relapse [14•]. Variability in participant age may impact results, as depression is less common in younger children compared to adolescents [29]. It is also possible that depressive symptoms assessed dimensionally may be more consistently linked to poorer treatment outcomes compared to the presence or absence of a depressive disorder diagnosis [28]. There is more consistent meta-analytic evidence of higher relapse rates among anxious youth with comorbid oppositional defiant or conduct disorder [14•]. Although systematic reviews have found mixed evidence regarding the effects of parental psychopathology on treatment outcomes for anxious youth [30, 31], a meta-analysis (N = 1188) found parent psychopathology predicted worse CBT outcomes in youth with anxiety disorders (substantial heterogeneity, I² = 53%) [27].

In terms of treatment characteristics, parent involvement in treatment has been theorized to improve outcomes, but there is more limited evidence in support of this. In one meta-analysis comparing CBT to other psychotherapies for adolescents, parent involvement was not a significant moderator.
The dose and focus of parent involvement may need to be more directly targeted. A meta-analysis [9] found that parent involvement (separate and together) was significantly associated with smaller pre- to posttreatment effect sizes, but only using child report [9]. There are several possible reasons for these mixed findings. First, there is considerable variability in the amount and type of parent involvement [9], which may make it difficult to assess specific aspects of having family in treatment that enhance outcomes for youth. Older participants may not need as much parent involvement in treatment as younger children, which could explain why a meta-analysis with adolescents did not find parent involvement to be a significant moderator of outcomes [25]. Additionally, CBT with parent involvement may offer fewer opportunities for in-session exposures and thus may be associated with smaller effects at posttreatment for some youth, as found in one meta-analysis [9]. This suggests that having parents involved may take time away from other aspects of treatment that more directly target anxiety symptoms, like exposures [9]. The dose and focus of parent involvement may need to be informed by individualized functional analysis, as some youth may find more benefit to having family involved in their treatment than others.

Finally, treatment modality (i.e., individual, group, family) has also been examined as a possible moderator of treatment outcomes for youth with limited evidence of differences across modalities. In a meta-analysis (N = 3386) exploring the effectiveness of different CBT modalities for anxious children and adolescents, individual CBT did not show a significant advantage over family CBT (k = 5; moderate heterogeneity, $I^2 = 49\%$) or group CBT (k = 4; moderate heterogeneity, $I^2 = 39\%$) in terms of remission [33]. Furthermore, recent meta-analyses with anxious youth did not find treatment modality to be a significant moderator of posttreatment outcome [25] or relapse rate at first follow-up [14•].

Neural Predictors of Treatment Outcomes

The investigation of neural predictors of response to treatment for internalizing disorders has been a burgeoning area of research over the past decade, with aims to identify who is most likely to benefit from a particular treatment, elucidate novel treatment targets, and ultimately inform personalized approaches to treatment. In terms of neural methods, electroencephalogram (EEG), event-related potentials (ERPs), and structural and functional magnetic resonance imaging (MRI/fMRI) each have complementing strengths as tools to work toward these aims. EEG/ERP is a non-invasive technique that records electrical neural activity at the scalp with millisecond temporal precision and greater feasibility in clinical translation due to reduced costs in comparison to other neural measures. In contrast, MRI/fMRI is used to examine brain structure and function via magnetic fields and radiofrequencies to capture changes associated with blood flow with excellent spatial resolution. Together, EEG/ERP and MRI/fMRI are complementary in providing objective assessments and offering additional explanatory power in conjunction with other more traditional clinical measures.

To date, most research using neuroscience methods to delineate the etiology of anxiety and identify intervention targets has focused on neural responses to threat. Circuits of interest include the amygdala and regions of the prefrontal cortex (PFC) and anterior cingulate cortex (ACC), which play regulatory roles in fear responses, attention, and action monitoring, respectively. A recent systematic review of 21 studies on neural indicators of CBT response in youth identified the amygdala, PFC, and ACC as brain regions key to predicting treatment outcomes in youth with internalizing disorders [34••]. Specifically, greater activation of the dorsolateral and ventrolateral PFC regions during threat processing tasks was associated with greater reductions in anxiety severity with treatment. Greater activation of the dorsolateral PFC and ventrolateral PFC, regions involved in appraising and regulating responses to threatening stimuli, potentially supports youth in successfully engaging in exposure treatments and leading to enhanced therapeutic outcomes. In addition, hyperactivation of the amygdala in response to threatening cues, reflecting greater threat reactivity, was associated with greater post-CBT-treatment improvement. On the other hand, lower activation of dorsal ACC and dorsomedial PFC, potentially reflecting difficulties with attentional control, during implicit threat processing has been linked with greater and earlier anxiety symptom reduction [35]. Together, this literature indicates that alterations in the amygdala, dorsal ACC, and dorsomedial PFC function may be indicators of more room for improvement at pretreatment and greater opportunity for treatment gains.

Expanding beyond a focus on threat processing, recent research has begun to examine motivational processes at the neural level in relation to treatment outcomes. In a recent investigation, greater reward responsiveness, as indicated by striatal activation assessed pretreatment, differentiated youth with anxiety disorders who responded to CBT (i.e., > 35\% symptom reduction) versus youth who did not [36]. Greater striatum response to reward anticipation has also been associated with greater reduction in anxiety symptoms in youth undergoing multiple forms of treatment for depression and comorbid anxiety [37]. However, these findings are mixed such that blunted reactivity to reward receipt measured by EEG has been associated with greater response to treatment,
particularly in predicting depression symptom reduction in youth with anxiety disorders [38]. These findings are similar to observations in adults with anxiety and depression [39] and conceptualized to suggest that initial dampened reward response may signify greater room for improvement across treatment. Taken together, the literature suggests that striatal activation to reward anticipation may be particularly important for supporting treatment engagement for youth with anxiety. Moreover, blunted responsiveness to reward receipt may be an indicator of potential to benefit from CBT (via reduction in depression symptoms) for youth with comorbid depression and anxiety. Replication of this research is needed to better understand its potential application and clinical impact in improving CBT outcomes for youth.

To date, neural predictors of CBT response identified in youth are largely similar to those that have been observed in adults. In a meta-analysis ($N=442$) of the literature on neural indicators of CBT treatment response in adults, the same brain regions as the systemic review in youth were identified (i.e., the PFC and ACC, along with the anterior insular cortex; no significant heterogeneity, $I^2=0.56–0.83$) [40]. Notably, although there is region overlap across populations, the direction of associations from pretreatment neural indicators to posttreatment outcomes may diverge for adults and youth. For example, a meta-analysis on CBT outcomes for adults concluded that hyperactivation in the ACC was associated with better treatment response, whereas a systematic review on CBT outcomes for youth suggested that ACC hypoactivation was associated with better treatment response [34••, 40]. These discrepancies may be due in part to differences in brain maturation because of protracted development of frontal regions including the ACC [41].

Future research will need to determine the clinical utility of these neuroscience methods so they can be effectively used to complement clinical assessment and treatment planning using personalized approaches. This will require replication of existing research examining neural predictors of treatment response so more definitive inferences can be made. Similarly, there is a need to establish normative values for neural measures of interest, similar to clinical assessments. Clinical practitioners utilizing these methods need to be able to consistently obtain clean data with known psychometric properties so that normative and cutoff values can be used to inform treatment planning. This work has begun in EEG/ERP and MRI/fMRI research with adults (e.g., [42]) but is in early stages. Advanced statistical approaches are also needed to foster measure refinement and translation to clinical applications. Specifically, machine learning approaches hold promise for detecting and aggregating features of brain function that optimally predict treatment response, and ultimately, predicting the likelihood of response to different types of treatment [43–45]. Indeed, an essential future direction of examining neural predictors of treatment outcome is going beyond prognostic prediction to also examine prescriptive prediction. These future directions have potential implications for the field’s ability to move beyond simply identifying youth who are more or less likely to benefit from a given treatment to instead identify the treatment approaches that are most likely to result in the greatest and most efficient symptom reduction for a particular patient.

Conclusions

Recent meta-analyses have continued to demonstrate the efficacy of CBT for treating anxiety disorders in children and adolescents, with evidence of moderate to large effects on symptoms [6, 7, 8•, 12, 13] for children even as young as preschool age [8•]. Furthermore, CBT is efficacious as an adjunct treatment to psychopharmacological intervention [19, 20••, 21, 22]. Yet, as with most forms of intervention, there is considerable individual variability in outcomes [6, 7, 8•, 11], and few consistent moderators and predictors have emerged in the clinical literature [14•, 25, 27, 28, 32, 33]. This hinders progress in terms of identifying which interventions work best for whom and optimizing intervention outcomes. Recent research has leveraged neuroscience methods including EEG and fMRI to elucidate novel, neural predictors of CBT outcomes for youth with anxiety disorders, with some consistent patterns emerging in brain regions involved in threat and motivational processing [34••, 36]. Despite the promise of these early findings, there is still much work to be done to bridge the gap between clinical neuroscience and clinical practice and determine the extent to which these methodologies can be applied to inform more personalized approaches to youth anxiety treatment.

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Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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