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Anxiety in youth with autism spectrum disorders: implications for treatment

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SUMMARY

Anxiety disorders are one of the most common psychiatric comorbidities among children and adolescents with autism spectrum disorders (ASD). There has been a recent proliferation of research examining the prevalence, phenomenology, assessment and treatment of anxiety disorders among youth with ASD. While there is currently very limited support for the use of pharmacological agents to treat anxiety among youth with ASD and comorbid anxiety, there has been overwhelming support across numerous modestly sized controlled studies for the efficacy of cognitive behavioral therapy. This review discusses advances in the treatment literature for anxiety in youth with ASD, and discusses the current evidence base for whether standard treatment needs to be adapted for this population.

Keywords

Anxiety; Autism; Autism Spectrum Disorder; Child; Adolescent; Pediatric; Treatment; CBT; Pharmacological treatment

Recent epidemiological data suggests that Autism Spectrum Disorders (ASD) affect up to 1 in every 68 children in the United States [¹]. Although prevalence rates range from 22-84% [²⁻⁵], meta-analytic studies have suggested that approximately 40% of youth with ASD experience a comorbid anxiety disorder [⁶], making it one of the most common co-occurring psychiatric conditions [⁴]. The literature on the prevalence, phenomenology, assessment and treatment of anxiety disorders in youth with ASD has grown exponentially over the past

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decade. This review aims to highlight some of the more recent and significant advances in the treatment of anxiety disorders in children and adolescents with ASD, and to highlight important areas for future investigation.

Autism Spectrum Disorders

The diagnosis of ASD is characterized by persistent deficits in social communication and social interactions (including socio-emotional reciprocity and nonverbal communication). Individuals with ASD also present with restricted and repetitive patterns of behavior, interests and activities, including stereotyped motor movements (e.g., hand flapping), speech (echolalia) and use of objects (e.g., lining up toys) [7]. Youth with ASD often demonstrate rigid and inflexible insistence on routines and sameness, ritualized patterns of behavior with restricted or fixated interests, as well as sensory hyper- or hypo-reactivity (e.g., indifference to temperature, excessive touching/smelling, intense aversive reaction to sounds or certain textures). With the transition to use of the 5th version of the Diagnostic and Statistical Manual [DSM-5; 7] in 2013, there have been some adjustments to the conceptualization and diagnosis of ASD. The one overarching diagnosis of ASD now encompasses the previous DSM-IV diagnoses of Autistic Disorder, Asperger's Disorder and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS), eliminating the categorical classification of ASDs and adding a severity specifier ranging from Level 1 ('Requiring support') to Level 3 ('Requiring very substantial support'). Youth who present with social communication deficits, but do not meet ASD criteria are usually evaluated for the new diagnosis of Social (Pragmatic) Communication Disorder [7].

Anxiety in Youth with Autism Spectrum Disorders

Anxiety is a common comorbidity among youth with ASD [4,6], adding to the overall level of burden experienced by the child and their family [8-10]. Most studies suggest equivalent or slightly milder severity of anxiety symptoms in youth with ASD in comparison to typically developing youth with anxiety [11-13]. While some anxiety presentations in the population more closely resemble anxiety diagnoses seen in neurotypical children and adolescents, in many cases, there can be considerable overlap between anxiety and ASD symptoms, and differential diagnosis in the context of symptom cross-over and heterogeneous presentations can be difficult [2,14,15]. The general consensus is that anxiety is not necessarily a core feature of ASD given that not all youth with ASD present with this symptom, and that anxiety responds better to treatment than core ASD deficits, however the co-occurrence of anxiety symptoms are common in this population [15]. Woodand Gadow [14] have proposed that in many cases, atypical or 'unique' variants of anxiety may exist in children and adolescents with ASD, encompassing the phenomenology of overlapping symptoms of anxiety related to ASD symptoms. We will discuss the common presentations of anxiety in children and adolescents with ASD, both in reference to disorder-based anxiety, and atypical anxiety.

Youth with ASD experience a range of different anxiety disorders, the most common being specific phobias, social anxiety disorder, Generalized Anxiety Disorder and obsessive compulsive disorder (OCD) [6]. Specific Phobias are by far the most frequent anxiety

disorder noted among youth with ASD [4,6]. Typical fears include fears of the dark, insects, and of needles and injections and in most cases the phenomenology is not dissimilar to typically developing youth.

Social anxiety is particularly interesting in youth with ASD from a phenomenological perspective. Despite objective deficits in social functioning, youth with ASD (particularly those who are older and higher functioning) often experience elevated levels of social anxiety [16,17]. Developmental models [17] have suggested that individuals with ASD have a range of risk factors that increase their propensity to experience social anxiety. Youth with ASD experience elevated physiological arousal that may increase their potential to become overwhelmed by social interactions, resulting in subsequent withdrawal behaviors that restrict the opportunity and potential for development of age-appropriate social skills. These social skill deficits further perpetuate the risk for negative social interactions with peers, in turn, exacerbating further physiological arousal. Notably, diagnosis of social anxiety in youth with ASD requires that the young person does not avoid social interactions because of a lack of interest (a feature common in youth with ASD), but because of high levels of fear about the potential negative outcomes that may arise from engaging in the social interaction. Interesting, in many cases, fear of negative evaluation is not an unrealistic concern given that youth with ASD often lack the complex social skills necessary for successful social engagement, especially during adolescence. Particularly among older children and adolescents who are a high functioning, social anxiety may be the result of improving insight about their social differences in comparison to peers [16,18].

The phenomenology of co-occurring OCD and ASD in youth remains understudied, however there are key areas of overlap between ASD and OCD symptomatology. Differentiating whether these symptoms are OCD-related, ASD-related, or the result of their co-occurrence can be challenging. For example, one study [19] found high levels of ritualistic behavior in youth with ASD (73%), however only 11% demonstrated distress related to their rituals. Complicating this clinical picture further, not all youth with OCD experience distress related to compulsions, particularly when they serve to neutralize or reduce distress, despite the objective interference and impairment that they cause. Youth with ASD and OCD experience similar levels of symptom severity as typically developing youth with OCD [20]. While some dimensional and subtyping studies have suggested that youth with ASD and OCD experience higher levels of hoarding obsessions, and compulsive ordering, hoarding and repetition than neurotypical youth with OCD [21], others studies have found few phenomenological differences [20]. These inconsistent findings are likely to reflect the difficulties inherent in distinguishing repetitive behaviors from compulsions, and fixated or restricted interests from obsessions in this population.

Interestingly, youth with ASD often experience atypical symptoms of anxiety that do not necessarily fit within a specific diagnostic category, and in many cases have some level of overlap with their ASD symptoms. For example, youth with ASD often experience intense levels of anxiety and distress related to changes in their routine or environment [8,22]. Similarly, youth may become anxious and agitated when there are barriers or obstacles that prevent them from engaging in a stereotyped behavior or compulsion [14]. It is also common for children with ASD to experience sensory hyper-responsivity, and become particularly

anxious in response to normal levels of sensory input [23]. For example, youth with ASD are often anxious about eating certain foods due to textural issues and some may even report being fearful of vomiting as a result [24,25]. Other common examples of anxiety related to sensory issues includes being fearful of loud noises (e.g., the vacuum, hand dryers) or particular clothing (e.g., requiring clothes to be 'too tight', sock to be pulled up, sensitivity to tags, or requiring clothing to be made of particular materials or colors). In some cases these symptoms of anxiety may be accounted for by a co-occurring anxiety disorder (e.g., specific phobia) if other criteria are also met, but in many cases, they tend to represent an atypical or 'not otherwise specified' presentation of anxiety.

Pharmacological Treatment for Anxiety in Children and Adolescents with ASD

Although pharmacological treatment using selective serotonin reuptake inhibitors (SSRIs) are an effective treatment for anxiety in neurotypical youth [26,27], research examining their use in children and adolescents on the autism spectrum is limited, and includes heterogeneous samples of youth and poor study methodology (e.g., non-randomized and uncontrolled open trials, retrospective chart reviews, unclear symptom level targets) [28]. Overall, there is little to no support for using pharmacological agents for treatment of anxiety in youth with ASD, with limited efficacy and high rates of negative side effects. Some small-scale studies have suggested modest efficacy for citalopram to reduce anxiety symptoms [29,30], although a large controlled trial of citalopram failed to find reductions in repetitive behaviors [31]. A study by Martin, Koenig, Anderson and Scahill [32] found no improvement in anxiety symptoms using fluvoxamine, although a study of fluoxetine found some improvement in repetitive behaviors [33]. A 2010 Cochrane review concluded that there was no current evidence in support of the use of SSRIs in youth with ASD, and worse, that there was emerging evidence of harm [34] with high rates of adverse side effects from SSRI use, including behavioral activation, insomnia and akathisia [30,32]. Buspirone, an anxiolytic medication, has shown preliminary efficacy and low rates of side effects in a case study [35] and small open-label trial [36], with another small open-label trial currently under investigation [37]. Unfortunately, trials have included anxiety, irritability, aggression and hyperactivity as treatment targets, limiting any strong conclusions about the potential of this medication for treatment of anxiety in ASD. Given the lack of efficacy, and high rates of negative side-effects, pharmacological treatment of anxiety in youth with ASD is not recommended as a first-line intervention.

Cognitive Behavior Therapy for Anxiety in Youth with ASD

As with typically developing children [38], cognitive behavioral therapy (CBT) has demonstrated robust efficacy for treating anxiety disorders in youth with ASD [39-43], although the effect size varies considerably between studies. To date, there have been 14 randomized controlled trials that have examined the efficacy of CBT for anxiety in youth with ASD [39], and more than 41 studies examining CBT for anxiety in ASD when including studies that utilized other methodologies (e.g., open trials) [44]. The results of two recent meta-analytic studies as well as a Cochrane review have suggested moderate effect

sizes for CBT treatment of anxiety in youth with ASD in comparison to no-treatment or active control conditions, although they note considerable heterogeneity in the studies and outcomes [39,44,45]. For example, some studies note large effect sizes [46-48] while others note medium [49-51] or small [52-54] effect sizes, and one small open trial even noted an increase in parent-rated (but not clinician-rated) anxiety over the course of treatment [55]. Of note, one study of group CBT treatment for anxiety in youth with high functioning autism had stronger effect sizes for CBT than most other studies [46], and when this study was removed in the meta-analysis, CBT showed a small to moderate effect [39]. Although one of the most recent meta-analysis did not find a difference in treatment effects based on child, parent or clinician reporting [39], the 2015 meta-analyses by Kreslins, Robertson [40], as well as other studies, have consistently found that children with ASD tend to report less severe anxiety symptoms, smaller treatment effects, and provide ratings that do not correspond to parent and clinician ratings [56], suggesting that children with ASD may not be the most reliable informants when assessing symptoms. This may be the result of impaired insight, emotional awareness and recognition, but is also somewhat consistent with findings in typically developing youth with anxiety, where preference is often given to parental and clinician reports of child functioning [57,58].

CBT appears to be effective regardless of whether the treatment is delivered in a group or individual format [39]. Group formats have demonstrated large effect sizes [39] and may have the added benefit of normalizing anxiety symptoms in the presence of other affected children and providing socialization and supportive peer interaction opportunities. However individual formats demonstrated similar efficacy, and may have the advantage for some children of a more flexible implementation than group settings allow, and can be tailored to the unique needs and interests of the child [39].

Unfortunately, most CBT trials have been conducted with moderate to high functioning youth with ASD, who have adequate verbal skills. While results are overwhelmingly promising in this population, it is unclear whether CBT is appropriate for lower functioning youth, those with moderate to low intellectual functioning, youth with minimal verbal skills, and those with aggressive and/or self-injurious behaviors. It is likely that amongst these groups of children, parental involvement would need to be much higher, and the use of more parent-management strategies (versus self-regulation and self-directed coping strategies) would be required.

Treatment Considerations and Modifications for Youth with ASD

Existing studies of CBT for anxiety in children and adolescents with ASD vary considerably in their format (e.g., group vs. individual treatment) and duration (6-32 sessions ranging from 60-120 minutes), although most tend to incorporate similar core treatment skills [39]. Similar to treatment of anxiety in neurotypical youth, in most cases the core treatment components of CBT for anxiety involves psychoeducation about the nature of anxiety (i.e., normalize the experience of anxiety, differentiate helpful vs. unhelpful anxiety, identify cognitive behavioral and physiological components of anxiety), cognitive therapy strategies (e.g., learning to identify and challenge unhelpful anxious cognitions), and behavioral strategies (e.g., graded exposure to feared situations utilizing a fear hierarchy, exposure and

response prevention strategies, and behavioral experiments to test catastrophic and anxious predictions), as well as psychoeducation and/or intervention with parents (e.g., reducing family accommodation of anxiety, building helpful parenting responses to anxious and anxious-oppositional behaviors). Lickel, MacLean, Blakeley-Smith and Hepburn [59] found that youth with ASD were able to competently perform some of the prerequisite skills for CBT, including discriminating between thoughts, feelings and behaviors, and were able to shift maladaptive cognitions, however they did show difficulty with emotional recognition skills, consistent with one of the core deficits of ASD.

While many treatment skills are similar to those used with typically developing youth, there are differing opinions about whether CBT needs to be adapted for implementation with anxious children with ASD [60]. Some studies demonstrated efficacy for treatment of anxiety in youth with ASD using standard anxiety CBT treatment protocols designed for typically developing youth, including Coping Cat [51,61] and Cool Kids [46,62]. Others have utilized ASD-specific treatment protocols such as the Multimodal Anxiety and Social Skills Intervention [MASSI; 63], Face Your Fears [64] or the Behavioral Interventions for Anxiety in Children with Autism [BIACA; 65]. Interestingly, a multi-site randomized controlled trial is currently underway examining differences between standard and ASD-specific treatment protocols for anxiety in children and adolescents in ASD and should provide important results for clinical decision making in the future [66].

Regardless of whether clinicians are utilizing a standardized CBT treatment, or an adapted treatment, there are some key clinical issues that often warrant attention when working with youth on the spectrum. Several recommendations have been made for adapting CBT, either within the scope of normal flexible and personalized delivery models, or adaptations and augmentations to standard CBT. Any treatment implemented with children will require some level of personalization and adaptation to suit the clinical presentation, developmental capacity and interests of the child in order to aid understanding, engagement and compliance. In the case of ASD however, clinicians may need to make more significant adaptations or augmentations to build on the child's strengths and/or compensate for ASD-related deficits. In cases of lower functioning children, clinicians may also need to incorporate additional treatment targets to address ASD symptoms that are likely to influence the child's treatment response and/or ongoing functioning. For example, many youth with ASD have difficulties with verbal skills and abstract thinking, skills which are often utilized within CBT for typically developing skills. As such, repetition of ideas within therapy, and well as the incorporation of more concrete examples and visual prompts (e.g., pictures, drawings, toys, puppets) such as written worksheets, emphasis on pictures and drawing are important [46,67-72]. Where possible, use of the child's 'special interests' can be especially advantageous given that it is usually highly engaging, accessible and salient for the child [68,69]. For example, a commonly used adaption to address impaired emotional recognition and verbal communication in ASD is to use the child's special interest and/or visual prompts, such as salient characters in a movie/game, to illustrate different severity levels of emotions (e.g., 'really mad like a creeper in Minecraft') rather than typical verbal likert scales. Special interests can also be used to explain therapeutic concepts in engaging and accessible ways for children (e.g., cognitive therapy involves 'collecting clues like Harry Potter to see whether anything bad is likely to happen'). Incorporating special interests is

highly reinforcing for the child, and may help to facilitate the child's engagement and enthusiasm to participate in treatment. Use of special interests may also facilitate therapist use of concrete and accessible metaphors for the child. Therapists will vary in their use of special interests to explain therapeutic content, use of special interests to reinforce therapeutic participation (e.g., as a reward for completing therapy activities), or to build therapeutic rapport and alliance. Regardless, flexible implementation of therapy in a way that engages the child, while also retaining treatment fidelity, is critical to successful treatment and therapy retention [73-75].

In addition to utilizing the child's strengths and special interests within treatment, in many cases, CBT for anxiety will require incorporating some level of focus on social skills deficits. Social skills deficits are one of the core features of anxiety in youth with ASD, and it has been often proposed that social skills deficits may compound the child's anxiety [17,63], especially in the context of recurring experiences of inappropriate or poor social skills resulting in failed attempts at engaging with others, or being met with negative reactions. Many of the key differences between use of standardized CBT and ASD-specific treatment protocols are in the addition of overt social skills training treatment components in the latter, rather than more subtle incorporation of social skills training within normal exposure therapy practice tasks. In many cases, the level of focus on social skills deficits depends on the baseline level of social skills that the child presents with. For example, anxious children, and children with ASD, often find it difficult to make eye contact. Regardless of whether poor eye contact is the result of social skills deficits, anxiety-related avoidance, or a combination of the two, the therapist will instruct the child to gradually increase their level of eye contact during social anxiety exposure tasks. Within this framework, hierarchies should be constructed to address both the core anxiety-related tasks, but to also encompass ASD-specific problems as well [52,69]. Within ASD-specific protocols for anxiety, there is often an overt focus on the addition of social skills training both in terms of didactic instruction about social 'rules' to help guide child behavior, as well as in vivo practice of social skills. This can include providing rules or structure about how to be a good host when a friend comes over (e.g., let the friend choose the game), or in vivo practice of reciprocity skills (e.g., learning how to ask questions and follow-up questions about something of interest to the other child) to facilitate social relationships. However, despite the widespread use of social skills training for youth with ASD, there is minimal empirical support for its efficacy [76], and dismantling studies and studies directly comparing standard and ASD-specific CBT are needed to assess the clinical utility of directly and independently addressing social skills training within an anxiety-based intervention.

Youth with ASD frequently show deficits in daily living skills, including personal skills (dressing, bathing), and functional skills at home (cleaning, putting things away) [77-81], skills that are important for prognosis into adulthood [82,83]. Some CBT protocols for youth with ASD will include direct intervention to address deficits in independent daily living skills [e.g., 65], and have shown positive outcomes for both anxiety and children's adaptive functioning, personal daily living skills and private daily routines (e.g., independent bathing) [84].

The role of parents within treatment for anxiety in youth with ASD can vary. Meta-analytic results for typically developing youth do not suggest notable differences between child-focused and family-focused treatment outcomes [85,86], and this is confounded by considerable heterogeneity in the type of parental involvement between studies ranging from reviewing child session content to active parent training in contingency management and parental anxiety management techniques. However, there is some evidence that child age and developmental capacity moderates this effect, with parental involvement superior for younger (but not older) children [87]. This is likely to generalize to youth with ASD, where increased levels of parental involvement in treatment may be indicated, especially in youth who have higher levels of dependence on parents and have poorer functional and daily living skills [60]. In a study of CBT for anxiety in children with Asperger's Disorder, youth who had their parents involved in treatment showed greater improvement than youth who did not have a parent involved [52]. Parental involvement in therapy may also be particularly relevant given the higher levels of critical and overinvolved parenting styles common amongst parents of youth with ASD [60,88]. In treatments for anxiety in youth with ASD, parents are often treated as co-therapist and are tasked with assisting their child to learn and implement treatment techniques outside of session to enhance skill generalization. In addition, maladaptive parenting practices resulting from the child's anxiety, ASD, or their co-occurrence, are targeted to facilitate treatment progress. For example, parents of youth with ASD typically need to provide more assistance, protection and guidance to their child than would be normative for a typically developing child of the same age. That being said, assisting the parent to differentiate adaptive protection and overprotection are often key points in reducing family accommodation of anxiety symptoms, and enhancing the child's adaptive and independent daily living skills [60,89].

Although some prominent anxiety treatment manuals developed for typically developing youth include physiological arousal reduction and relaxation components, relaxation and breathing retraining skills are controversial in the treatment of anxiety disorders given the potential to be used as a safety behavior that can interfere with normal exposure and habituation processes [90,92]. However, among treatment protocols for youth with ASD, relaxation skills are often utilized. The rationale for the use of relaxation for youth with ASD mainly focused around two issues. Firstly, youth with ASD experience high levels of physiological hyper-reactivity and sensitivities that are often linked to exaggerated emotional reactions (anger, tantrums, exaggerated startle and fear reactions), and the development of self-soothing strategies are proposed as important to facilitate emotion regulation [77,93]. Secondly, youth with ASD may be less able to engage with other strategies to manage their anxiety, particularly cognitive restructuring where youth are required to use a verbal process to identifying anxious cognitions, generate disconfirmatory evidence relating to the feared outcome, and to ultimately generate a more adaptive perspective or thought. This process relies upon executive functioning and cognitive flexibility skills [94,95], skills which are often impaired in youth with ASD [96]. In order to facilitate exposure therapy, alternative strategies, including relaxation, have been proposed as one way to reduce anxiety to allow approach behaviors and reduce avoidance [46].

Expert commentary

Research in the area of treatment for anxiety in children and adolescents with ASD has advanced considerably over the past decade. The question of *whether* CBT works for children and adolescents on the spectrum appears to have been answered with a surge in clinical trials in recent years. The most current Cochrane review of CBT for childhood anxiety disorders in 2015 included both typically developing and ASD youth, and found that children and adolescents treated using CBT were 7.85 times more likely to be in remission of all anxiety diagnoses at the end of treatment than wait-list controls [43]. When examining this exclusively in youth with ASD, the ratio was even higher (Odds Ratio = 16.74). The advancements in CBT treatment research among youth with ASD have been very promising over recent years. The current question regarding treatment tends to focus around the adage of which form and which treatment components of CBT work best, and for whom.

Unfortunately, despite the considerable investment by governments and special interest groups into establishing and improving the efficacy of treatment for anxiety in children and adolescents with ASD, there is still a substantial gap between this knowledge and the first-line treatments that are likely to be received by families. Common and concerning trends include families being informed that significant anxiety is a part of their child's ASD diagnosis and cannot be addressed, the commonplace prescription of medication with limited supporting data (including SSRIs), or the referral for behavioural interventions lacking empirical support for anxiety (e.g., play therapy, Applied Behavior Analysis, social skills training and sensory integration therapy). When families are referred for treatments that do not address their child's anxiety concerns, they are likely to become disillusioned in the health care system, and there may be a range of negative outcomes for their child resulting from delayed access to evidence-based and effective treatments. Clearly, if families are able to access skilled clinicians who are able to provide CBT, the outcomes are likely to be promising for children, and greater focus will need to be placed on dissemination of effective treatments in coming years.

Five-year view

Over the coming five years, there are several areas that warrant further empirical and clinical attention. One of the outstanding treatment-related questions is whether or not ASD-specific treatments are necessary for the treatment of anxiety in youth with ASD. Important results from a randomized controlled trial examining the benefits of ASD-specific treatment over standard CBT treatment for anxiety in children with ASD will be available in the coming years, [66] and will facilitate clinical decision making about the need for treatment adaptation, as well as identifying which treatment works best based on different child characteristics (i.e., which treatment works best for which child). However, this is unlikely to provide absolute instruction. With the introduction of DSM-5 [7] and the National Institute of Mental Health Research Domain Criteria (RDoC), along with the shift towards dimensional assessment and diagnosis, there is clear scope to begin to understand which treatments work better, and for whom. For example, youth who demonstrate significant and objective social skills deficits may be more likely to benefit from specific social coaching above and beyond standard CBT, especially where this would maximize the potential for

positive social interactions that are likely to reinforce continued social participation. However youth who experience specific phobias may be less likely to benefit from the inclusion of social skills training. ASD severity, age, and skill deficits may be more informative markers of whether treatment needs additional adaptations beyond normal idiosyncratic and personalized approaches within treatment [74,75]. Given the moderate to high functioning nature of youth included in current CBT trials, there is a need to understand whether CBT skills, or an adaptation of these skills, is effective for lower functioning youth, those with minimal verbal skills, moderate to low IQ, and those with aggressive and/or self-injurious behaviors. It may be that greater emphasis on parent-management techniques are most appropriate amongst these populations, rather than a child-focused coping skills model, and future research with these groups is important to address the treatment needs of youth across the spectrum of Autism.

With the burgeoning interest by funding bodies and scientists into biomarkers of psychopathology, there is likely to be an increased output of neuroimaging and experimental therapeutic studies in the coming years. For example, the past decade has seen a significant increase in research examining whether youth with ASD demonstrate excessive mouth-gaze and impaired eye-gaze that may impact facial recognition and recognition of social cues, with mixed findings [97]. Studies disentangling developmental differences in neurological functioning that may account for the different trajectory of youth with ASD, including functional and structural differences that may overlap with anxiety are likely to remain of interest. While excessive focus on the 'cause/s' of ASD are unlikely to significantly alter the lives of youth with ASD and anxiety, a focus on functional processes may highlight potential avenues for enhancing treatment methods or outcomes. Understanding individual and ASD-related differences in the processing of fear-related stimuli may assist with identifying neurological or functional differences that could be utilized or targeted more directly in treatment.

Although existing trials of pharmacotherapy suggest little efficacy and high rates of side effects, they are still routinely prescribed in clinical practice. There is some concern that existing trials are inadequate in their methodology to fully exclude any future use and utility of SSRI medications, and a large-scale double-blind, placebo controlled trial of an SSRI for the treatment of anxiety (including social anxiety, specific phobia, generalized anxiety disorder and atypical anxiety) in children and adolescents with ASD should be conducted. Even if this trial provided negative findings, based on efficacy, tolerability or both, this would be an important trial to conduct, and would provide robust evidence to guide clinical decision making.

Perhaps the area of most importance over the coming years, is a need to focus on bridging the gap between knowledge and practice. Improving parent and clinician access to information about symptoms of anxiety in youth with ASD, as well as the evidence-based treatment options, (e.g., the effectiveness of pharmacotherapy vs. CBT) are important to facilitate and overcome barriers to help-seeking. Efforts to aid the dissemination and implementation of evidence-based treatments outside of specialized research clinics is critical. Many well-meaning clinicians, unfortunately, will deliver non-evidence based treatments to anxious youth on the spectrum. With considerable potential to improve the

functioning and quality of life for child and families, it is important to improve access to CBT. Improving clinician access to training in CBT for anxiety, as well as improving knowledge and understanding of ASD and anxiety, are critical areas to address to begin to bridge this gap between knowledge and practice. In addition, refining existing treatment models of CBT for ASD is important given that families with a child on the spectrum are often already over-burdened with medical, educational and allied health treatment responsibilities. Ensuring the most time and cost-efficient treatments are readily available for these families has the potential to reduce additional stress as well as improving functioning and quality of life.

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Reference annotations

* Of interest

** Of considerable interest

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Key issues

- Anxiety is one of the most common psychiatric comorbidities among children and adolescents with ASD.
- Specific phobias, social anxiety, generalized anxiety and obsessive compulsive disorder are the most common anxiety presentations in youth with ASD, although atypical anxiety symptoms that overlap with ASD symptomatology are common.
- There is little to no evidence at this time supporting the use of pharmacological agents to treat anxiety in youth with ASD.
- CBT shows consistent efficacy for reducing anxiety symptoms in children and adolescents with ASD.
- Promising effects have been found for standard CBT, and ASD-specific adaptations of CBT treatments.
- It is unclear whether CBT needs to be modified for children with ASD, although studies are currently examining this issue.
- Treatment modifications may need to be personalized based on the child's presentation, skills and deficits.
- Treatment mediators and moderators have yet to be elucidated.