

Assessment and Treatment of Anxiety in Youth With Autism Spectrum Disorders

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abstract

OBJECTIVES: Anxiety is one of the most prevalent co-occurring symptoms in youth with autism spectrum disorder (ASD). The assessment and treatment recommendations proposed here are intended to help primary care providers with the assessment and treatment of anxiety in ASD.

METHODS: The Autism Speaks Autism Treatment Network/Autism Intervention Research on Physical Health Anxiety Workgroup, a multidisciplinary team of clinicians and researchers with expertise in ASD, developed the clinical recommendations. The recommendations were based on available scientific evidence regarding anxiety treatments, both in youth with ASD and typically developing youth, and clinical consensus of the workgroup where data were lacking.

RESULTS: Assessment of anxiety requires a systematic approach to evaluating symptoms and potential contributing factors across various developmental levels. Treatment recommendations include psychoeducation, coordination of care, and modified cognitive-behavioral therapy, particularly for children and adolescents with high-functioning ASD. Due to the limited evidence base in ASD, medications for anxiety should be prescribed cautiously with close monitoring of potential benefits and side effects.

CONCLUSIONS: Assessment and treatment of clinical anxiety in youth with ASD require a standardized approach to improve outcomes for youth with ASD. Although this approach provides a framework for clinicians, clinical judgment is recommended when making decisions about individual patients.

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Anxiety is one of the most prevalent and impairing co-occurring conditions in youth with autism spectrum disorder (ASD).¹⁻³ A recent meta-analysis indicated that 39.6% of youth with ASD have at least 1 anxiety disorder.⁴ Despite this burden, youth with ASD face barriers in accessing timely and appropriate mental health treatment, which places increasing demands on primary care providers to manage anxiety in these children.⁵

Diagnosing anxiety in youth with ASD can be more challenging than in typically developing (TD) youth because of cognitive and language impairments, compromised reporting of emotions, overlapping symptoms between anxiety and ASD, and unique behavioral expressions of anxiety in the ASD population. In addition to challenges with assessment, the field is faced with limited proven treatments to target anxiety in youth with ASD. The Autism Speaks Autism Treatment Network (ATN) Anxiety Workgroup recently authored a systematic review of pharmacologic and nonpharmacologic anxiety treatment studies in ASD that were published through June 2013.⁶ These results showed modest evidence for the efficacy of cognitive-behavioral therapy (CBT) and lack of randomized placebo-controlled trials investigating pharmacologic treatments for anxiety in youth with ASD. The few existing studies that focus on anxiety are open-label or retrospective chart reviews. This finding is in contrast to data in TD youth, which support the use of both medications and therapy.⁷⁻⁹

Most primary care providers lack specific training in managing youth with ASD and co-occurring psychiatric conditions.¹⁰ On the basis of this finding, coupled with the lack of anxiety treatments for youth with ASD, the Anxiety Workgroup sought to develop a systematic approach to the assessment and treatment of anxiety that primary

care providers use in their clinical practice. The workgroup was composed of 7 authors of this article. The goal was to help clinicians develop a systematic approach to the assessment of anxiety in this population, to provide treatment recommendations, and to help clinicians decide when to refer to a mental health specialist.

METHODS

The ATN/Autism Intervention Research Network on Physical Health Anxiety Workgroup developed the current assessment and treatment approach through a systematic multi-iterative process. The ATN/Autism Intervention Research Network on Physical Health is a consortium of 14 ASD centers throughout the United States and Canada focused on improving the clinical care of youth with ASD. The Anxiety Workgroup is composed of a multidisciplinary group of clinicians and researchers (child psychiatrists, developmental pediatricians, and a clinical psychologist) with extensive clinical experience in working with this population.

The workgroup held a series of conference calls from April 2014 to November 2014 to discuss best practices for both assessment and treatment of anxiety in youth with ASD. The group reviewed relevant studies pertaining to anxiety and ASD and discussed clinical practice patterns. For the assessment process, evidence was gleaned from manuscripts on the topic indexed in PubMed and/or PsychINFO, clinically relevant articles that were not indexed in PubMed or PsychINFO, and book chapters that were published between 2000 and 2014. Treatment recommendations were based on findings from the systematic review conducted by Vasa et al,⁶ anxiety treatment studies in ASD published from June 2013 to January 2015, and studies on

treatment of anxiety in TD youth. Both assessment and treatment recommendations were informed by clinical consensus when data were lacking. For each recommendation, clinical consensus was achieved through an iterative process. After extensive discussion, a written draft of each recommendation was circulated to all members for feedback. Recommended changes were discussed during subsequent conference calls, incorporated into the written draft, and redistributed to the workgroup members for further review. The process continued until all workgroup members reached consensus with the final revision.

RESULTS AND DISCUSSION

Assessment of Anxiety

The recommendations below present a systematic process to assess anxiety. Conducting a full assessment may take a prolonged visit or multiple visits. Practitioners whose schedule does not allow adequate time may wish to delegate this assessment to a mental health professional. The recommendations below correspond to Fig 1.

Recommendation 1: Perform a Developmentally Appropriate Multi-Informant and Multi-Method Assessment of Anxiety

Current evidence recommends the use of multiple assessment modalities and informants when assessing anxiety in children with ASD.^{11,12} This process includes data from clinical interviews and rating scales gathered from multiple informants (eg, child, parent, and teachers) as well as behavioral observations whenever possible. Assessment of anxiety in this population can be more laborious than in TD youth because of potentially compromised language and cognitive functions in the child and the presence of multiple complex co-occurring conditions that overlap with anxiety. It is also important to

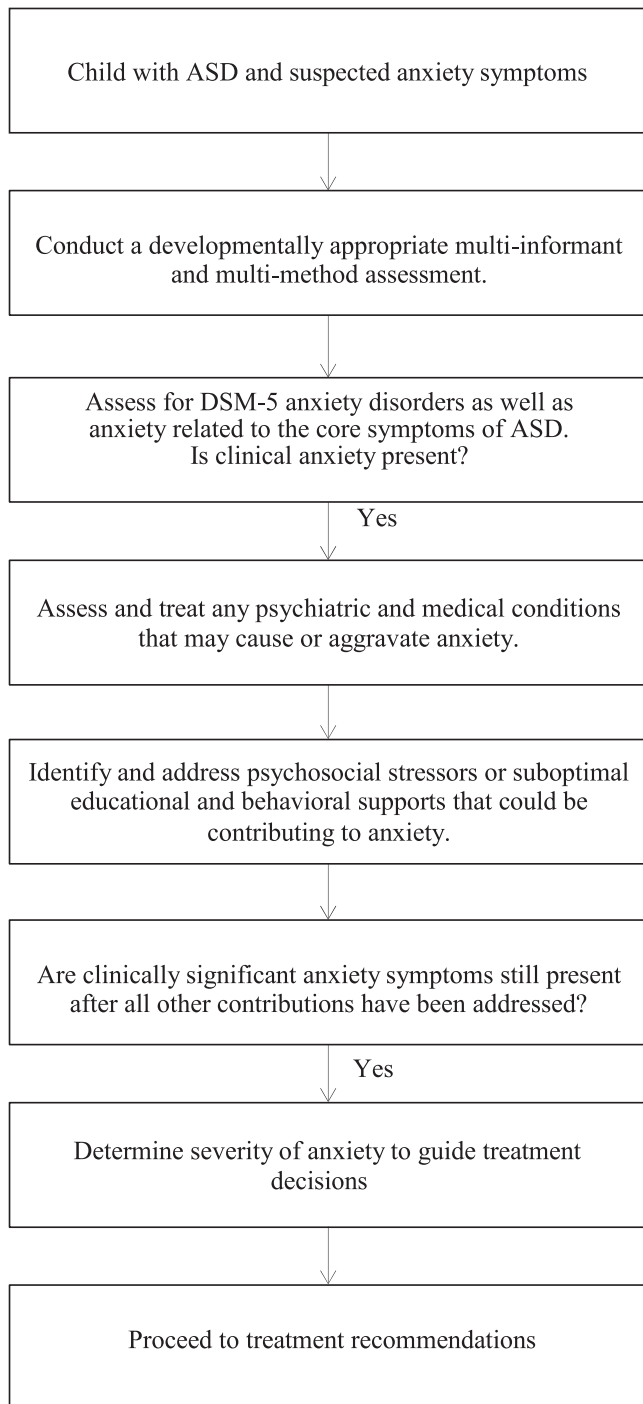


FIGURE 1
Assessment of anxiety in youth with ASD.

evaluate the anxiety symptoms in the context of child and family stressors.

Child self-report. Children with ASD may differ in their ability to self-report symptoms of anxiety due to age, verbal fluency, and cognitive ability.¹³ If the child appears to be

capable of providing self-report, it is important to assess the child's ability to understand and express emotions (eg, "Do you know what I mean by nervous or scared?" "Tell me a time when you were nervous") and provide developmentally appropriate

explanations of these emotional terms when needed.¹⁴ Some children may respond better to forced choice responses (ie, those requiring a "yes" or "no" response) than open-ended questions. Other children may be able to provide responses using visual analog scales rather than through verbal response. If emotional insight is compromised, results must be interpreted cautiously.

Parent report and other caregiver information. Clinicians must rely on accurate reporting of children's anxiety symptoms by parents and other caregivers. If child self-report is compromised, the evaluation must rely on reported observed behaviors.¹⁵ These may include avoidance and crying in response to specific stimuli or contexts, freezing behavior, fearful affect, clinginess, and increased repetitive behaviors and/or vocalizations. Irritability, tantrums, disruptive behavior, aggression, worsening sleep problems, and self-injury may also suggest the presence of anxiety. Parents who have an anxiety disorder may have enhanced perceptions of anxiety in their child.¹⁶ Sometimes, there may be disagreement between parent and child reports.¹⁷ It is therefore important for clinicians to collect collateral information from school staff and other caregivers in the form of narratives and behavior reports to supplement their findings.

Anxiety instruments. There are few well-validated tools for assessing anxiety in youth with ASD, and as such, clinicians often depend on measures used in TD children when assessing anxiety in ASD. Some scales such as the Screen for Child Anxiety Related Emotional Disorders (SCARED)¹⁸ show comparable psychometric properties between youth with ASD and TD youth, whereas others, such as the Multidimensional Anxiety Scale for Children (MASC),¹⁹ show factor structures that differ between the 2 groups. Preliminary data on the

Spence Children's Anxiety Scale (SCAS) indicate that it may serve as an effective anxiety-screening tool in youth with ASD.²⁰ Data from 2 systematic reviews indicate some support for the use of the following additional anxiety scales in children with ASD: the Revised Child Anxiety and Depression Scale (RCADS), the Child and Adolescent Symptom Inventory, Fourth Edition (CASI-4R), and the Pediatric Anxiety Rating Scale (PARS).^{21,22} However, both reviews noted measurement limitations across these scales. Furthermore, a recent study reported that some of these scales may not detect atypical fears.²³ In summary, data from anxiety instruments used in TD children should be interpreted cautiously when applied to youth with ASD.

Examination. In the office, clinicians should conduct a physical and mental status examination when evaluating for anxiety. Elevated heart rate or blood pressure may reflect situational anxiety related to the medical procedure or office visit. Other signs of anxiety include tremors, nail biting, bald spots secondary to hair pulling, and skin lesions due to skin picking. A palpable thyroid, fine skin or hair, and/or brisk tendon reflexes suggest checking the thyroid status as a possible cause of anxiety symptoms. Mental status examination may reveal poor eye contact, negative affect (eg, fear, irritability), and changes in communication (eg, stuttering, increased vocalizations, decreased verbal exchanges). The presence of disruptive behaviors may reflect anxiety; however, these behaviors may also reflect a desire to escape from the situation and therefore require careful assessment. Some children may not exhibit signs of anxiety on examination even though they experience anxiety in other settings.

Recommendation 2: Assess for Specific Anxiety Disorders and Anxiety Symptoms Related to the Core Symptoms of ASD

Many youth with ASD meet criteria for anxiety disorders according to the *Diagnostic and Statistical Manual, Fifth Edition* (DSM-5).²⁴ The most common DSM-5 anxiety disorders are social anxiety disorder, generalized anxiety disorder, and specific phobia.² A substantial number of children with ASD also exhibit atypical anxiety symptoms that are connected to the core symptoms of ASD and may not fit neatly into DSM-5 categories.²⁵ Examples of atypical anxiety symptoms include anxiety about sensory stimuli, transitions, or social situations without accompanying fear of negative evaluation. Thus, the assessment of anxiety in children with ASD should include a focus on both categorical and atypical symptoms.

Anxiety and ASD symptoms can overlap. For example, social avoidance may represent behavioral avoidance of feared stimuli, which suggests social anxiety, or social indifference, which is a core feature of ASD.²⁶ Ritualistic and repetitive behaviors are core ASD symptoms and are also present in certain anxiety disorders, including obsessive-compulsive disorder, generalized anxiety disorder, and separation anxiety disorder.²⁴ These rituals may serve to reduce anxiety or may be a preferred activity unrelated to negative affect.²⁷ Clinicians should therefore inquire about the function of the ritualistic behaviors. A referral to a behavioral psychologist, who can conduct a functional behavioral analysis, may help differentiate these etiologies.

Clinicians can also ask questions to help tease out whether overlapping symptoms are explained solely by ASD or are consistent with a co-occurring anxiety disorder. Some of these questions include

asking about behavioral signs of anxiety that may accompany the symptom in question (eg, is the social avoidance associated with fearful affect, irritability, or physiologic symptoms?). It is also important to assess baseline ASD symptoms to differentiate preexisting ASD characteristics from new-onset anxiety symptoms (eg, has the child always avoided crowds or is this a new behavior?). Other questions to ask include whether ASD symptoms have intensified (eg, has the frequency of repetitive behaviors increased recently?) and whether there is a relationship between exposure to specific stimuli and anxiety symptoms.

Recommendation 3: Assess and Treat Other Psychiatric and Medical Conditions That May Cause or Aggravate Anxiety

Youth with ASD may present with other types of psychiatric symptoms such as inattention, hyperactivity, irritability, aggression, self-injury, and tantrums.^{1,2} These symptoms may be a manifestation of anxiety (eg, children who are anxious about schoolwork may exhibit irritability at school) or may be related to another disorder that is triggering the anxiety (eg, symptoms of attention-deficit/hyperactivity disorder at school may lead to academic struggles and subsequent anxiety about schoolwork). Treating other conditions that may exacerbate anxiety should therefore be part of the treatment plan and should be considered before treating anxiety directly.

Co-occurring medical disorders are prevalent in youth with ASD but may also reflect the presence of anxiety. For example, gastrointestinal²⁸ and sleep problems²⁹ may cause or aggravate anxiety, particularly if symptoms are more frequent or severe or may be caused by anxiety. Complex partial seizures can present with anxiety-like symptoms, including fear, misperceptions, and

irritability.³⁰ Some medications (eg, psychostimulants, bronchodilators, allergy medications) can also cause anxiety and may need to be changed. Any medical issues affecting anxiety therefore warrant treatment.

Recommendation 4: Address Psychosocial Stressors or Suboptimal Behavioral and Educational Supports That May Be Contributing to Anxiety

Many children with ASD have a strong need for sameness and prefer predictable routines and schedules.²⁶ Changes in the environment can therefore cause significant distress and anxiety. These changes can be minor (eg, desks are moved in class) or substantial (eg, new school, loss of a one-to-one aide, loss of in-home behavioral support services, change in a parent's job schedule).

Anxiety may also result from a mismatch between the child's needs and the types of supports in place in his/her daily life. For example, inadequate educational supports or high academic expectations may cause increased stress due to academic challenges.³¹ Unrecognized learning, gross or fine motor, or speech and language difficulties may aggravate such stress. Many children with ASD experience bullying and peer victimization in school, which may lead to significant anxiety.³²

Stressors in the family environment must also be evaluated. Parents of youth with ASD experience greater stress than parents of children with Down syndrome and TD children.³³ Stressors can include caregiver burden, lack of sleep, limited social and community engagement, and worries about the future.³⁴ Parental anxiety may contribute to anxiety in children, through modeling of anxious and overprotective parenting behaviors.¹⁵

Inquiring about recent stressors and working with parents to alleviate these stressors is critical. Clinicians can help with educational advocacy (eg, talking to school staff or writing letters indicating the need

for increased services at school), suggest strategies to stabilize the home environment (eg, increasing structure and predictability), accessing resources (eg, behavioral therapy, respite care), and promoting parental self-care (eg, taking breaks, seeking personal mental health and medical treatments). The child's anxiety level should be reassessed to determine if symptoms have decreased after modifying these stressors.

Recommendation 5: Assess the Degree of Anxiety-Related Impairment

After collecting all of the data, the clinician should assess if anxiety-related impairment is present (eg, How much does anxiety interfere with daily functioning? Is impaired functioning present across 1 or multiple settings?). Assessing the contribution of anxiety symptoms (eg, schoolwork avoidance or behavioral challenges at school and home) to the overall impairment and functioning of the child with ASD will help to prioritize treatment.

Treatment of Anxiety

If clinical anxiety persists despite relieving potential sources of anxiety or if stressors cannot be immediately modified, then treatment is recommended. Clinicians and parents must decide together what the best treatment approach will be. Potential treatment barriers should be explored (eg, insurance constraints, parent work schedules, access to providers, and transportation issues). Due to limited treatment data in ASD, a specific treatment algorithm is not offered but rather various treatment recommendations are presented with the caveat that clinicians tailor treatment on the basis of child and family circumstances and clinical judgment.

Recommendation 1: Psychoeducation and Coordination of Care Are the First Steps of Treatment

Educating youth and families about anxiety symptoms is an important

first step. Other points to discuss include delineating specific and measurable treatment outcomes (eg, decreased avoidance of feared stimuli, more responsive to psychosocial interventions when anxious, sleeping in own room every night). Coordinating the treatment plan with parents and care providers (eg, therapists, school staff) is recommended to track progress.

Recommendation 2: Anxiety Can Be Treated With Modified CBT Techniques

Preliminary data suggest that modified CBT (MCBT) is an efficacious treatment of children and adolescents with high-functioning ASD and DSM-5 anxiety disorders.³⁵ MCBT can be administered individually or in a group and often includes parental involvement.

CBT in TD youth involves many components, including affective education, cognitive restructuring, reducing avoidance behaviors, relaxation, modeling, and exposure to the feared stimuli (with response prevention). Some youth with high-functioning ASD can understand basic cognitive concepts of CBT and therefore may be responsive to both the cognitive and the behavioral elements of MCBT.³⁶ In ASD, special CBT adaptations are needed to facilitate understanding of cognitive and emotional concepts. These include the use of visual supports and concrete language, the use of written materials and lists, opportunities for repetition and practice, incorporating special interests, video modeling, and more active parent engagement in therapy.³⁵ Behavioral therapy with exposure may be particularly useful for youth who have language and cognitive difficulties, thereby precluding participation in the cognitive components of treatment.³⁷

Some families may have limited access to mental health professionals with expertise in ASD and MCBT protocols, in which case medications may be an option. Sometimes, a child

may be resistant or severely anxious during therapy (eg, exposure to a feared stimulus results in severe tantrums). In these situations, parents and clinicians must decide together whether medication should be tried to facilitate engagement in therapy.

Recommendation 3: Certain

Medications Can Be Considered for the Treatment of Anxiety

Table 1 presents a summary of medications that could potentially be considered for the treatment of anxiety in youth with ASD. Because these medications have not been rigorously studied in youth with ASD, the doses presented in Table 1 are based on data in TD children and adolescents. The recommendations, however, are to start medications at low doses and titrate slowly with close monitoring (eg, monthly office visits) of both benefits and adverse effects. Most important, we recommend that primary care providers have a low threshold for seeking consultation from a developmental/behavioral pediatrician or child psychiatrist when prescribing psychotropic medications. Consultation could be requested either before starting the medication or during the titration process, especially if higher doses are used. Mental health professionals can assist pediatricians with titration and safety monitoring, and help tease out the complex developmental, psychosocial, and medical issues that can affect treatment outcomes. If medications are ineffective or poorly tolerated, gradual discontinuation is recommended. Liquid preparations are available for slower titration or if pills cannot be swallowed.

Medications with efficacy in TD children can be tried for anxiety in ASD. Robust evidence supports

TABLE 1 Summary of Medications for the Treatment of Anxiety in Youth With ASD

Symptoms ^a	Medication ^b	Dose Range ^b		References		
		Starting Dose	Maximum Dose			
Core anxiety symptoms	Sertraline ^c	12.5 mg daily	200 mg daily	Reviews in typically developing youth: Mohatt et al (2013), Strawn et al (2014)		
	Fluoxetine ^c	2.5–5 mg daily	60 mg daily			
	Citalopram ^c	2.5–5 mg daily	40 mg daily			
	Escitalopram ^c	1.25–2.5 mg daily	20 mg daily			
Specific anxiety symptoms ^d						
	Sleep disturbance	Melatonin	2 mg hs	10 mg hs	Gueneo et al (2011)	
Physiologic symptoms ^f		Clonidine	0.05 mg hs	0.2 mg hs	Nguyen et al (2014)	
		Trazodone ^e	12.5–25 mg hs	100 mg hs		
	Behavioral dysregulation ^f		Clonidine ^f	0.05 mg hs for 1 week then bid-qid	0.1 mg tid-qid	No data in TD or ASD youth; recommendations based on clinical consensus
			Guanfacine ^f	0.05 mg hs for 1 week then bid-qid	1 mg tid	
			Clonidine ER ^f	0.1 mg hs or qam	0.2 mg hs or qam ^g	
			Guanfacine ER ^f	1 mg hs or qam	4 mg hs or qam ^g	
Situational anxiety ^g		Propranolol	10 mg bid-tid or prn	30 mg tid	Reviews by: Mahajan et al (2012), Ji and Findling (2014)	
		Clonidine	0.05 mg hs for 1 week then bid-qid	0.1 mg tid-qid		
		Clonidine ER	0.1 mg daily	0.2–0.3 mg daily		
		Guanfacine	0.5 mg hs for 1 week then bid tid	1 mg tid		
		Guanfacine ER	1 mg hs ^g	4 mg hs or qam	No data in TD or ASD youth; recommendation based on clinical consensus	
		Lorazepam	0.25–0.5 mg prn	2 mg prn		
		Propranolol	5–10 mg prn	20 mg prn		

bid, twice daily; ER, extended-release; hs, bedtime; prn, as needed; qam, each morning; qid, 4 times per day; tid, 3 times per day.

^a Specific anxiety symptoms refer to individual or limited symptoms of anxiety, whereas core anxiety symptoms refer to the entire syndrome of cognitive, affective, and physiologic changes associated with anxiety.

^b Maximum doses are based on data in TD children and adolescents. Higher doses in this table should only be used in consultation with a specialist versed in their use, such as a child psychiatrist or developmental-behavioral pediatrician.

^c Discuss side effects including risk of behavioral activation. Higher doses may be needed for fast metabolizers. Slow metabolizers may need lower doses.

^d Behavioral dysregulation refers to symptoms of irritability, aggression, property destruction, and self-injury. For severe behavioral dysregulation, refer to a mental health specialist or follow the ATN pathway for treatment of irritability and problem behaviors.

^e There are no data to support the use of trazodone. It is only recommended in children aged >8 years. The risk of priapism should be discussed with the family.

^f For short and ER clonidine and guanfacine preparations, monitor blood pressure and heart rate at each visit. Check for orthostatic hypotension if dizziness, light-headedness, or falls are reported. Guanfacine ER can be started in the evening initially due to the possibility of sedation and then switched to morning, if needed. Alternatively, it can be started directly in the morning if tolerated by the patient. Guanfacine is preferred over clonidine during daytime hours because of its longer half-life and lower potential for sedation.

^g Lorazepam is a short-acting benzodiazepine (6–8 hours). For situational anxiety, it should be given 30 min before the event. There are no data on the use of propranolol in children and adolescents, but it is used by some experts for the treatment of situational anxiety.

the efficacy of selective serotonin reuptake inhibitors (SSRIs) for the treatment of anxiety disorders (separation anxiety, generalized anxiety, and social phobia) in TD youth.⁷ Indeed, SSRIs are the most effective pharmacologic treatments for anxiety disorders in TD youth,

although benefits may not be seen for several weeks after treatment initiation.

SSRIs are frequently prescribed in youth with ASD³⁸; yet, there is a lack of double-blind placebo-controlled trials supporting their efficacy for anxiety

in this population.⁶ Data from SSRI trials in youth with ASD report high rates of behavioral activation, which manifests as increased activity level, impulsivity, insomnia, or disinhibition without manic symptoms.³⁹ This behavioral activation typically occurs at the beginning of SSRI treatment or with dose increase and resolves with reducing the dose or discontinuing the medication. Other prescribing considerations include a family history of bipolar disorder, drug interactions, and the black box warning of suicidal ideation. Given these factors, certain SSRIs (shown in Table 1) are preferred over others. In summary, SSRIs should be prescribed cautiously in youth with ASD, with close monitoring.

Medications can be used to treat specific anxiety-associated symptoms based on evidence in ASD as well as expert clinical consensus. Several studies discuss the management of sleep disturbance in youth with anxiety and ASD.^{40,41} Insomnia secondary to anxiety can be treated initially with melatonin, and if ineffective, there is preliminary evidence indicating that clonidine, a short-acting α -agonist, may help with insomnia. Although no data are available, low-dose trazodone can also be considered. Antihistamines with anticholinergic effects (eg, diphenhydramine) should be avoided for chronic sleep difficulties due to the potential for delirium and constipation. Referral to a sleep specialist should be considered as necessary if these interventions are ineffective. Some children with

anxiety may exhibit significant physiologic arousal symptoms including increased heart rate, blood pressure, sweating, and muscle tension. Although no data are available, α -agonists and propranolol could be considered to reduce such physiologic symptoms.

Anxiety can also result in behavioral dysregulation, which can be characterized by irritability, aggression, property destruction, and self-injury. α -Agonists (clonidine, guanfacine, guanfacine extended release), which improve symptoms of attention-deficit/hyperactivity disorder in youth with ASD, may potentially reduce some of these behaviors.⁴²⁻⁴⁴ The ATN pathway for the treatment of accompanying irritability and problem behaviors can also be followed to manage these behaviors.⁴⁵

Youth with ASD frequently experience situational anxiety such as during family events, holiday time, blood draws, and other medical procedures. There are no data on pharmacologic treatments for situational anxiety. Short-acting benzodiazepines (eg, lorazepam) or a β -blocker (eg, propranolol) can be considered temporarily with close attention to sedation, cognitive impairment, and behavioral activation.

Recommendation 4: Refer to a Mental Health Clinician if Anxiety Is Extremely Impairing or Is Not Responding to Interventions

Children with complex presentations or partial or no

response to medications should be referred to an ASD mental health clinician (eg, a child psychiatrist, developmental pediatrician, psychologist, and others). If the child's anxiety triggers self-injury and/or lloperment, treating clinicians should initiate appropriate interventions to keep the child safe. Appropriate intervention may include a referral to an inpatient or partial hospitalization program.

SUMMARY

The proposed assessment and treatment strategies provide a useful starting point for clinicians to develop a standardized approach to the assessment and treatment of anxiety in youth with ASD. These recommendations can be updated and specific treatment algorithms can be developed as research on the phenomenology, risk factors, and treatments for anxiety becomes available.

ABBREVIATIONS

ASD: autism spectrum disorder
ATN: Autism Treatment Network
CBT: cognitive behavioral therapy
DSM-5: *Diagnostic and Statistical Manual, Fifth Edition*
MCBT: modified cognitive behavior therapy
SSRI: selective serotonin reuptake inhibitor
TD: typically developing

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