Review

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Comorbid autism spectrum disorder and anxiety disorders: a brief review

Brian A Zaboski[1] & Eric A Storch*,[2]

[1]School of Special Education, School Psychology & Early Childhood Studies, University of Florida, PO Box 117050, Norman Hall 1403, Gainesville, FL 32611, USA

[2]Menninger Department of Psychiatry & Behavioral Sciences, Baylor College of Medicine, Houston, TX 77030, USA

* Author for correspondence: eric.storch@bcm.edu

Appearing in 40% of the cases of autism spectrum disorder (ASD), comorbid anxiety presents unique challenges for practitioners by amplifying problem behaviors such as social skills deficits, resistance to change and repetitive behaviors. Furthermore, comorbid ASD/anxiety strains familial relationships and increases parental stress. Research indicates that the neurobiological interactions between anxiety and ASD require comprehensive assessment approaches, modified cognitive behavioral therapy and carefully managed pharmacological interventions. Meta-analyses indicate that cognitive behavioral therapy with exposure is an effective treatment option when adequately accounting for social, familial and cognitive variables. The purpose of this focused review is to update readers on the latest research advances in comorbid ASD and anxiety, including prevalence, assessment, psychosocial and pharmacological treatment.

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The *Diagnostic and Statistical Manual of Mental Disorders* (5th Ed., DSM-5) [1] classifies autism spectrum disorder (ASD) as a neurodevelopmental disorder with three primary characteristics: deficits in social communication (criterion A) and restricted or repetitive behaviors/interests (criterion B) that originally present in early development (criterion C). Since publication of the DSM-5, autism, Asperger's syndrome and pervasive developmental disorder not otherwise specified have been subsumed under the broader category of ASD [1].

The frequency with which anxiety disorders present comorbid with ASD contributes considerable complexity. For instance, in individuals with ASD, anxiety is associated with sleep problems [2], self-injurious behavior and parental stress [3], insistence on sameness [4] and sensory under- and over-responsiveness [5]. Thus, treatment of comorbid ASD/anxiety necessitates updated research and evidence-based practice principles. Accordingly, the purpose of this report is to synthesize the current research on comorbid ASD and anxiety, including prevalence rates, assessment strategies, treatments and research directions.

Prevalence

Approximately 40% of the cases with ASD are diagnosed with at least one anxiety disorder [6]. The most common comorbid anxiety disorders include social phobia (17–30%), specific phobias (30–44%), generalized anxiety disorder (15–35%), separation anxiety disorder (9–38%) and obsessive-compulsive disorder (OCD; 17–37% [6,7]). Initial explanations for these ranges (e.g., varying assessment methods, diagnostic definitions and sampling procedures [7]) have been supplemented by proposals that the ranges reflect overlapping phenomenology among ASD and anxiety disorders. For instance, Kerns *et al.* [8] proposed that anxiety may differ through interactions with ASD, such that it is either typical (i.e., symptoms consistent with DSM criteria) or atypical (i.e., anxiety symptoms not associated with traditional DSM criteria), thereby expressing itself differently across populations.

The interaction between ASD and anxiety may also explain the variability in the prevalence rates. First, there is considerable overlap in symptoms [9]. For instance, social anxiety, characterized principally by a fear of negative evaluation by others and avoidance of social situations [1], may be mistaken as a social communication deficit in ASD. Repetitive behaviors within ASD may overlap with compulsions in OCD, and cognitive deficits common

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to ASD (e.g., memory) may cause compulsive behavior, as well [9]. Preliminary research also suggests that gene polymorphisms may modulate the effect of anxiety [10], and that anxiety may express itself differently across settings and observers [11]. Genetic overlap between ASD and some of the DSM-5's other psychiatric diagnoses provide evidence that many mental illnesses are not categorically distinct [12,13]. Indeed, this raises the question about whether ASD and anxiety are even distinct diagnoses. On balance, treatments for anxiety in youth with ASD (and without) are transdiagnostic in nature and approaches (e.g., exposure) apply to a spectrum of anxiety presentations.

Assessment

Comorbid anxiety complicates assessment due to the presence of core ASD symptoms, such as social communication deficits, and the potential for symptom overlap (e.g., repetetive behaviors in OCD; communication deficits due to social anxiety) [14]. Vasa *et al.* [15] provided specific assessment recommendations for this comorbid presentation by synthesizing expertise from members of the USA and Canada's Autism Intervention Research Network on Physical Health Anxiety Workgroup to provide a *"useful starting point for clinicians to develop a standardized approach to the assessment and treatment of anxiety in youth with ASD"*. Clinicians must consider that assessing individuals with ASD requires the consideration of several unique factors. For instance, individuals with ASD are more likely to experience cognitive deficits and may communicate nonverbally or struggle to articulate internal experiences [16], which may impair a child's ability to articulate her inner experience of anxiety. Use of parent and teacher reports may also mask the prevalence of anxiety if raters confuse behaviors associated with anxiety as symptoms of ASD (e.g., rituals vs repetitive behaviors) [17].

Practitioners should utilize comprehensive assessment procedures with multiple methods and multiple informants [15]. This should include clinical interviews and rating scales from patients, caregivers, teachers and other family members. Assessors should investigate and determine which anxiety diagnoses are most likely, while recognizing the weaknesses of available instruments. For example, few anxiety instruments have been validated for individuals with comorbid ASD/anxiety other than the Screen for Child Anxiety Related Disorders (SCARED) [18], which showed preliminary data. Morevoer, there are few instruments validated for assessing individuals with ASD and anxiety, which forces researchers and clinicians to assess anxiety using instruments normed for typically developing children [19]. This is problematic, given the overlap and difficulty disentangling anxiety from symptoms of ASD [8]. For example, an adolescent with ASD and OCD is likely to experience repetetive behaviors, as these are core symptoms of ASD. The Obsessive Compulsive Inventory-Revised (OCI-R [20]) shows some promise differentiating the repetetive behaviors resulting from ASD and the compulsions that result from the OCD. For instance, individuals with ASD and OCD report higher scores on the OCI-R's obsessing, checking and ordering subscales [21]. Obsessions and compulsions related to OCD are often anxiety provoking, unwanted and unpleasant [22]; thus, assessing an individual's emotional responses to these symptoms is critical.

After determining the presence of anxiety, Vasa *et al.* [15] recommended that assessments consider other comorbid diagnoses and medical conditions (e.g., medical or behavioral) that may exacerbate anxiety and, if present, to treat them first (or concurrently if needed). For instance, sleep disturbances, irritability, aggression and self-injurious behaviors can impede the direct treatment of anxiety [15]. Next, psychosocial factors, including the family's role in the patient's anxiety, should also be evaluated, as these can interfere with treatment. For example, the presence of behavior problems is associated with depression and anxiety in parents [23], who are essential in treatment planning [24]. Similarly, mismatches between child need and educational supports can exacerbate behaviors that worsen with [25]. Family accommodation, or overly protective responses to anxiety that prevent an individual from utilizing adequate coping skills, also presents a problem worthy of an assessor's attention [26]. In one study, 97.5% of parents reportedly accommodated their child's anxiety, with most instances occuring once per week [24]. Moreover, clinicians need awareness of a patient's cognitive functioning, as this can place limitations on treatment strategies [27].

Psychosocial & behavioral interventions

The significant impairment associated with comorbid ASD and anxiety demands effective intervention strategies. A number of controlled trials indicated that cognitive behavioral therapy (CBT) is an effective treatment modality. In their meta-analysis of 14 studies ($n = 511$) [28] observed that the effect size of CBT with youth diagnosed with comorbid ASD and anxiety was moderate ($g = 0.47$). They also reported that overall effect sizes decreased from $d = 0.84$ to $d = 0.71$ when child-reported measures were included, suggesting that children with ASD may struggle to accurately report on their internal states. Follow-up data are limited in randomized controlled trials, though

preliminary data are promising, with large treatment gains (d = 0.80–0.83*)* observed after a 3-month follow-up period [29].

Treatment with CBT has been conducted in group or individual format, with anywhere between 6–32 sessions that lasted 1–2 h [27]. CBT for this population appears most effective when emphasizing the following core components: psychoeducation, exposure to feared triggers and cognitive restructuring [28]. Psychoeducation includes providing education on ASD, cognitive and physiological reactions to anxiety, accommodation and treatment for anxiety. The hallmark of exposure to feared triggers is the creation of a fear hierarchy, or a graded list of exposures that address prevalent fears. Because unique interests (e.g., rocks, Harry Potter and action figures) are a core characteristic of ASD, these should be used to reinforce approach behaviors and encourage patients to cope with challenging situations [27]. Cognitive restructuring or disputing maladaptive thinking by helping patients recognize the relationship between thoughts and feelings, is an effective intervention if modified to a child's developmental and cognitive level [30]. Concrete examples that incorporate personal interests and relate directly to patients' lives often assist individuals with ASD. Finally, clinicians should prioritize treatment plan goals with evidence of impairment [15]. For instance, if a patient's compulsive 8 h prayers prevent her from functioning, then that should be the initial treatment focus unless prevented by more pressing medical or psychosocial concerns.

When used with individuals with ASD, clinicians and researchers are encouraged to develop a modified CBT treatment approach that aligns with a patient's skillset, interests and developmental capacity [31]. Typical modifications include concrete behavior plans, incorporating a child's special interests into treatment, parental involvement and a broad treatment plan that addresses the core ASD symptoms as well as the anxiety [31]. Notably, such approaches are applicable for the range of anxiety manifestations, capitalizing on research advances that direct clinicians away from categorical approaches. Young children with ASD may struggle with cognitive restructuring, increasing the effectiveness of more concrete behavioral intervention plans in some cases. Additionally, cognitive variables (e.g., memory, vocabulary and concentration) require flexibility, such as frequently repeating and reviewing ideas, providing concrete examples and utilizing visual aids [27]. Parents commonly report accommodating anxiety by avoiding activities, reassuring children (e.g., that nothing bad will happen) rather than allowing them to experience the anxiety-provoking situation on their own, or changing family routines [24]. Preliminary data suggest that decreasing family accommodation is associated with decreases in anxiety pre- to post-treatment (r = 0.41) [24], and that lower family supportiveness and organization is associated with slower treatment outcomes [32].

Finally, individuals with comorbid ASD/anxiety often require social skills training. In addition to core social skills deficits related to ASD, high anxiety places individuals with ASD at risk for loneliness [33], which may further prevent patients from practicing important social skills (e.g., empathizing and inferring another's thoughts). Consequently, CBT, which relies on some of those skills, may be less effective [34]. The UCLA PEERS Program for young adults has shown promise in a randomized clinical trial with 16, 90-min sessions that emphasize peer conflict resolution, romantic relationships and managing friendships [35]. Compared with a delayed treatment group, the social skills treatment group improved in overall knowledge of social skills (d = 2.57*)* and monthly get-togethers (d = 0.92) on self-report measures. Follow-up data showed maintenance of most treatment gains after 16 weeks.

Pharmacological interventions

Serotonin and norepinephrine reuptake inhibitors and selective serotonin reuptake inhibitors (SSRIs) are effective for several types of anxiety disorders, including panic, generalized anxiety disorder and social phobia in typically developing youth [36]. Meta-analyses have also shown that antidepressants, including fluvoxamine, sertraline, paroxetine, duloxetine, fluoxetine and venlafaxine are effective when compared with placebo controls (d = 0.64) [37]. Specifically, dosing guidelines are based on those for typically developing youth with anxiety/OCD; a full discussion is beyond the scope of this manuscript. As such, the reader is referred to practice guidelines for a full discussion [38,39].

Although not indicated for anxiety in youth with ASD, atypical antipsychotics have demonstrated efficacy and have a US FDA indication for treating irritability and aggression among youth with ASD, which may reflect anxiety symptomology [40,41]. Benzodiazepine use has been popular; however, the small number of randomized controlled trials coupled with side effects like drowsiness and irritability do not support their usage [42]. Thus, while SSRIs and serotonin and norepinephrine reuptake inhibitors appear most effective for typically developing youth and atypical antipsychotics show promise, the added complexity of ASD leaves the literature on pharmacotherapies with comorbid anxiety wanting.

In a systematic review of treatments for children and adolescents with ASD/anxiety, Vasa *et al.* [42] reported that pharmacological interventions have not been well researched. Despite the wide utilization of SSRIs, common side

effects such as increased impulsivity, insomnia and activity level have been reported. Current pharmacological recommendations, including low doses of SSRIs with frequent symptom monitoring and cross-collaboration with other providers, are based on anxiety outcome studies for typically developing children and youth rather than comorbid ASD/anxiety [15].

Conclusion

ASD with anxiety is a challenging psychiatric comorbidity to treat and assess. Preliminary evidence suggests that ASD with anxiety is amenable to CBT, particularly when clinicians target familial accommodations that exacerbate/maintain anxiety and incorporate behavioral intervention plans into treatment. Pharmacological interventions show promise for typically developing populations, but additional research is required to establish the efficacy of medications for individuals on the spectrum. Because comorbid ASD/anxiety remains a nascent and growing area of study, practitioners are encouraged to remain updated on the latest scientific findings.

Future perspective

As demonstrated in this focused review, researchers continue to generate theories and hypotheses to elucidate and overcome the challenges inherent in assessing and treating comorbid ASD/anxiety; however, several questions remain. First, variability in prevalence data of anxiety should be clarified. Additional research investigating the interactions of ASD and anxiety would be helpful; in addition to large epidemiological studies clarifying different prevalence rates for narrow, DSM-defined anxiety and broader, more atypical anxiety [8]. Relatedly, research elucidating the diagnostic utility of the DSM-5 categories should be considered, as these dichotomous categories may overlook important neurobiological overlap between the diagnoses. Second, psychometrically sound anxiety assessments, sensitive to the different symptom presentations for individuals with ASD are crucial. Third, more

Executive summary

Prevalence
- Autism spectrum disorder (ASD) and anxiety greatly overlap and the explanation of the overlap is unclear.
- Genetic studies show that ASD overlaps with other psychiatric illnesses.
- Overlap may be an artefact of categorical classifications.

Assessment
- Overlap between core symptoms of ASD and anxiety complicates assessment.
- Individuals with ASD may have cognitive delays and self-report instruments may inaccurately capture anxiety.
- A multimethod approach is highly recommended.
- The SCARED and OCI-R show promise for assessments.
- Psychosocial factors, including family accommodation, should not be overlooked.

Psychosocial interventions
- Cognitive behavioral therapy (CBT) with modifications can effectively treat individuals with comorbid ASD/anxiety.
- Three important components of CBT include psychoeducation, exposure and cognitive restructuring.
- Four common modifications include concrete behavior plans, incorporating a child's special interests into treatment, parental involvement and a broad treatment approach.
- Decreasing family accommodation appears to improve treatment outcomes.
- Social skills training may be required to remediate communication deficits.

Pharmacological interventions
- Selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors show promise for anxiety in typically developing populations.
- Atypical antipsychotics might help in treating other associated symptoms with ASD such as irritability and aggression.
- Additional research on pharmacological interventions is needed.
- Ongoing medication and symptom monitoring are strongly encouraged when pharmacotherapy is indicated.

Conclusion
- Treating and assessing ASD with anxiety involves unique considerations.
- Family-based CBT continues to show promise.
- Pharmacotherapy is an effective intervention for individuals in the typically developing population.
- However, additional research is required to establish the effectiveness of pharmacological interventions for children and adolescents with ASD/anxiety.

research clarifying the efficacy and effectiveness of CBT with individuals with ASD is sorely needed. Moreover, randomized clinical trials systematically studying the effect of treatment modifications for ASD/anxiety (e.g., increased emphasis on exposure vs cognitive restructuring) would be helpful. Fourth, large scale treatment studies are needed to inform practitioners and researchers of efficacy and side effects of pharmacotherapy for comorbid ASD/anxiety, as well as treatment moderators.

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