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Anxiety Disorders and Obsessive-Compulsive Disorder in Individuals with Autism Spectrum Disorder

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Abstract
Purpose of Review This review aims to synthesize the most recent research on anxiety disorders and obsessive-compulsive disorder (OCD) in individuals with autism spectrum disorder (ASD) and discuss the relationship between these conditions and challenges for assessment. Furthermore, implications for treatment and future directions are discussed.
Recent Findings Research suggests that anxiety disorders and OCD are highly prevalent in individuals with ASD. However, the significant overlap of ASD features with anxiety and OCD symptomology makes differential diagnosis of these disorders particularly challenging. Though several treatments for anxiety have been adapted for youth with ASD (e.g., cognitive behavior therapy), pharmacological treatments and treatments for adults are still marked undeveloped.
Summary Despite the high prevalence of anxiety disorders and OCD in ASD and some recent advances in assessment and treatment, research is needed to clarify the multifaceted relationship of these conditions and develop tailored assessment and treatment approaches appropriate for a full range of individuals with ASD.

Keywords Anxiety · Obsessive-compulsive disorder · Autism spectrum disorder · Repetitive behaviors

This article is part of the Topical Collection on *Anxiety Disorders*

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Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and social reciprocity, as well as repetitive behavior and restricted interests [1].

In addition to the core symptoms of ASD, comorbid psychiatric conditions are highly prevalent, aggravating impairment, and complicating diagnosis and treatment [2•, 3, 4••]. There is considerable evidence that individuals with ASD are at heightened risk for anxiety and anxiety disorders, which can cause persistent distress, exacerbate ASD symptoms, and increase behavioral problems [5–7, 8•]. Despite the high prevalence of anxiety symptoms in this clinical population, and the impact of these symptoms on overall well-being, the precise relationship between anxiety and ASD requires clarification.

Disentangling symptoms of ASD and anxiety and determining risk factors associated with the development of anxiety

in ASD is a critical priority, given the tremendous impact of anxiety on well-being and quality of life in this population. Higher levels of anxiety are associated with the occurrence of depression, disruptive behaviors, aggression, self-injury, and parental stress [9•]. Without accurate assessment and diagnosis in this population, anxiety and associated impairments are likely to go untreated and worsen with time [10].

Obsessive-compulsive disorder (OCD) is often reported in individuals with ASD, yet repetitive behaviors and intrusive, recurrent thoughts are present in both conditions and difficult to differentiate [2•, 11–16]. Establishing if some individuals with ASD present a clinical picture that warrants a separate diagnosis of OCD is challenging for clinicians, and there is ongoing debate concerning the nature of repetitive behaviors in ASD versus those observed in OCD [17•]. This review provides a broad overview of the literature on the prevalence, presentation, assessment, and treatment of anxiety and OCD in autism. We discuss possible relationships between anxiety and ASD and examine how repetitive behaviors are similar in ASD and OCD. Finally, we address challenges related to assessment and offer clinical guidelines for differential diagnosis and treatment of anxiety and OCD in individuals with autism.

Prevalence of Anxiety and OCD in Autism

Reports on the prevalence of impairing anxiety in individuals with ASD have varied significantly, with estimates ranging from 11 to 84% [2•, 18–20]. Estimates of OCD are somewhat narrower, ranging from 2.6 to 37.2% in children and adolescents with ASD [2•]. A recent meta-analysis of 31 existing studies concluded that 39.6% of young people with ASD had clinically elevated levels of anxiety or at least one anxiety disorder [2•]. Based on this meta-analysis, which utilized Diagnostic and Statistical Manual-Fourth edition (DSM-IV) criteria for anxiety disorders, which included OCD, rates of anxiety disorders in ASD are more than two times higher than those in typically developing children [21, 22]. In more detail, specific phobia (29.8%), OCD (17.4%), and social anxiety and agoraphobia (16.6%, respectively) were reported to be the most common anxiety disorders in youth with ASD. However, current prevalence rates using the DSM-5 have yet to be established [1].

The range of prevalence rates reported for anxiety disorders and OCD in ASD is likely influenced by the clinical heterogeneity of individuals with ASD, including the broad spectrum of intellectual and verbal abilities. For example, some studies have found anxiety in ASD to be positively correlated with intelligence quotient (IQ), whereas others have found no relationship or, in some cases, a negative correlation [18, 23, 24, 25•]. Furthermore, other studies have found that only specific anxiety symptoms (e.g., generalized, separation, and panic-related worries) were associated with higher IQ in individuals with ASD [23]. A similar mixture of findings is also evident regarding the relationship of anxiety in individuals with ASD and verbal abilities [10, 26, 27]. Some evidence suggests that assessment methods (questionnaires versus interviews) contribute to the wide range of estimates, as higher prevalence rates of generalized anxiety are reported in studies that used questionnaires compared to studies that used interviews [28, 29]. Moreover, overlapping symptoms and the sometimes unconventional presentation of anxiety in ASD likely contribute to inconsistent prevalence estimates, especially given that most studies have relied on anxiety measures not designed for this population [18, 30].

Presentation and Origins of Anxiety Disorders in ASD

The range of manifestations of anxiety that have been documented in ASD is large and heterogeneous, encompassing both classic and unconventional presentations, such as fears of change or novelty, worries surrounding circumscribed or specialized interests, and unusual phobias [31]. The variability of such manifestations as well as the overlap of many anxiety and autism symptoms poses considerable challenges to the ascertainment and classification of anxiety symptoms in ASD. For example, expressions of anxiety such as social withdrawal and ritualistic behaviors can be superficially similar to the core social deficits of ASD making the differentiation of these conditions difficult. Features that are common although not pathognomonic in ASD may also affect the expression of anxiety symptoms. For example, individuals with ASD who are minimally verbal and present with co-occurring intellectual disability may be unable to report their internal states (e.g., worry) and instead demonstrate anxiety through nonspecific behaviors (e.g. avoidance, disruptive behavior, tension). Similarly, ASD-related difficulties detecting, making sense of, emoting, and verbally reporting internal feelings and emotions may also alter the presentation of anxiety in verbally fluent individuals [32, 33]. Behaviors such as screaming, which might reflect manifestations of anxiety in a nonverbal child or child with limited emotion recognition, might also reflect learned patterns of behaviors aimed at escaping demands, obtaining attention, or other instrumental purposes that are *not* accompanied by anxious feelings [34, 35]. In this way, anxiety symptoms may be both altered in presentation and obscured by their co-occurrence with ASD.

Importantly, it remains unclear whether anxiety in ASD reflects a manifestation of the same etiological factors that cause core autistic symptoms, a causally unrelated co-occurring condition, a consequence of the challenges faced by individuals with ASD in their social environment, or a combination of different factors [8•, 36, 37].

Evidence supporting the notion that the co-occurrence of ASD and anxiety reflect a shared etiology (i.e., what causes ASD also causes anxiety) includes the presence of structural and functional abnormalities in brain structures such as the amygdala, hippocampus, ventromedial prefrontal cortex, and insula, in individuals ASD and those with anxiety [38, 39•]. However, causal pathways linking shared abnormalities to the clinical presentation of comorbid ASD and anxiety are unclear, and the fact that not all individuals with ASD have co-occurring anxiety speaks against a simple, shared etiology account.

Another possible scenario is that anxiety emerges a consequence of the social communication symptoms characterizing ASD. For example, impaired understanding of others' actions, communications, and expectations might result in experiencing the social world and its demands as unpredictable, chaotic, and ultimately anxiety-provoking [40–42]. Similarly, hypersensitivity to sensory stimuli (e.g., loud noises) that are common in ASD might lead to aversion and subsequent anxious responses to situations that normally would not provoke anxiety (e.g., advertisement jingles, balloons popping, vacuum cleaners). Although there is evidence supporting this scenario, if anxiety is the inevitable consequence of having ASD, again it is not clear why not all individuals with ASD have anxiety [37, 43]. Alternatively, it is possible that features that are frequently, but not universally associated with ASD, confer the increased risk of anxiety in ASD. These include intellectual disability, depression, obsessive-compulsive features, tic disorders, and emotional regulation issues, all of which are frequently associated with both ASD and anxiety [4••, 36, 44]. However, anxiety does not appear to be exclusively occurring in subgroups characterized by specific comorbidities or clinical profiles.

Importantly, though less often discussed, adverse life experiences may also increase the risk for anxiety in individuals with ASD [45]. For example, individuals with ASD frequently experience limited opportunities to express preferences and make choices, are at greater risk for being bullied, and exhibit extensive unmet needs throughout the lifespan and across dimensions of social, psychological, and medical support [46–49]. Although none of these potential relationships alone provides a conclusive explanation, a likely scenario is that the high prevalence of anxiety in ASD reflects the interplay between different, co-occurring risk factors.

Repetitive Behaviors, OCD and ASD

Repetitive behavior is a defining feature of both OCD and ASD and, in both conditions, refers to a set of behaviors that are performed repetitively and are considered to be inappropriate or odd [14]. In OCD, obsessions are intrusive, recurrent thoughts (often related to contamination, organization, or sexual/religious themes) that cause marked anxiety. Compulsions are typically performed in response to these intrusive thoughts and serve to relieve anxiety. Examples of compulsions include handwashing, checking, or other repetitive routine activities. For individuals with OCD, these repetitive behaviors are unwanted and bothersome.

In ASD, repetitive behaviors vary in type and severity and include stereotyped motor behaviors, such as hand flapping, rocking, shaking fingers in front of their eyes, or more complex behaviors, such as insistence on following the same routine in everyday life, lining up objects, and watching the same video over and over [17•]. Notably, and in contrast to OCD, some repetitive behaviors in ASD may not cause distress, but rather represent preferred or comforting activities for those on the spectrum. Even when linked to positive affect, it should be emphasized that repetitive behaviors in ASD can be time-consuming and lead to problem behaviors (e.g., noncompliance, tantrums, and aggression) when the individual is interrupted or asked to stop the behavior [16, 17•].

Given that both conditions are characterized by repetitive behaviors, discerning which behaviors are part of ASD and which reflect a comorbid OCD can be challenging [14]. In order to better understand the overlap between these two conditions, studies have investigated types of repetitive behaviors in individuals with ASD and OCD [11, 13–15]. Studies found that individuals with OCD show higher levels of obsessions and compulsions and greater symptom severity compared to individuals with ASD, and that these two clinical populations can be distinguished based on the content of their repetitive thoughts and behaviors [11, 13–15]. For example, McDougle et al. (1995) investigated the types of repetitive behaviors in 50 patients with ASD and 50 patients with OCD, and found that participants with ASD were less likely to experience thoughts with aggressive, contamination, sexual, or religious content [11]. Similarly, Ruta et al. (2010) found that OCD individuals reported higher frequencies of contamination and aggressive obsessions, and checking compulsions compared to ASD individuals who, on the other hand, displayed slightly higher frequencies of hoarding obsessions [13].

Challenges with Assessment of Anxiety and OCD in ASD

Measurement and assessment of anxiety disorders and OCD in autism can be complicated by the social impairments characteristic of ASD, such as deficits in communication, insight, ability to recognize emotions, or a co-occurring intellectual disability [5, 8•, 9•, 39•].

A high proportion of individuals with ASD present a co-occurring intellectual disability (IQ < 70) [50]. Generally, a low IQ in this subset of the population is associated with language impairments. For individuals who are minimally verbal, the diagnostic process must rely on information gathered from

parents, teachers, or other caregivers. However, parent or teacher reports of anxiety in minimally verbal individuals with ASD are inferential, and thus may overestimate or underestimate the presence of anxiety and OCD. In fact, it may be difficult for parents to recognize anxiety or obsessive-compulsive symptoms in their child with ASD, but it is also possible that parents misinterpret ASD features to be anxiety or obsessive-compulsive symptoms. For example, behaviors such as screaming, crying, and throwing self to the floor can be interpreted as manifestations of anxiety; however, these behaviors could also reflect learned patterns of behaviors that are aimed at escaping demands or obtaining attention, and are not accompanied by anxious feelings. Similarly, repetitive behaviors, such as making lists or watching the same video over and over may appear to be part of OCD; however, these behaviors in ASD are usually experienced as an enjoyable and rewarding activity, and are not associated with distress [17•, 34, 35].

On the other hand, assessment challenges exist also with individuals that are verbally fluent. As mentioned above, it is possible that even individuals with average language skills may be unable to describe their emotional and internal states or recognize the connection between obsessions and compulsions due to deficits in emotion recognition or insight which complicate self-report instruments as well as the ability of parents and clinicians to understand a child's worries [17•, 39•]. As such, even with verbal children, clinicians and practitioners must often rely on observable behavior, rather than self-reports.

Many of the currently available measures to evaluate anxiety and OCD were initially developed and standardized for typically developing children; therefore, it is possible that these measures may not adequately differentiate between autism and anxiety or obsessive-compulsive symptoms [39•]. However, a number of instruments exist to support the identification of anxiety symptoms in ASD [8•, 39•, 51]. Brief, informant report measures include the Child and Adolescent Symptom Inventory (CASI), which was designed to exclude potentially overlapping anxiety and ASD symptoms; the Autism Spectrum Disorders-Comorbidity for Adults scale (ASD-CA); and the Anxiety Scale for Children with Autism Spectrum Disorder (ASC-ASD) [5, 23, 52, 53]. Bearss et al. (2015) also recently described the use of focus group transcripts generating 52 candidate items for the initial development of a parent-oriented outcome measure of anxiety symptoms in youth with ASD [54].

Although a number of standard anxiety questionnaires, such as the Multidimensional Anxiety Scale for Children, (MASC-C), the Revised Children's Anxiety and Depression Scale (RCADS), the Screen for Child Anxiety and Related Emotional Disorders (SCARED), and Spence Child Anxiety Scale (SCAS), among others, have been used with youth on the autism spectrum, these tools were not specifically designed for ASD and research on their psychometric properties in this population is mixed [8•, 55–59]. In addition to these brief questionnaires, the Anxiety Disorders Interview Schedule with Autism Spectrum Addendum (ADIS/ASA) offers a more comprehensive assessment of anxiety in ASD, including a systematic approach for differentiating anxiety and ASD symptoms [60]. Moreover, the Comorbidities Interview (ACI) Interview offers an adaptation of the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) for youth with ASD, though research has only examined the validity of the depression, attention deficit hyperactivity disorder (ADHD), and OCD sections thus far. Finally, Witwer et al. (2012) found that the Children's Inventory for Psychiatric Syndromes-Parent Version (CIPS) demonstrated good inter-rater reliability for specific phobias as well as generalize, separation and social anxiety, though agreement was more limited for OCD, ADHD, and mood disorders as well as for generalized anxiety disorder in youth with IQ < 70 [61].

Regarding measures for OCD in ASD, the Children's Yale-Brown Obsessive Compulsive Scales for ASD (CYBOCS-ASD) has been shown to be a reliable measure to evaluate repetitive behaviors in youth with ASD [16, 62]. Other tools to evaluate repetitive behaviors in ASD include the Autism Diagnostic Interview-Revised (ADI-R), the Repetitive Behaviour Questionnaire (RBQ), the Repetitive Behaviour Interview (RBI), and the Repetitive Behaviour Scale-Revised (RRB-R) [63–66].

Overall, given that our understanding of the psychometric properties of existing and newly developed measures is still evolving, caution should be exercised in interpreting assessment results, and integration of information from multiple sources, including caregiver report and direct observation, is recommended. Current research is also exploring the viability of tools detecting physiological measures such as heart rate, skin conductance responses, or heart rate variability which might provide future avenues to overcome the barriers inherent to current assessment techniques.

Current Approaches to Treatment

Research suggests that cognitive-behavioral therapy (CBT), an empirically supported treatment for anxiety, is highly effective for treating youth with anxiety, ASD, and average to above average IQs [67, 68]. Empirically supported CBT programs that have been adapted specifically for youth with ASD and anxiety aim to enhance child engagement, comprehension, retention, and generalization of CBT skills by increasing parent involvement; using interactive, visual, or multimodal teaching strategies, and incorporating special interests into sessions [69]. Augmenting traditional CBT strategies with social skills training and parent management techniques have also been used to address broader deficits that potentially contribute to and/or exacerbate anxiety [69]. Research in

treating adults with anxiety and ASD is more preliminary, but also suggests that CBT approaches and mindfulness techniques may be promising [70••, 71]. Behavioral treatment for individuals with OCD and ASD has received much less attention in the literature, but existing research suggests that obsessive-compulsive symptoms can improve with CBT [72]. Finally, single-subject studies also support behavioral treatments for phobic avoidance in those with ASD and intellectual impairments; however, larger clinical trials have yet to be conducted [73].

Selective serotonin reuptake inhibitors (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) is considered the first line of psychopharmacological treatment for anxiety disorders or OCD in the general population [74]. However, research on the use of SSRIs in individuals with anxiety or OCD and ASD is lacking and there is some evidence that individuals with ASD are particularly vulnerable to the behavioral activation side effects of SSRIs, including impulsivity, insomnia, and overall increased activity [75, 76]. Prescribing SSRIs for individuals with ASD and anxiety or OCD should therefore be approached cautiously.

Conclusion

In this paper, we reviewed recent research examining the relationship between anxiety and OCD in individuals with ASD, including challenges for assessment and implications for treatment. While there is some evidence lending insight into the relationship between anxiety disorders, OCD and ASD, there remains a need for more refined frameworks and practice parameters, including fine-grained models of how and why these conditions occur in ASD tested via longitudinal research designs, and clinical tools to identify and address symptoms of anxiety throughout the lifespan.

In this review, we have discussed several complexities that are inherent to differential diagnosis of anxiety, OCD, and ASD, which make true comorbidities particularly difficult to assess. During the diagnostic process, it has to be considered that autism symptoms might be so prominent in the individual's clinical presentation, that parents and professionals may not even consider the possibility of an anxiety disorder in an individual with ASD. On the other hand, it is possible that ASD symptoms might be misattributed to underlying anxiety or OCD by caregivers and professionals. Given the high incidence of these conditions in ASD, there is an obligation for the field to continue the development and validation of screening instruments that are specifically designed to quickly and accurately evaluate clinical levels of anxiety and OCD symptoms in individuals with ASD.

Moreover, investigation of physiological measures of anxiety in ASD is especially appealing in light of the cognitive and verbal deficits that are prevalent in this population. Research has begun to explore the use of physiological measures as biomarkers of anxiety in youth with ASD, and preliminary findings suggest that cardiovascular reactivity may be one option [77–80]. Identification of simple and reliable biomarkers for anxiety also holds promise for providing a convenient outcome measure for clinical trials of anxiety in ASD.

Despite some initial support for the use of CBT for anxiety and OCD in ASD, most anxiety treatment studies for children with ASD target high-functioning children, leaving effective treatments for children with lower verbal and IQ skills largely unknown. Moreover, the use of behavioral and psychopharmacological interventions for these conditions in this population lacks robust, large clinical trials with longer term outcome, and this should be a focus of future research [67]. Fortunately, these studies are under way (e.g., the Translational Adolescent and Childhood Therapeutic Interventions in Compulsive Syndromes project (TACTICS)) [81••].

Recently, research has suggested several novel behavioral treatments for comorbid ASD and anxiety that extend beyond traditional CBT programs. For example, social skills training, which does not explicitly target anxiety symptoms, has been shown to significantly reduce social anxiety in adolescents with ASD [82, 83]. Similarly, treatments that aim to improve executive function (e.g., flexibility and emotion regulation) for children with ASD have been shown to improve symptoms of anxiety [84–86]. Mindfulness-based treatments are also beginning to show promise for reducing anxiety in this population [71, 87].

Consideration of other co-occurring conditions will be important in designing interventions that improve overall functioning for children with ASD. Many children with ASD struggle with other behavioral and mental health problems that may or may not be related to anxiety, including ADHD, depression, disruptive behavior, feeding disorders, and sleep disorders [3, 4••]. It will be important to design interventions that target pivotal areas of the child's behavioral and emotional functioning, which may have collateral effects on several other domains and improve the child and family's overall quality of life.

In the past decade, advances in the understanding and early identification of ASD promoted a shift from reactive to preventative efforts in the treatment of core ASD symptoms [30, 88, 89]. This approach capitalizes on the opportunity to target symptoms of ASD during early sensitive periods when neurodevelopmental trajectories can be advantageously altered [90]. Extending the same logic to the issue of anxiety, some early intervention programs for infants and toddlers with or at-risk for ASD use evidence-based strategies to teach and facilitate skills that improve coping and resilience and may prevent or attenuate the escalation of anxiety symptoms, such as emotion regulation [91]. The development of theory-driven preventative approaches to anxiety in ASD holds the potential

to bridge the gap between ASD early intervention approaches and CBT practice and minimize the debilitating burden associated with anxiety in this population.

Compliance with Ethical Standards

Conflict of Interest Valentina Postorino, Giacomo Vivanti, Jessica Bradshaw, Martina Siracusano, and Luigi Mazzone declare that they have no conflicts of interest.

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Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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