# Comorbidity of ADHD with Anxiety Disorders and Obsessive Compulsive Disorder

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## Prevalence and Morbidity

Child psychiatric disorders have heavily overlapping symptom presentations. It is not atypical for a child to present with multiple symptoms that fall into various diagnostic categories. Comorbidity, however, is defined in epidemiologic samples as an occurrence of co-diagnosis greater than chance. Clinical samples may be useful for looking at mechanisms of comorbidity, but always overstate the amount of comorbidity, because of biases related to the referral of more complex cases to clinics for assessment and treatment. The prevalence of combined ADHD and anxiety is high in clinically referred samples, over 30% [1, 2].

In large epidemiologic samples, both ADHD and anxiety occur at estimated rates of 5–10% each. If truly non-comorbid, one out of 100 or more children would have both. However, these disorders are highly comorbid, with a three times odds ratio for ADHD and anxiety, compared to an 11 times odds ratio for ADHD and conduct disorders, and a five times odds ratio for ADHD and depression [3]. OCD often begins in prepubertal children, and the prevalence of pediatric OCD is about 2–3% [4]. More than 50% of pediatric patients with OCD have been found to have at least one comorbid psychiatric disorder [5], with approximately 30% meeting criteria for

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ADHD [6]. An earlier age of OCD onset predicts increased risk for ADHD. Much more attention has been paid to the comorbidity of externalizing disorders such as conduct disorder with ADHD than to comorbid anxiety or OCD with ADHD.

## Etiological Factors

### Theoretical Approaches to Comorbidity

As Caron and Rutter have described [7], true comorbid presentations my arise by several different means. *First, separate diagnoses may have shared risk factors*. This is especially true in psychiatric disorders because they are often multifactorial, and causative factors are not specific to only one disorder. Second, separate risk factors for each disorder may themselves tend to co-occur (for instance, parental substance use disorders and traumatic exposure). Third, one disorder could create a risk for the other through a causal chain (e.g., ADHD and its associated chronic school failure triggers long-term anxiety, or creates the need for OCD symptoms as a counter-measure to cope with ADHD's inattentive symptoms). Fourth, the two disorders when they occur together may represent a distinct variety of one of the disorders or a truly separate disorder itself, requiring new treatments or having outcomes that are distinct from either of the two disorders occurring alone [7]. Accordingly, Jensen and colleagues have also discussed ways to examine comorbidity of disorders through their phenomenology and temporal relations between symptoms; other comorbidities; demographic, psychosocial, environmental, and family factors; genetics and temperament; and treatment response and clinical outcome [1].

In reviewing studies on comorbidity, one must keep in mind the potential artifacts related to confounding data and different approaches to the data. Firstly, the bias toward increased comorbidity when using clinical samples has already been mentioned [7]. Secondly, using dimensional rather than categorical measures of symptoms related to the diagnoses in question may be helpful. There are times when both dimensional and categorical approaches may also be useful, though this has generated some controversy [8]. The development of Research Domain Criteria (RDoC) [9] allows the study of diagnosis-crossing concepts such as emotion dysregulation, which may help elucidate biological mechanisms of comorbidity [10].

Next, studies should consider a developmental perspective, looking at the age that symptoms develop, or how comorbidity may change or develop over time [11]. In addition, nonspecific overlapping symptoms may be hallmarks of different diagnoses. For instance, anxious children may have situational inattention, impulsivity, and motor restlessness. Children with ADHD may eventually develop anxieties regarding school performance or peer relationships that may or may not meet full diagnostic status for a syndromal anxiety disorder. Likewise, the obsessions and compulsions of OCD may cause distractions, task avoidance, or restlessness, mirroring the symptoms of ADHD. Also important is to be mindful of contradictory information between informants, which may confound categorization of comorbidity. For example, in the Multimodal Treatment Study of ADHD, findings were different depending on whether analyses used parent- or child-reports of anxiety [12].

A further concern is the problem of severity of diagnosis, which may intensify relationships between separate diagnoses. In some studies, worsening anxiety symptoms lead to more long-standing functional problems with ADHD [13]. There is a high prevalence of ADHD in youth with both OCD and tic disorders, and such children with all three diagnostic categories have more severe symptomatology [14]. However, the presence of ADHD does not seem to alter clinical presentation or OCD or vice versa [15]. Some studies merge multiple anxiety diagnoses into one category or use atypical concepts of ADHD such as "sluggish cognitive tempo" [16]. Finally, it is possible that a third diagnosis explains comorbidity in a particular case, such as anxiety and inattention frequently co-occurring with autism [17], obsessive compulsive symptoms associated with Tourette's syndrome [18], or depression arising from chronic anxiety, as the true comorbid factor [19].

## Neurobiology

There is a strong neurobiological basis for ADHD as a diagnosis, such that various biological deficits involving prefrontal systems contribute to various inattentive, hyperactive, and/or impulsive symptoms [20]. First, the dorsolateral prefrontal cortex modulates attention, cognition, and motivation through connections with the thalamus, cerebellum, and circuitry back to the cortex via multiple feedback loops [21]. Second, the orbital and medial prefrontal cortex circuitry connect to the amygdala, nucleus accumbens, and brainstem and modulate attentional processes dependent on reward and emotion. These two types of circuitry have been labeled as "cold" and "hot" processing, with the "cold" processing being more background in nature and the "hot" processing being dependent on emotional reactivity factors [22]. Involved neurochemical systems have included catecholamines, intermediary glutamate and GABA, and more recently, serotonin in the orbitofrontal cortex for attentional processes [23].

The neurobiology of pathological anxiety involves dysregulation in the anterior limbic network, which includes the orbitofrontal, ventrolateral, and ventromedial prefrontal cortices, with connections to the insula, anterior cingulate, and amygdala. Neurochemical systems also overlap with those for attentional processes. Pathological anxiety is thought to be largely related to excessive responsiveness in the amygdala, but other structural and connectivity problems may also play a role [24].

The paradox is that anxiety, associated with behavioral *inhibition* and its related neural systems, often *co-occurs* with ADHD, associated with systems of behavioral *disinhibition*. Both systems share frontal connectivity, as described above, through different but overlapping subcortical networks. The frontal cortex may be a governor for excessive amygdala responsiveness, and the anterior cingulate may modulate dual processes related to both cognitive and emotional systems [25]. The striatum may be an important mediator between what at first appear to be disparate circuits [20]. From a pharmacological perspective, excessive norepinephrine from high doses of stimulants (and possibly in high-anxiety states) may lead to decreasing attentional responses [26].

In order to tie attention processes and anxiety dysfunction, Levy postulates the nucleus accumbens as being central. In her view, poor cortical inputs from impaired frontal reward and punishment circuitry affect nucleus accumbens firing, which further leads to amygdala hyperactivity [27]. McNaughton and Corr offer an alternative, more behavioral, explanation, positing that underactivity of the prefrontal cortex's functions related to behavioral inhibition puts patients with ADHD at greater risk of experiencing situations that involve imminent threats. The experience of such imminent threats, in turn, leads to activation of subcortical anxiety circuits, which lack the inhibitory functions associated with prefrontal cortex [28].

The neurobiology of ADHD and OCD is vastly different. Frontostriatal dysfunction is present in both disorders; however, neuroimaging shows *hypoactivation* with *decreased* functional connectivity in ADHD and *hyperactivation* with *increased* functional connectively in OCD [29]. Specifically, ADHD-specific deficits are seen in the parietal lobes, caudate and posterior cingulate, while there is disorder-specific dysfunction of the dorsolateral prefrontal cortex in OCD [30].

## Risk Factors and Associations

ADHD comorbid with anxiety or OCD is a conceptually complex phenotype that is not static, but instead appears to have several possible developmental trajectories. Genetic, psychosocial, familial, perinatal, temperamental, and cognitive correlates (and even the psychopathology itself, i.e. ADHD and OCD or anxiety disorders) may serve as risk factors for development and as moderators of outcome.

The most relevant studies examining the genetic influence on ADHD with comorbid disorders are latent class analysis (LCA) in twin studies and familial association studies. The few LCA studies do not show a differential clustering of internalizing symptoms in either the predominantly inattentive subtype (ADHD-I) or the combined subtype (ADHD-C) of ADHD [2]. Several familial association studies have provided evidence suggesting that ADHD and anxiety disorders are transmitted independently in families [31]. Male probands with ADHD and anxiety were much more likely to have first-degree family members with anxiety than probands with "pure" ADHD [32]. An inability to correlate symptom severity between ADHD and internalizing disorders for affected children and their parents also suggests independent transmission [33]. A familial study of children with ADHD and comorbid anxiety has suggested a strong association of child anxiety with maternal anxiety, but not with paternal anxiety [34]. Having a father with psychiatric illness significantly increases the risk of a child with ADHD having a comorbid internalizing disorder (including anxiety disorders) [35].

Shared genetic risk factors have been found for comorbid ADHD and OCD as part of a clinical triad also including tic disorders [36]. Geller and colleagues have used familial risk analysis to examine children with OCD, ADHD, and both disorders and their first-degree relatives. The studies suggested that comorbid ADHD and OCD could be a distinct familial subtype in which the disorders are genetically

transmitted together [37, 38]. It is important to remember that familial association studies cannot fully separate genetic from environmental sources of family transmission [2].

There is evidence to suggest that the perinatal period may influence the development of ADHD with OCD or anxiety. High levels of antenatal anxiety were predictive of ADHD symptoms and self-reported anxiety in children [39]. ADHD with comorbid anxiety has been associated with hyperemesis and maternal use of stimulant medication while pregnant [40]. OCD has been associated with perinatal complications, such as prolonged labor and edema during pregnancy [41], but there is little information regarding perinatal complications producing ADHD with comorbid OCD. There is a male preponderance seen in both ADHD and pediatric OCD. Even the first few years of a child's life may be clinically predictive. Irritability, temperamental emotionality, and high activity level at age 3 are associated with later onset of comorbid ADHD and internalizing disorders [11].

It is possible that a particular group of vulnerable children develop both ADHD and anxiety symptoms in response to psychosocial and familial stressors. Jensen and colleagues found that children with ADHD and comorbid depression or anxiety have both higher levels of life stress (including parental separation and divorce) and higher levels of maternal psychiatric symptoms [42]. These children also have more school and social difficulties [43], lower self-esteem [44], and are at greater risk for developing suicidality [45]. Conversely, another study found the opposite, that there was no additional social impairment in children with ADHD and anxiety compared to ADHD alone [46]. Families of children with ADHD and anxiety were found to be more insular, more dependent, and to have a more controlling family environment [47].

With respect to response inhibition and impulsivity, anxiety has been found to only partially mitigate impulsivity in ADHD [48]. Behaviorally, ADHD is considered an externalizing disorder, characterized by impulsivity and risk taking, while OCD is an internalizing disorder, characterized by behavioral restraint and harm avoidance. This seemingly puts the disorders on opposite poles of the spectrum, and has been referred to as the impulsive-compulsive continuum of behavior [49]. Accordingly, one would hypothesize that more patients with OCD have ADHD-I than ADHD-C. While there are few studies to prove this hypothesis, one study found the contrary (69% of youth with ADHD and OCD had ADHD-C and 24% had ADHD-I) [50].

The evidence regarding the effect of comorbid anxiety on cognitive performance in children with ADHD has been conflicting. A comparison of children with both ADHD and anxiety to children with either "pure" ADHD or normal controls found no significant difference in information processing between the two ADHD groups [51]. Conversely, some studies show children with ADHD and comorbid anxiety have greater difficulty with tasks of working memory and effortful processing [52], as well as emotional regulation [53]. It has been theorized that anxiety may serve to preempt storage within the working memory system, while paradoxically also improving motivation and performance [52]. The relationship between ADHD, anxiety, and working memory is increasingly complex, and the relationships may vary depending on the ADHD subtype [54]. Finally, studies suggest that children

with sluggish cognitive tempo (SCT) (daydreaming, staring, mental fogginess, apathy, and physical hypo-activity) are more likely to have comorbid anxiety [16].

In both ADHD and OCD there are performance deficiencies in executive function, particularly working memory and response inhibition. Studies have suggested that these deficiencies, although similar, are due to different underlying mechanisms [55]. The obsessions and compulsions of OCD can lead to symptoms resembling ADHD. The executive overload theory of OCD explains this inattention as being caused by exhaustion of the executive system from organizing rigid compulsive rituals and controlling obsessive thoughts [29].

## Assessment and Differential Diagnosis

### Symptom Presentation and Diagnosis

There is frequently an overlap between ADHD, OCD, and anxiety symptoms, which poses a diagnostic challenge. These disorders can share symptoms of inattention and poor performance at school. Moreover, anxiety can emerge in response to the social and academic deficits caused by ADHD [56]. The hyperactivity of ADHD can include fidgeting, restlessness, and over-activity so that the child appears to be "driven by a motor." Children with anxiety can often appear restless, keyed-up, or on edge, and have concentration problems due to excessive worry. Children with OCD might have externalizing symptoms similar to those seen in ADHD, like trouble sitting in class or paying attention to directions. Unlike children with ADHD, the hyperactivity and inattention would be due to intrusive anxious thoughts [57]. The developmental time course of the disorders can aid in diagnosis. ADHD is usually discovered in early childhood, preceding symptoms of anxiety and OCD [50]. ADHD-like symptoms associated with internal distractions would occur *after* the emergence of OCD as a direct result of the obsessions and compulsions. If ADHD-like symptoms pre-date the OCD symptoms, then true comorbidity is more likely [50]. Children with ADHD and comorbid anxiety or OCD often have cumulative impairment from the combination of these disorders [43].

Diagnostic assessment requires a detailed developmental history and psychiatric interview with guardians and the child. Since much of information in children comes from secondary informants, teachers and other caregivers can also share their observations of the child's behavior. Assessment strategies for diagnosis can include global scales like the Child Behavior Checklist and Behavioral Assessment System for Children (now known as the ASEBA) forms [58]. There are many standardized, disorder-specific scales for anxiety pediatric anxiety disorders such as Multidimensional Anxiety Scale for Children (MASC) [59] and the Screen for Child Anxiety Related Disorders (SCARED) [60]. For assessing OCD, there is a more commonly used measure done by interview, the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) [61], and a brief questionnaire modified from an adult questionnaire for pediatric ages called the Short Leyton Obsessional Inventory for Children and Adolescents [62]. Finally, to assess ADHD, there are

multiple parent and teacher measures available, including the Vanderbilt [63, 64], the Conners 3 [65], the Iowa Conners [66], or the SNAP-IV [67].

There are no specific labs tests or imaging studies recommended, however, the medical exam should include assessment for hearing and vision problems, thyroid dysfunction, and neurological abnormalities. The clinician should carefully review any psychological testing already completed to rule in or rule out learning disabilities. If the patient is prepubertal in age, with an abrupt onset and episodic course of OCD symptoms or tic-like movements, emotional lability or other psychiatric symptoms (e.g., anxiety, nighttime fears and bedtime rituals, hyperactivity, and oppositionality), and a history suggestive of recent streptococcal throat infection, the clinician might consider additional testing for the so-called Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) syndrome [68]. Please also see Table 3.1 in Chap. 3 for further review of PANDAS.

## Treatment

### Psychosocial Treatment

To date, there are no evidence-based psychosocial treatments for youth with both ADHD and comorbid OCD or anxiety. Our understanding of treatment has come mainly from the NIMH-funded Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA) study [69]. This study suggested that children with ADHD and comorbid anxiety might benefit more from behavioral therapy than children with ADHD alone. Behavioral treatment for children with comorbid parent-rated anxiety was as effective as medication management and combined treatment, all of which surpassed community care. Of note, the MTA's behavioral treatment targeted symptoms of ADHD (including aggression, academic productivity, and social skills) and did not specifically address anxiety symptoms [70]. The MTA cooperative group concluded that behavioral treatment should be added for those children with ADHD, strong negative affectivity, and disruptive behaviors. They posited that reducing core ADHD symptoms may lead to improvement of internalizing symptoms such as anxiety. For children with ADHD and comorbid phobic symptoms, however, adding cognitive behavioral therapy (i.e., restructuring and exposure) was recommended [12].

Outside of MTA, only a handful of studies have examined psychosocial treatment response in youth with both ADHD and anxiety disorders, with mixed results. Several studies of CBT-based treatments did not show a difference in treatment response between youth with anxiety and those with comorbid ADHD [71]. However, the Child/Adolescent Anxiety Multimodal Study (CAMS) suggested that comorbid ADHD hinders the effectiveness of CBT for pediatric anxiety [72]. Children with specific phobias and comorbid ADHD also responded less well to brief intensive CBT in comparison to children without ADHD [73]. CBT with exposure and response prevention (ERP) is the first-line treatment for OCD in children. Some have raised concerns that behavioral treatments for ADHD, such as increased

structure and organization, might trigger or worsen checking rituals and other compulsive behaviors of OCD [29]. The exposures in ERP and coding of corrective information from the therapy, as well as the habituation processes key to CBT, may also be less effective in patients with ADHD because of their inattentive, hyperactive, and impulsive symptoms. For these reasons, family CBT-based interventions may be more beneficial than individual CBT in anxious children with high levels of ADHD symptoms [74].

A few other studies have designed unique psychosocial treatment modalities to address co-occurring ADHD and anxiety or obsessive compulsive disorders. A modified cognitive behavioral family-based approach with additional psychoeducation sessions for ADHD resulted in a decrease in anxiety symptoms, but no improvement in ADHD symptoms [75]. More recently, an integrated approach that combined parent training (Barkley's Defiant Child) with a modified family-based CBT approach (Cool Kids Program) has been developed. Improvements in both anxiety and ADHD were noted, though gains were limited for ADHD symptoms [76]. Neuropsychological remediation (i.e., working memory training) may target cognitive difficulties that are common to both ADHD and anxiety [53]. Finally, based on an association between childhood anxiety, ADHD, and sensory over-responsivity (characterized by hypersensitivity to sensory stimuli), occupational therapy can be helpful within a larger treatment plan [77].

## Psychopharmacological Treatment

Stimulants are the first-line medication to treat ADHD and selective serotonin reuptake inhibitors (SSRIs) are the preferred treatment for anxiety disorders and OCD [72, 78]. These medications have proven efficacy in randomized controlled trials for their respective disorders, but are not necessarily effective for comorbid conditions. In contrast, atomoxetine offers a single medication that can be used to treat symptoms of both anxiety and ADHD.

### Stimulants

Stimulants decrease the core ADHD symptoms of hyperactivity, impulsivity, and inattention. The therapeutic effects are rapid, and stimulants have proven efficacy and safety in randomized controlled trials. Amphetamine and methylphenidate are the stimulants that have received U.S. Food and Drug Administration (FDA) approval for the treatment of youth with ADHD [78].

The studies that have been conducted using stimulants in children with ADHD and comorbid anxiety or OCD have had mixed results. This is likely due to methodological differences or variations in medication titration [12]. Several mainly older studies suggest that stimulant use in children with ADHD and anxiety led to higher dose requirements [79], more side effects, and a poorer response to the drug [80]. Some researchers feel that children with both disorders might make up a distinct population who have a different response to medication than children with ADHD alone [32, 81]. Conversely, more recent studies have found stimulants produce

comparable improvements in children with and without anxiety [81–83] or an even better response to treatment when comorbid anxiety is present [84]. Side effects to stimulants were not significantly greater, and anxiety was not exacerbated in anxious children taking stimulants [12, 83]. In contrast, findings from the few studies regarding the effects of stimulant treatment on OCD have been more consistent. Several case studies suggest that stimulants may exacerbate OCD symptoms or anxiety [85]. Relative to OCD without comorbid ADHD, OCD *with* ADHD is associated with an earlier age of onset of the OCD, more severe and persistent OCD symptoms [86], poorer treatment outcomes [86, 87], and a greater likelihood of relapse of the OCD symptoms after an initially favorable treatment response [4].

Monotherapy with stimulants has not been found to be an effective treatment for anxiety disorders without ADHD, but many studies have shown improvement in anxiety when symptoms of ADHD are treated. This improvement is likely secondary to improvement in ADHD symptoms and associated anxiogenic situations due to the interpersonal and academic problems associated with ADHD. A recent meta-analysis found lower rates of anxiety in children with ADHD given stimulants versus placebo as well as a dosing effect where higher stimulant doses led to lower rates of anxiety [88]. In a study by Abikoff and colleagues, some children with ADHD and comorbid anxiety treated with methylphenidate no longer suffered from anxiety after receiving the stimulant, indicating that impairment in function can improve on stimulant monotherapy for some patients with this comorbid presentation [82].

### Nonstimulants

The nonstimulant Atomoxetine, a norepinephrine reuptake inhibitor (NRI), is approved by the FDA to treat ADHD in children and adults. Two randomized controlled trials comparing atomoxetine with placebo for treating pediatric ADHD with comorbid anxiety showed that atomoxetine was efficacious in reducing ADHD symptoms and well tolerated [89, 90]. There was also reduction in anxiety symptoms in clinician- and self-rated scales [90]. Of note atomoxetine takes several weeks to achieve maximum benefit, which is an important clinical consideration [91]. There is no evidence to suggest that atomoxetine is effective in treating OCD.

The evidence base for treatment of children with anxiety has been established for selective serotonin reuptake inhibitors (SSRIs) [72]. The FDA has approved the SSRIs Fluvoxamine, Sertraline, and Fluoxetine for use in children with OCD. In addition, Paroxetine, Citalopram, and Escitalopram have also shown efficacy relative to placebo [92]. There is scant evidence that SSRI monotherapy is useful in treating ADHD symptoms. A small open label pilot study suggested moderate improvement after 6 weeks of fluoxetine in children with ADHD [93], however no further studies are available to support this. A clinical consideration when using SSRIs is the possibility of activation. This is an increase in activity level without a change in mood or manic symptoms, which could be mistaken for worsening ADHD. Symptoms of activation appear early in the course of treatment, or with dose increases. Such symptoms generally dissipate with a decrease in the SSRI's dose or with discontinuation [94]. Another potential concern is the black box warning for all antidepressants regarding the risk of new or worsening suicidal ideations

or behavior [95]. Fortunately, the risk benefit ratios are more favorable for OCD and especially for anxiety disorders relative to MDD in children or adolescents on antidepressants considering the higher base rate of suicidal ideations or behaviors in depressed patients [96], but still suggest the need for clinicians to closely monitor their patients with anxiety disorders or OCD being treated with antidepressants.

Regarding other medication options, Bupropion is an antidepressant with noradrenergic and to a lesser extent dopaminergic properties that has shown modest efficacy in ADHD and has been used off-label for the treatment of ADHD in children [97]. Given the fact that bupropion has no serotoninergic effects, it would not likely be effective for OCD, and the common notion is that it is also not effective for anxiety disorders. However, its mechanism of action is similar to atomoxetine's, which as previously noted has been shown to have some benefit for anxiety. Moreover, one large randomized placebo controlled trial in adults suggested that bupropion's efficacy for anxiety disorders in patients with major depressive disorders was comparable to sertraline's [98]. Tricyclic antidepressants (TCAs) have individually been used to treat ADHD, anxiety, and OCD (most commonly clomipramine) [86]. However, there are no studies evaluating their effectiveness in youth with ADHD and comorbid anxiety or OCD, and their side effects and potentially lethality if taken in overdoses make them rarely used in current clinical practice. The long-acting α2-adrenergic agents guanfacine extended release and clonidine extended release have been FDA approved as monotherapy and adjunctive treatment of ADHD in children 6–17 years old. Guanfacine has been shown to improve traumatic stress related symptoms and PTSD nightmares in children and adolescents [99]. A recent case study described a child with comorbid ADHD and OCD who had a good response to guanfacine for impulsivity and inattention when a previous stimulant trial was poorly tolerated [100].

### Combination Pharmacotherapy

Medication combinations are commonly used when patients present with multiple symptoms from comorbid disorders, although the evidence to support this practice is not conclusive. A randomized double-blind study of children with ADHD and anxiety or mood symptoms found similar improvement in patients on atomoxetine alone versus atomoxetine plus fluoxetine. Fluoxetine did not seem to have a direct effect on ADHD symptoms [89]. The combination was well tolerated, but was not superior to atomoxetine monotherapy for anxiety symptoms. If a child was already being treated with fluoxetine, the authors felt that the addition of atomoxetine could be useful. Abikoff and colleagues explored the combination of both methylphenidate and fluvoxamine to treat comorbid anxiety and ADHD. The study suggested a high rate of response in ADHD symptoms to methylphenidate, but no additional benefit for anxiety with the addition of Fluvoxamine versus placebo [82]. When using medication combinations it is important to monitor for possible medication interactions. There are no formal studies examining combination pharmacotherapy for ADHD with comorbid OCD.

### General Recommendations

The Texas Medication Algorithm Consensus Panel recommends a trial of stimulant with addition of SSRI if necessary for continued anxiety symptoms in children with ADHD and comorbid anxiety [101]. A combination of medication and psychotherapy is usually indicated [82]. Stimulants have been found to be well tolerated and effective for ADHD in children with comorbid anxiety [70, 82]. Some children may show decreased anxiety when their ADHD symptoms are controlled. Atomoxetine can also be considered, but stimulants have more rapid onset, higher efficacy and usually do not increase symptoms of anxiety. If one disorder is more impairing than the other, it is reasonable to treat the more impairing disorder first [91]. A baseline review of systems is helpful, as children with ADHD and anxiety often have pretreatment physiological symptoms (i.e., headaches and stomachaches) that can be misinterpreted as medication side effects when not properly identified up front [83]. Based on the worsening anxiety on placebo seen in some RCTs, re-challenging a child who has experienced increased anxiety on a stimulant would be reasonable as such anxiety may be unrelated to medication [88]. Children with ADHD and comorbid OCD whose OCD symptoms *worsen* on a stimulant may respond better if their ADHD is instead treated with guanfacine [101].

## Concluding Remarks and Critical Next Steps

ADHD that is comorbid with anxiety or OCD seems to have distinct risk factors, but also clear moderators of co-occurrence. Both the ADHD and either the anxiety disorder(s) or OCD must be recognized when they co-occur so that adequate treatment approaches are considered. Combination therapy using psychotherapy and psychopharmacology will in all likelihood produce the most favorable treatment outcomes, but additional clinical studies are needed. Further research should also attend to sequencing and combining treatments, both medication and psychosocial, for these highly prevalent comorbid conditions. Finally, more attention should be given to the longer-term outcomes of these common comorbidities.

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