# Chapter 6
# Associated Comorbid Conditions

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Comorbidity is defined as the co-occurrence of two (or more) independent clinical diagnoses in the same person (Matson & Nebel-Schwalm, 2007). Comorbidity in ASD means that, in addition to meeting the full criteria for autism disorder, the child receives a diagnosis of another disorder such as a mood disorder, attention-deficit/hyperactivity disorder (ADHD), or obsessive compulsive disorder (OCD). The identification of comorbidity in ASD has important clinical-therapeutic implications. If a child does have another disorder, that comorbid disorder should receive specific treatment in addition to the interventions and educational strategies that the child receives based on the autism diagnosis. For example, individuals with HFASD who have comorbid psychiatric conditions may demonstrate a more complex neurodevelopmental disorder than those with HFASD alone (Matson & Nebel-Schwalm, 2007). Some research indicates that comorbidity may occur at higher frequencies among individuals with HFASD than for lower functioning individuals on the spectrum (e.g., Mayes, Calhoun, Murray, Ahuja, & Smith, 2011, for comorbid depression and anxiety disorders). Thus, the existence of a comorbid disorder may significantly impact the design of educational and treatment plans to address the social-emotional and cognitive-academic functioning of children with HFASD.

Although ASD does co-occur with different psychiatric disorders such as ADHD, mood disorder, anxiety disorder, OCD, and others, the exact rates of co-occurrence are somewhat unclear due to several complications. The first complication is methodological. The vast majority of individuals who participated in empirical studies were recruited through clinical referral rather than the wider community, suggesting that those who came to a clinic for diagnosis most likely exhibited more severe symptomology than those who did not. This selection bias may have resulted in elevated rates of psychiatric comorbidities reported for ASD. Second, differential diagnosis is challenging because many symptoms overlap between ASD and other psychiatric disorders. For example, inattention is a feature of both ASD and ADHD; social withdrawal

characterizes both ASD and depression; obsessions and rituals appear both in ASD and in OCD, and so on. Adding to this complexity is the difficulty involved in establishing valid, specialized screening and evaluation measures and psychiatric diagnostic tools to account for the complex possible overlaps between ASD and other psychiatric disorders (e.g., Stewart, Barnard, Pearson, Hasan & O'Brien, 2006).

In this chapter, I describe the major related conditions that have been empirically explored as comorbid with HFSAD: ADHD, mood disorders, anxiety disorders, and OCD. For each of these comorbid conditions, this chapter: (a) provides its clinical description; (b) discusses its symptom overlap with HFASD; (c) furnishes guidelines for making differential diagnosis; and (d) describes its frequency of comorbidity with ASD. Finally, I describe the instruments commonly utilized to evaluate comorbidity in HFASD. This review mainly covers findings related to HFASD or to the contribution of IQ to comorbid conditions in ASD.

## Major Comorbid Diagnoses

### HFASD with Comorbid ADHD

**Definition of ADHD**. The estimated prevalence of ADHD in school-age children ranges between 3 and 7%, indicating a very common childhood neurodevelopmental disorder. According to the *DSM-IV-TR* (APA, 2000), a child with ADHD may be predominantly the inattentive type (e.g., fails to attend to details, loses things, gets distracted, is disorganized) or the hyperactive-impulsive type (e.g., moves or speaks excessively, fidgets, intrudes into others' activities, has difficulty staying seated), or may be the combined type. Children's diagnostic type depends, among other factors, on meeting criteria for at least 6 out of the 9 symptoms listed for each of the two types (inattentive and/or hyperactive-impulsive).

Some ADHD symptoms overlap with some HFASD symptoms, thus hindering differential diagnosis. More specifically, HFASD and the predominantly inattentive type of ADHD seem to share symptoms such as difficulties in following instructions, problems in listening when spoken to directly, and executive-functioning difficulties like poor planning and organizational skills (Mayes, Calhoun, Mayes, & Molitoris, 2012). Overlap between HFASD and the predominantly hyperactive-impulsive type of ADHD may exist regarding symptoms such as excessive talking, problems awaiting one's turn, or interrupting others (e.g., Reiersen & Todd, 2011).

**Differential diagnosis**. A closer look at symptom quality and underlying mechanisms may help in determining a differential diagnosis between ADHD and HFASD. For one, the source of

distraction to attention is usually external in ADHD (e.g., noises, other's activity), whereas it is usually internal in HFASD (e.g., a strong preference for one' own idiosyncratic interests like spending hours reading a book). Inattention in HFASD takes the form of over-focusing on particular stimuli of interest and under-focusing on other aspects of the situation (most likely social aspects of stimuli like facial expression, intonation, or body gesture). Yet, such inattentiveness alone would not lead to a consideration of comorbid ADHD (Murray, 2010). In addition, symptoms of hyperactivity are not considered to be defining characteristics of HFASD. Hyperactivity in ASD may be seen in highly repetitive motor stereotypies or as a result of anxiety or agitation during highly demanding social or sensory environments, but these would not be considered indicators of the hyperactive-impulsive ADHD type among individuals with HFASD (Murray, 2010).

**Prevalence of ADHD in HFASD**. The *DSM-IV-TR* (APA, 2000) disallows the co-existence of ADHD and ASD in the same person, but empirical studies have demonstrated evidence of a high prevalence of ADHD in individuals with HFASD, whether community-based studies (e.g., Mattila et al., 2010; Reiersen, Constantino, Volk, & Todd, 2007; Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 2008; Simonoff et al., 2008) or clinic-based research (e.g., de Bruin, Ferdinand, Meester, de Nijs, & Verheij, 2007; Gadow, DeVincent, & Pomeroy, 2006; Lee & Ousley, 2006; Leyfer et al., 2006; Mattila et al., 2010; Sturm, Fernell, & Gillberg, 2004; Yoshida & Uchiyama, 2004). For example, Yoshida and Uchiyama (2004) found that 69% of school-age children with HFASD in their clinic-based sample (CA = 7-15 years) met diagnostic criteria for ADHD: 38% with inattentive type, 8% with hyperactive-impulsive type, and 23% with combined type. Similar results emerged from Sturm et al.'s (2004) study of the medical and psychiatric records of school-age Swedish children with HFASD (CA = 5-12 years), where 75% met criteria for ADHD, of whom the majority (95%) showed attention problems and about half (56%) demonstrated hyperactive-impulsive problems. Similar findings emerged in Lee and Ousley (2006) for smaller clinical samples defined as HFASD; 7 of the 12 children and adolescents with Asperger Syndrome (58%) met criteria for ADHD, and 10 of the 13 children and adolescents with PDD-NOS (77%) met ADHD criteria. In their study, as in the former findings, the inattentive type of ADHD was the most common type in Asperger Syndrome (42%) and in PDD-NOS (46%).

Likewise, de Bruin et al. (2007) reported that 45% of school-age children with PDD-NOS

(CA = 1.5-12.11 years; *M* = 8.5 years; full IQ = 55-120, *M* = 91.22; with diagnosis verified by ADOS; Lord et al., 2000) met the criteria for ADHD: 15% inattentive type; 8.5% hyperactive-impulsive type; 21.3% combined. Yet, as their IQ range indicates, not all of these participants were high-functioning, even if their mean IQ exceeded retardation level. Similar percentages (53%) of ADHD comorbidity were reported by Gadow et al. (2006) for a clinical sample of children with ASD (CA = 3-12 years; 35% autism; 22% Asperger Syndrome; and 43% PDD-NOS), although no specific percentages were reported for the more cognitively able children in the sample. In a like manner, Leyfer et al. (2006) also found that 31% of their ASD sample (CA = 5.1-17.0; *M* = 9.2) met the criteria for comorbid ADHD; however, this percentage referred to the whole sample, whereas only 67.7% of the sample met criteria for HFASD (IQ > 70).

Population-based studies unsurprisingly show lower frequencies of comorbidity. Providing a somewhat different point of view to the co-occurrence of ADHD and HFASD, Reiersen et al.'s (2007) twin study (*N* = 495) demonstrated elevated autistic traits in children with ADHD from the general population, as measured by the Social Responsiveness Scale (Constantino & Gruber, 2005). Although it is difficult to determine if these children with autistic traits would have met the full criteria for ASD, this finding is interesting and supports the link between the two disorders. Another study derived from a population-based twin sample in the UK reported 41% ADHD comorbidity in individuals with Asperger Syndrome (Ronald et al., 2008). Mattila et al. (2010) found that 38% of their Finnish participants with Asperger Syndrome or HFASD in a combined community- and clinic-based sample (*N* = 50, CA = 9-16 years) met criteria for ADHD, with 68% showing ADHD combined type and 32% showing inattentive type (and none meeting criteria for hyperactive-impulsive type). A similar picture emerged for each sample separately: In the community-based sample (*n* = 18, CA = 12-13 years), 33% met criteria for ADHD, comprising 83% combined type and 17% inattentive type. In the clinic-based sample (*n* = 32, CA = 9-16 years), 40% met criteria for ADHD, comprising 62.3% combined type and 37.5% inattentive type. Simonoff et al. (2008) found lower rates of ADHD (28.2%, with 84% combined type) in their large population study of children with ASD (*N* = 112, CA = 10-14 years), but many of these participants were not high-functioning (IQ = 19-124; *M* = 72.7). Interestingly, no associations emerged between IQ and ADHD in their study.

In sum, clinic-based studies specific to HFASD have indicated rates of comorbidity with ADHD that range from 40% to 75%, whereas studies that were not HFASD-specific yielded

somewhat lower rates (31-53%) resembling the rates obtained for community-based HFASD-specific samples (33%). Thus, even if it is difficult to precisely estimate the prevalence of ADHD in individuals with HFASD, it is clear that a significant percentage of children with HFASD do meet a diagnosis for ADHD. This clear outcome justifies the modified perception suggested in the 2013 *DSM-V* (APA, 2012) to allow the co-occurrence of these two diagnoses.

Moreover, when these two disorders co-occur, they may affect children's social and adaptive functioning as well as their executive control, leading to a more severe clinical profile and possibly to poorer outcomes, especially socially. For example, children's autism-linked insistence on playing games with peers that are oriented toward their own peculiarities may be exacerbated, or vice versa, by their ADHD-linked tendency to move quickly between peer activities (Murray, 2010). Thus, children with HFASD who demonstrate comorbid ADHD features may require specialized intervention efforts for both disorders, indicating that treatments should be tailor-made (Murray, 2010; Reiersen & Todd, 2011).

**HFASD with Comorbid Mood Disorders**

Higher IQs have been linked with greater levels of depression in individuals with ASD (see review in Szatmari & McConnell, 2011). For example, in a study of adults with ASD (CA = 18-44 years), Sterling, Dawson, Estes, and Greenson (2008) found that individuals with less social impairment, higher cognitive ability, and higher rates of other psychiatric symptoms were more likely to report depressive symptoms. Indeed, researchers have suggested that individuals with HFASD are at higher risk of developing comorbid mood disorders than their less cognitively able counterparts, due to their more developed awareness of their social deficit and isolation (e.g., Hedley & Young, 2006). Barnhill and Smith-Myles (2001) found that adolescents with Asperger Syndrome who felt responsible for their social failure at school experienced heightened levels of depression. This subsection describes the most common mood disorders: major depressive disorder and dysthymic disorder.

**Definition of mood disorders.** Most studies on comorbidity of mood disorders with HFASD have reported co-occurrence with major depressive disorder (MDD), and several studies also pinpointed comorbid dysthymic disorder in HFASD; therefore, clinical categories are next detailed for these two depression categories. Clinical symptoms of MDD according to the *DSM-IV-TR* (APA, 2000) include depressed affect and/or diminished interest or pleasure in almost all life activities for a minimum of 2 weeks, plus at least 5 of the following 9 symptoms almost

daily, which cause clinically significant impairment in important areas of functioning (social, occupational, etc.): (1) depressed mood during a large part of the day; (2) lowered interest or enjoyment in all or most activities; (3) substantial unintended changes in weight; (4) too much or too little sleep; (5) noticeable psychomotor abnormalities; (6) energy loss; (7) experiencing feelings of unimportance or extreme guilt; (8) reductions in concentration, decisiveness, or ability to think; and (9) continuing ruminations about death (APA, 2000). Dysthymic disorder is diagnosed in cases where, over a minimum of two years, the person reveals milder but consistent depressed mood for most of each day. During this period of time, the person must show at least 2 of the following symptoms: under- or over-eating, sleep problems, fatigue, low self-esteem, lack of concentration or decisiveness, and sense of hopelessness. A diagnosis of dysthymic disorder is not given with MDD for the first two years, and neither diagnosis should be made if manic or hypo-manic episodes are present (APA, 2000).

The diagnostic criteria for depression are similar in children and adults; however, symptom profile may differ with age. Children and adolescents may manifest agitation, irritability, and bad temper, whereas adults may exhibit sadness or depressed mood. In addition, somatic complaints and social withdrawal are more frequent in children than in adults (APA, 2000). A recent nation-based survey by the National Comorbidity Survey–Adolescent Supplement showed a prevalence of 11.2% for major depression among adolescents (CA = 13-18 years) in the USA (Merikangas et al., 2010). In children, clinical depression affects girls and boys at about the same rate, but over the lifespan major depression is twice as common in females as in males, with overall population rates of 8-12% (e.g., Kessler et al., 2003, 2005).

**Differential diagnosis**. Social withdrawal is a common symptom for both HFASD and depression. In addition, individuals with HFASD are characterized by atypical and restricted means of emotional expression, such as inadequate, flat, or mechanical intonation; atypical range and clarity of facial expression; and difficulties in expressing and communicating emotions (e.g., Begeer et al., 2008; Hubbard & Trauner, 2007; see also Chapter 1 on social cognition and emotions). On the one hand, these atypical emotional expressions may mask depressive symptoms at times, but on the other hand, they may mislead significant others to conclude that the individual with HFASD has depression even when that is not the case (e.g., Ghauziddin, Ghauziddin, & Greden, 2002; Matson & Nebel-Schwalm, 2007). Other symptoms like sleep and appetite disturbances may also characterize both disorders (Stewart et al., 2006).

Change in symptoms' severity or profile is a key guide toward differential diagnosis between HFASD and depression. Symptoms may indeed overlap between the two disorders, but they are chronic in HFASD and not episodic as in most cases of depression (Mayes et al., 2011). The most common symptoms found to signify depression in HFASD according to Stewart et al.'s (2006) review of studies up to 2003 were: depressed mood (reflected in sad facial expression and an increase in crying and irritability); loss of interest in activities; and deterioration in adaptive functioning, especially in self-care behaviors and personal hygiene. Interestingly, symptoms such as worthlessness, guilt, diminished ability to concentrate, and suicidal thoughts – which are frequent in individuals with depression – were not frequent in HFASD (Stewart et al., 2006). Along with fatigue and hypoactivity (slowing down or even stopping one's usual activities), individuals with HFASD may also become more active. They may show an increase in the intensity and severity of symptoms like obsessive-compulsive behaviors (e.g., Ghaziuddin, Weidmer-Mikhail, & Ghaziuddin, 1998) or aggression, irritability, and oppositional behaviors (e.g., Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Lainhart, 1999; Matson & Nebel-Schealm, 2007). Kim et al. (2000) found that children with HFASD and comorbid depression (CA = 9-14 years) demonstrated higher levels of aggressive behavior that had an influence on parental participation in social activities, as well as on the child's relationships with teachers, peers, and family members.

**Prevalence of mood disorders in HFASD**. Mood disorders are a prevalent comorbid condition in children, adolescents, and adults with HFASD (e.g., Ghauziddin et al., 1998; Kim et al., 2000; Leyfer et al., 2006; Mayes et al., 2011; Mazefsky, Conner, & Oswald, 2010; McPheeter, Davis, Navarre, & Scott, 2011; Sterling et al., 2008; Wing, 1981), and they are more likely to appear in families with a history of depression (Ghauziddin & Greden, 1998). Furthermore, among children with HFASD (mean CA = 11 years, mean IQ = 75.3) depression was linked with a higher frequency of negative life events (e.g., bereavement, parental marital discord) in the 12 months before onset of depression (Ghauziddin, Alessi, & Greden, 1995). Measuring depression, Kim et al. (2000) reported that 16.9% of children with Asperger Syndrome and HFASD (CA = 9-14 years, IQ > 70) scored at least two standard deviations above the mean of a random community sample ($N$ = 1751). Several other studies demonstrated even higher depression rates in HFASD at similar ages. For example, Mayes et al. (2011) collected maternal reports on children's depressed mood, yielding rates of 54% for children with HFASD,

compared to 42% for children with LFA and only 19% for children with TYP (*n* = 233; CA = 6-16 years, *M* = 8.3; mean IQ = 103).

In order to understand the rates of depression in HFASD, it is important to make a distinction between a syndromal profile of depression, which meets the full *DSM* criteria (APA, 2000) for MDD, and a sub-syndromal profile, which falls short of meeting the *DSM* criteria (Leyfer et al., 2006). Syndromal rates of depression were somewhat lower (10%) than sub-syndromal rates (24%) in Leyfer et al.'s study (CA = 5-17 years, *M* = 9.2), but only two thirds of that sample were high-functioning (full IQ > 70). Based on a sample including only youngsters with HFASD (CA = 10-17 years, *M* = 11.90; verbal IQ =71-147, *M* = 106.35; full IQ = 71-144, *M* = 104.84), Mazefsky et al. (2010) reported that 32% met criteria for syndromal or sub-syndromal diagnosis under the "any depression" category (including dysthymia and depression not otherwise specified), whereas only 19% met criteria for a full MDD syndromal diagnosis. Also, 40% of Green, Gilchrist, Burton, and Cox's (2000) sample of adolescents with Asperger Syndrome had chronic unhappiness, but only an additional 5% met criteria for MDD. Thus, it seems that children with HFASD more often tend to show depressed mood or a sub-syndromal profile of depression rather than a full-blown MDD. Alternatively, current methodologies may not be reliably capturing the symptoms of MDD in HFASD, due to the lack of specific depression measurements adapted to HFASD.

Among adults with HFASD, percentages of depression are somewhat higher than those of children or adolescents. In Sterling et al.'s (2008) sample based mostly on adults with HFASD (CA = 18.33-44.75, *M* = 26.82), 43% exhibited a significant level of depressive symptoms. These authors found that individuals who qualified for a mood disorder diagnosis were older, more cognitive able (had higher verbal and full IQs), and scored higher on the ADOS social domain (Lord et al., 2000) than individuals who did meet the diagnostic criteria. Wing (1981) reported that depression was the most common comorbid psychiatric diagnosis among adults with Asperger Syndrome, occurring in 30% of her sample (*N* = 34). Ghauziddin et al. (1998) reported similar rates of depression (37%) for a sample including individuals between the ages of 8 and 51 years (*M* = 15.1 years; mean verbal IQ = 105.9; mean full IQ = 102.7), where 23% met criteria for MDD, 11.4% met criteria for dysthymic disorder, and 2.8% (*n* = 1) met criteria for bipolar disorder.

Most of the reported rates of depression were derived from clinic-based samples; however,

a more recent study (McPheeter et al., 2011) estimated the prevalence of depression among children with ASD ages 4-17 years using a national US sample of 125,000 parents during 2003-2004. Forty percent of these parents reported having been told by a health care provider that their child had depression or anxiety in addition to autism, although the frequency of such reports was low in early childhood (5.6% of ages 4-6; 48.4% of ages 7-10; and 46.0% of ages 11-17. (See similar reports in Ghauziddin et al.'s 2002 review.) However, these outcomes should be taken with caution because (a) information is lacking on how diagnoses were obtained, (b) percentages referred to the whole ASD spectrum, without differentiating HFASD, and (c) these data mixed depression and anxiety diagnoses. Indeed, anxiety is another frequent comorbid disorder in individuals with HFASD, as described next.

**HFASD with Comorbid Anxiety Disorders**

Among the various anxiety disorders, the following have been considered to co-occur more frequently with HFASD (APA, 2000): a specific phobia (i.e., significant fear of a distinct, well-defined object/situation) or a social phobia (i.e., significant fear of a potentially embarrassing performance/social situation); a generalized anxiety disorder (i.e., disproportionate anxiety or worry about multiple incidents or activities, which is hard to control and continues for a minimum of 6 months on more days than not); and OCD (i.e., repeated unwelcome compulsions like hand washing or obsessions like intrusive thoughts, which require a significant investment of time or lead to discernible distress or impairment). Thus, in this section, I focus on these anxiety disorders.

**Definition of anxiety disorders**. All people experience anxious feelings from time to time, but fear or tension are considered pathological when they are intense, excessive, irrational, and uncontrollable, and when they affect people's ability to manage daily tasks and relate to others. Anxiety may be accompanied by a range of physical and affective symptoms such as increased heart rate, tensed muscles, rapid breathing, and intensive fear without a noticeable reason. Such anxiety may lead to a change in the person’s behaviors (e.g., avoidance) and cognitions (e.g., compulsive thoughts).

Anxiety disorders are common within the general population. Eighteen percent of adults in the USA show an anxiety disorder at some point in their lives, and 4.1% of them present a severe disorder (Kessler et al., 2005). A full quarter (25.1%) of adolescents in the general population (CA = 13-18 years) exhibit an anxiety disorder, of which 5.9% are severe (Merikangas et al.,

2010). Among these adolescents, percentages range for the different anxiety disorders, from 2.2% for generalized anxiety disorder to 19.3% for specific phobia. The earliest onset is defined as young as 6 years, with elevating risk toward older adolescence, and among adolescents whose parents were divorced or separated (Merikangas et al., 2010). Like in the case of mood disorders, anxiety disorders are more common in females than males across the lifespan (e.g., Kessler et al. 2005; Merikangas et al., 2010).

**Differential diagnosis.** Avoidance of social interaction is a characteristic of individuals with ASD, yet is not necessarily a sign of social phobia. Crowded situations involving many people are an overwhelming and fearful situation for many children on the autism spectrum, as are noises that may provoke distress (e.g., school bell, vacuum cleaner). Thus, social and specific phobias are not easy to differentiate from HFASD. Even more difficult is the challenge of differentiating between OCD and HFASD because both disorders share the existence of obsessive and compulsive behaviors as a defining criterion.

***Differential diagnosis between HFASD and OCD***. The key to differential diagnosis between HFASD and OCD is twofold, referring to emotional reactions and to contents. First, in OCD but usually not in HFASD, the obsessive-compulsive preoccupation is painful, and performing the compulsion results in anxiety reduction or prevention, whereas in ASD it may provide some gratification and pleasure. Thus, children's emotional reaction to the preservative thoughts may be a criterion for differential diagnosis (Spiker, Lin, Van Dyke, & Wood, 2012; Wood & Gadow, 2010). However, for some children on the spectrum, repetitive behaviors can increase in frequency and intensity during stressful situations or as a reaction to change or during transitional periods, which only adds to the complexity of differential diagnosis based on emotional reaction (Wood & Gadow, 2010). As a result, children's emotional reaction cannot be the only criterion for differential diagnosis, and the contents of the obsessions should also be considered.

Contents of obsessions and compulsions may differ between OCD and HFASD. Taylor and Hollander's (2011) recent review of work in the field provided a helpful summary of repetitive behaviors for which the OCD and ASD may be comparable or dissimilar. Their classification of repetitive stereotypic behaviors in ASD into high order (cognitively mediated) versus low order (primitive brain processes) may specifically help in differential diagnosis of the two disorders. High-order repetitive behaviors include complex behaviors such as circumscribed interest and

preoccupation, a need for sameness, adherence to rituals and routines, and repetitive language, whereas low-order behaviors include repetitive sensory and motor behavior such as stereotypical movements (e.g., body rocking, finger flicking, hand flapping) and repetitive use of objects (Taylor & Hollander, 2011).

Taylor and Hollander's review reported that low-order repetitive sensory and motor behaviors such as touching, rubbing, stereotypical body movements, repetitive use of objects, unusual sensory interests, and self-injuring behaviors were only linked to ASD. High-order behaviors in the category of sameness (e.g., resistance to change) were also linked to ASD. However, high-order cleaning behaviors and fear of contamination, as well as forbidden thoughts, such as thoughts about aggression, sex, religion, and somatic symptoms were identified as unique to OCD. Nevertheless, both high- and low-order subtypes of repetitive behaviors can be identified in OCD; for example, intrusive repetitive thoughts may be considered high-order behaviors (e.g., of harm - “Did I hurt him?” – or of doubt - “Did I close the oven?”), whereas engagement in repetitive actions (e.g., hand washing) may be considered low-order repetitive behaviors, thus impeding differential diagnosis. Several symptoms that were found to overlap between OCD and ASD included hoarding and higher order symmetry like repeating, counting, or checking.

***Differential diagnosis between specific and social phobia and HFASD.*** Not many studies have explored the types of fears that characterize children with ASD. Parental reports (Evans, Canavera, Kleinpeter, Maccubbin, & Taga, 2005) highlighted that children with ASD exhibited a distinct profile of fear and anxiety compared to children with Down syndrome and to children with TYP matched for CA and MA (mean CA = 9.20; mean MA = 5.53; mean IQ = 59). This ASD profile included more situational fears such as fears of crowded transportation and medical situations (e.g., shots, blood tests, physician's exam) but fewer fears of harm or injury (e.g., fears of one's own or a parent's death, fear of fire). In addition, externalizing problem behaviors like conduct, impulsive, and hyperactive symptoms were associated with these fears only in ASD. Likewise, Matson and Love (1990) also identified a fear profile for ASD (CA = 2.5-17.0 years) that differed qualitatively from the fear profile of CA-matched children with TYP. Children with ASD feared thunderstorms, dark places, large crowds, dark rooms or closets, going to bed in the dark, and closed places; whereas children with TYP feared failure or criticism (social anxiety), harm and injury, small animals, and punishment.

These two studies are helpful in starting to delineate a fear profile in ASD, but their participants were not high-functioning. Specific examination of fear profiles for more cognitively able children is important because they may differ (e.g., including higher rates of social anxiety, for example in Gillott, Furniss, & Walter, 2001), based on their higher social awareness and understanding.

Symptoms of social phobia and those of ASD may be differentiated based on the phobia's content. If the anxiety has social attributions (negative evaluation from peers or worry about "looking stupid"), it is more likely a social phobia, whereas in ASD such anxiety, as described in the profiles above, usually relates to non-social aspects of the situation, such as unfamiliar people, noise, or changes in routine (e.g., Szatmari & McConnell, 2011).

In sum, differential diagnosis of ASD from the various anxiety disorders (mainly specific and social phobia or OCD) relies heavily on clinical judgment of the anxiety's content and functionality. Hence, careful attention should be given to the identification of genuine versus apparent comorbidity of anxiety disorders (specifically of OCD) together with HFASD.

**Prevalence of anxiety disorders in HFASD.** Although exact prevalence rates of anxiety disorders in HFASD may be unclear due to overlapping symptoms, Wood and Gadow's (2010) research review concluded that prototypical manifestations of clinical anxiety may be identified in children and adolescents with HFASD. These authors also emphasized this anxiety's significant impact on life quality regardless of the ASD symptoms' severity, thereby underscoring the need for serious consideration of comorbidity. Several empirical studies have reported a higher prevalence of anxiety disorders in HFASD compared to TYP (e.g., Gillott et al., 2001; Kim et al., 2000; Kuusikko et al., 2008; Mattila et al., 2010; Mayes et al., 2011; Mazefsky et al., 2010; Russell & Sofronoff, 2005) and a higher prevalence in HFASD compared to LFA (e.g., Mayes et al., 2011; Sukhodolsky et al., 2008).

For example, Kuusikko et al. (2008) examined differences in self-reported social anxiety and parent-reported internalizing difficulties between Finnish children (CA = 8-12 years) and adolescents (CA = 12-15 years) with HFASD ($n$ = 21 HFA and $n$ = 35 Asperger Syndrome) and their age-mates from a large community-based TYP sample ($n$ = 353). The self-report findings pinpointed a higher risk for social anxiety in the sample of adolescents with HFASD, where over half (57.1%) exceeded the clinical cut-off scores for social anxiety versus only 17% of the TYP sample. This difference did not emerge for the younger children in the study. Differently,

according to parent reports using the Child Behavior Checklist (CBCL, Achenbach & Rescorla, 2001), both younger and older participants with HFASD were rated higher than the TYP group on internalizing symptoms that exceeded the USA-defined clinical borderline status. Between half and three fourths of the HFASD group were rated with clinically elevated internalizing symptoms on the CBCL's total internalizing scale and on its subscales (e.g., withdrawn, somatic, anxious/depressed subscales). Thus, the adolescent age group with HFASD appears to be at specific risk for developing social anxiety, whereas internalizing difficulties (including both depression and anxiety) should be a concern in HFASD across development. Interestingly, to exclude possibly overlapping symptoms between HFASD and social anxiety, Kuusikko et al. analyzed their measures twice, once with the original scales and a second time using a revised scale that accounted for symptom overlap. Both analyses yielded comparable outcomes.

Similarly, significant percentages of children and adolescents with HFASD (CA = 9-14 years) extracted from a large random community sample ($N$ = 1751) scored at least two standard deviations above the population mean for anxiety disorders based on parental report: 13.6% for generalized anxiety disorder and 8.5% for separation anxiety (Kim et al., 2000). Two other studies reported anxiety disorders among about 40% of HFASD samples, as follows: Mattila et al. (2010) reported anxiety disorders in 42% of a combined community and clinic sample of HFASD in Finland (CA = 12-13 years in the community-based study and 9-16 years in the clinic-based study). Specific phobias were the most common anxiety disorder, in 28% of the participants (e.g., fears of animals, darkness, heights, confined spaces, bridges, needles, injections), and OCD was presented in 22% of the participants. Interestingly, 14% of the participants revealed two to three different concurrent anxiety disorders. According to maternal reports in Mazefsky et al. (2010), 39% of clinic-based adolescents with HFASD (CA = 10-17 years) met the criteria for lifetime history of an anxiety disorder (e.g., syndromal and sub-syndromal generalized anxiety disorder, social phobia, or specific phobia).

Somewhat higher percentages of anxiety symptoms (79%) were reported in Mayes et al. (2011) based on maternal reports for children with HFASD and for children with anxiety disorder (CA = 6-16 years). Interestingly, in this study, the frequency of mother-reported anxiety symptoms was similar for children in the two groups, attesting to the high prevalence of anxiety in HFASD. In addition, as found for depression rates, Mayes et al. (2011) reported that more children with HFASD had symptoms of anxiety than children with LFA. Differences in anxiety

were also reported between participants with LFA (IQ < 70, *n* = 106) and HFASD (IQ > 70, *n* = 48) in Sukhodolsky et al.'s (2008) large sample of parental reports for children and adolescents with ASD (*N* = 171; CA = 5-17 years). Altogether, 43% of the participants met the cut-off criteria for at least one anxiety disorder, with the HFASD group showing a significantly higher prevalence of generalized anxiety disorder (25%) and of overall anxiety disorders (58%) compared to the LFA group (4% and 39%, respectively).

Higher IQs have been linked with greater anxiety in ASD (see review in Szatmari & McConnell, 2011). Indeed, researchers have conjectured that individuals with HFASD may be at higher risk for developing comorbid anxiety than their less cognitively able peers, as a result of their greater awareness of their social deficit and isolation (e.g., Hedley & Young, 2006). Gadow, DeVincent, & Schneider, (2008) found that higher IQ was associated with more severe anxiety in children with PDD-NOS, and Sukhodolsky et al. (2008) underlined an association between higher levels of anxiety in children with HFASD and greater impairment in social responsiveness and more frequent stereotypical behaviors. In a like manner, greater anxiety symptoms were related with social skill deficits in Bellini (2004).

Taken altogether, rates of any anxiety disorders (syndromal or sub-syndromal) in HFASD differ somewhat between studies, due to difficulties in differential diagnosis related to overlapping symptoms and variability in the methods used to determine comorbid status along the different studies. However, a common parameter in all studies is that anxiety frequently co-occurs with HFASD and that the child with both comorbid conditions is at greater risk for maladjusted social functioning. Thus, comorbid anxiety disorders may increase the social impairment of children with HFASD and impede their actual social involvement with peers in natural social situations (White, Oswald, Ollendick, & Scahill, 2009). Adolescents with HFASD seem to be at greater risk for such influences (Kuusikko et al., 2008).

The picture is even more dramatic when looking at the higher rates of overall mood and anxiety disorders in HFASD, placing the child and especially the adolescent with HFASD, and even the adult with HFASD, as well as their families, at greater risk for negative short- and long-term outcomes. Regarding childhood, this comorbidity is associated with higher levels of withdrawal, non-compliance, and aggression and with increasing stress and conflict on the family (Matson & Nebel-Schwalm, 2007). These outcomes coincide with recent efforts to develop effective treatment endeavors that target reductions in anxiety and depression and

increases in social competence in order to enhance these individuals' social participation (see more in Chapter 6 on social intervention).

## Measurements to Assess Comorbidity in HFASD

As mentioned above, the development of instrumentation to tap comorbid conditions in HFASD continues to remain inadequate in terms of ruling out the possible overlapping criteria between HFASD and other psychiatric disorders while implementing a dual diagnosis. However, several instruments have been used for ASD (not for HFASD specifically), and some preliminary efforts were made to validate these diagnostic tools for the ASD population and to pinpoint cut-off scores that would identify potential risk for comorbid conditions. Importantly, higher scores on such screening instruments would still need to be clinically verified. The next section provides a short review of such instruments, divided into general and specific measures for assessing psychopathology.

### General Measures of Psychopathology

**The *Child Behavior Checklist* (CBCL).** The 113-item CBCL (Achenbach & Rescorla, 2001) is frequently used to evaluate various emotional and behavioral disorders across the lifespan. It can be implemented as a questionnaire or as an interview, and it includes forms for self-report or for reports by significant adults (e.g., caregivers, teachers, other professionals) who are familiar with the child. Two versions are available: the preschool checklist version (termed the CBCL—1.5-5 years or CBCL—Preschool) and the school-age checklist version (termed the CBCL—6-18 years or CBCL—Youth). Each version contains two empirically derived overall broad-band syndrome scales – internalizing and externalizing – and eight norm-referenced narrow-band syndrome scales that were derived through factor analysis of data from the general pediatric population. Three subdomains (withdrawal, somatic complaints, and anxiety/depression) form the broad-band internalizing syndrome, which evaluates emotional problems. Two subdomains (delinquency and aggressiveness) form the broad-band externalizing syndrome, which evaluates behavior problems. The remaining three other mixed syndrome scales (social difficulties, thought problems, and attention problems) do not belong to either broad-band scale because they had sizeable factor loadings on both broad domains in Achenbach and Rescorla's (2001) factor analyses. A "Total Problems" scale quantifying overall impairment is also obtained.

Despite the fact that its psychometric properties have not been extensively evaluated in

ASD, the CBCL has been used in autism research to evaluate comorbid psychiatric conditions, for example in Kuusikko et al. (2008) to assess the internalizing syndrome and its three subdomains or in Schroeder, Weiss, and Bebko (2011) to assess psychiatric comorbidities in individuals with Asperger Syndrome. Previous studies showed that the caregiver form of the CBCL—Youth checklist could differentiate between youngsters with ASD and with other psychiatric conditions (e.g., Duarte, Bordin, de Oliveira, & Bird, 2003; Mazefsky, Anderson, Conner, & Minshew, 2011; Petersen, Bilenberg, Hoerder, & Gillberg, 2006). Also, two recent studies that evaluated the psychometric qualities of the preschool and school-age checklist versions among children with a confirmed diagnosis of ASD supported both versions' factorial validity for the broad-band and subdomain syndromes (Pandolfi, Magyar, & Dill, 2009, 2012, respectively). The CBCL—Youth checklist's diagnostic accuracy was sensitive but low on specificity in differentiating ASD symptoms from other emotional behavioral symptoms. That is, only general scale elevation was noted, which may be taken as evidence of a significant emotional and/or behavioral problem; however, the general low specificity found for usage of the CBCL—Youth with the ASD population underscores the need for further diagnostic assessment using measures specific to ASD and to particular emotional and behavioral disorders. Only further assessment can complement the CBCL to differentiate between ASD symptoms and the presence of co-occurring emotional and behavioral disorders (ADHD, depression, anxiety) that may require specific treatment.

**The *Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children (6-18)—Present and Lifetime Version* (K-SADS-PL) and the *Autism Comorbidity Interview—Present and Lifetime Version* (ACI-PL).** The K-SADS-PL is a semi-structured "gold standard" diagnostic interview (Kaufman et al., 1997; Lauth et al., 2010) designed to assess current and past psychiatric disorders, including: affective disorders (e.g., MDD, dysthymia); psychotic disorders; anxiety disorders (e.g., generalized anxiety disorder, OCD, social phobia); behavioral disorders (e.g., ADHD); substance abuse disorders; eating disorders; tic disorders; and ASD (PDD-NOS and Asperger Syndrome). The K-SADS-PL is administered by interviewing the parent(s) and then the child, and then compiling summary ratings that include all information sources (parent, child, school, and other). The K-SADS has also been used in ASD studies to evaluate comorbid psychiatric disorders (e.g., Joshi et al., 2010; Mattila et al., 2010).

In light of the paucity of "gold standard" measures for validly and reliably assessing present and lifetime psychopathology in ASD, Leyfer et al. (2006) recently suggested the ACI-PL as a modification to the K-SADS-PL. The ACI-PL is a parent interview adapted in several ways for specific use with ASD: (1) This scale considers the unique way in which psychiatric symptoms may be manifested in ASD, such as MDD expressed through increased agitation, self-injury, and temper outbursts, rather than simply by showing depressed mood. (2) The scale regards children's described behaviors or emotional reactions as psychiatric symptoms only if they differ qualitatively and quantitatively from the children's baseline behaviors or emotions; that is, symptom manifestation is measured as change from baseline. For example, coding for social phobia in the ACI-PL requires that children's fear and/or avoidance relate to situations' social aspects (e.g., fear of "looking stupid") rather than its non-social aspects (e.g., noise). Thus, the ACI-PL distinguishes impairment due to comorbid psychiatric disorders from impairment due to core features of ASD. (3) The scale acknowledges that ASD makes some questions irrelevant in some children (due to limited language or self-reflection capabilities); therefore, symptoms are only probed if a child is capable of demonstrating them (e.g., increased guilty feelings are not an applicable symptom of depression in a child who does not understand guilt). Moreover, criteria for sub-syndromal disorders are applied (i.e., when significant psychiatric impairment falls just short of meeting full *DSM* criteria, APA, 2000). Utilization of sub-syndromal criteria enables identification of treatment needs that may be overlooked by relying solely on *DSM* criteria.

Altogether, the ACI-PL modification includes the addition of an introductory section that explores children's behavior and emotion at baseline, as well as supplementary questions at the beginning of each disorder section assessing further observable features and applicability of symptoms to the child. Leyfer et al. (2006) examined the instrument's psychometric qualities for 109 fairly high-functioning children (67% had full IQ > 70, CA = 5-17 years) with a diagnosis of autistic disorder based on the ADI-R (Lord et al., 1994), ADOS (Lord et al., 2000), and *DSM-IV-TR* (APA, 2000) criteria. The ACI-PL demonstrated good inter-rater reliability, test-retest reliability, and criterion and concurrent validities for the diagnosis of MDD, OCD, and ADHD. Recently, using the ACI-PL, Mazefsky et al. (2010) was able to identify high percentages of depression and anxiety in youth with HFASD (CA = 10-17 years). Further validity and reliability testing are needed for *DSM* disorders across the age, IQ, and verbal ability spectrums found in

autism and for sub-syndromal disorders.

**The *Behavior Assessment System for Children—Second Edition* (BASC-2).** The BASC-2 (Reynolds & Kamphaus, 2004) is a standardized multidimensional rating system using children's self-reports, teacher ratings, and/or parent ratings to assess a broad range of children's skills, adaptive behaviors, and problem behaviors at home and in the community. It is available for three age ranges: preschool (2-5 years), child (6-11 years), and adolescent (12-21 years). The BASC-2 provides information on nine clinical scales – aggression, anxiety, attention problems, atypicality, conduct problems, depression, hyperactivity, somatization, and withdrawal – and five adaptive scales: activities of daily living, adaptability, functional communication, leadership, and social skills. Together, the nine clinical and five adaptive scales are used to generate four composites: externalizing problems, internalizing problems, behavioral symptoms index, and adaptive skills. To supplement interpretation of the core scales, additional scales were added: six new clinical scales (anger control, bullying, developmental social disorders, emotional self-control, executive functioning, and negative emotionality), one adaptive scale (resiliency), and seven new content scales. Of these, the "developmental social disorders" content scale is of particular relevance to HFASD because it captures aspects of ASD like deficits in social skills, interests, activities, and communication.

BASC-2 items are oriented toward *DSM-IV-TR* (APA, 2000) symptomology and can be used in screening and as part of a comprehensive assessment procedure. This measure has been shown as reliable and valid for persons age 2 through 24 years of age; children with ASD were included in the general and clinical norm samples as well as in the reliability and validity studies (Reynolds & Kamphaus, 2004). Solomon, Miller, Taylor, Hinshaw, and Carter (2012) used the BASC-2 to assess the depression, anxiety, and internalizing problems (a composite of anxiety, depression, and somatization items) among boys and girls with HFASD (CA = 8-18 years). They found a specific risk for affective disorders in the teen years for girls with HFASD. Adolescent girls with HFASD had higher internalizing symptoms compared to boys with HFASD and to girls with TYP, and higher symptoms of depression than girls with TYP. Volker et al. (2010) explored the prototypical profile on the BASC-2 of students with HFASD ($n$ = 124; CA = 6-16 years, mean IQ = 105) and found significant differences between HFASD and TYP groups on all BASC-2 parent version scores except for the somatization, conduct problems, and aggression scales. Mean HFASD scores were in the clinically significant range on the behavioral symptoms

index, atypicality, withdrawal, and developmental social disorders scales. Screening indices suggested that the developmental social disorders scale was highly effective in reliably differentiating between HFASD and TYP. Even so, the task remains to explore the instrument's ability to discriminate between HFASD and other childhood disorders. Thus, the sensitivity and specificity data obtained by Volker et al. would not necessarily apply to screening for other potential comorbid clinical conditions.

**The *Diagnostic Interview Schedule for Children-IV* (DISC-IV).** The DISC-IV (Schaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) is a highly structured respondent-based interview to assess more than 30 childhood and adolescent psychiatric disorders (e.g., anxiety, mood disorders, schizophrenia, disruptive behavior disorders) derived from the *DSM-IV* (APA, 1994) and the *ICD-IO* (World Health Organization, 1992). The DISC-IV includes two versions: the parent version (DISC-IV-P) for parents of children ages 6-17 and the child version (DISC-IV-C) to be administered to children ages 9-17. The DISC-IV showed moderate to good reliability (Shaffer et al., 2000). Using a Dutch version of the DISC-IV-C to assess anxiety disorders, mood disorders, schizophrenia, and disruptive behavior disorders in a sample of children ages 6 to 12 with ASD, a high prevalence of at least one comorbid psychiatric condition (80.9%) was found (de Bruin et al., 2007). However, despite the sample's mean full IQ score in the high-functioning range (91.22), not all participants were high-functioning (full IQ ranged from 55 to 120), and the psychometric qualities of the Dutch DISC version have yet to be explored.

**The *Child Symptom Inventory-4* (CSI-4)**. The CSI-4 (Gadow & Sprafkin, 2002) offers a teacher and a parent version of a behavior rating scale that assesses the behavioral symptoms of a broad range of childhood psychiatric disorders (e.g., ADHD, oppositional defiant disorder, conduct disorder, generalized anxiety disorder, and MDD) based on *DSM-IV-TR* classifications and symptoms (APA, 2000), providing indication of diagnosis and severity for each disorder. The findings of numerous studies indicate that the CSI-4 (targeting children age 5-12) demonstrates satisfactory psychometric properties in community-based normative, clinic-referred non-ASD, and ASD samples (see literature review in Gadow & Sprafkin, 2009). This scale was extensively used in children with ASD, but with mixed IQ capabilities, not specific to HFASD. These studies showed the scale's construct validity for ADHD, oppositional defiant disorder, separation anxiety, and tics (see summary in Gadow, DeVincent, Olvet, Pisarevskaya, &

Hatchwell, 2010). Confirmatory factor analysis supported the internal validity of the *DSM-IV* model of behavioral syndromes in a large sample of children with diagnosed ASD (*N* = 730; Lecavalier, Gadow, DeVincent, & Edwards, 2009). Parent and teacher ratings have shown modest convergence. A revised version – the CSI-4R – was recently suggested, to combine the CSI-4 with its sister symptom inventory for adolescents (ASI-4, targeting 12-18 years) in a single measure spanning ages 5-18 years (the Child and Adolescent Symptom Inventory-4R; CASI-4R, Gadow & Sprafkin, 2012). Another version of the symptom inventory is also available for children as young as 3-5 years (the *Early Childhood Inventory-4;* Sprafkin, Volpe, Gadow, Nolan, & Keely, 2002).

**Measures to Assess Specific Psychopathologies**

Several measures have been used in the study of HFASD to evaluate specific psychiatric disorders, including the following:

(1) The *Children's Depression Inventory* (Kovacs, 1992) is a self-report assessing depression level in children ages 7 to 17, which also provides evaluation of areas relevant to depression (negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem). Kovacs (1992) reported a Cronbach alpha of 0.86 for this inventory in a normative sample, and Hedley and Young (2006) presented similar results for children with Asperger Syndrome (see also Solomon et al., 2012).

(2) The *Conner's Rating Scales—Third Edition* (Conners, 2008) consists of observer ratings (parents, teachers, caregivers) and adolescents' self-reported ratings to assess ADHD and to evaluate problem behaviors in children and adolescents. Ronald et al. (2008) utilized the parents' version of this scale to identify ADHD traits and suspected cases in individuals with Asperger Syndrome, and the scale showed good internal consistency (Cronbach alpha = .92).

(3) The *Children's Yale-Brown Obsessive Compulsive Scale* (Scahill et al., 1997) is a semi-structured parent and child interview assessing a range of possible OCD symptoms, for obsessions (e.g., contamination, aggression, hoarding/saving, magical thoughts/superstitions, and possible obsessive thoughts—somatic, religious, sexual) and for compulsions (e.g., cleaning/washing, checking, repeating, counting, ordering/arranging). This scale has shown good internal consistency (Cronbach alpha = .90) and a significant correlation with other measures of OCD in the general population. In Zandt, Prio, and Kyrios (2009), children with HFASD (CA = 7-16; mean verbal IQ = 96.45) scored lower on both the obsession and compulsion scales

compared to children with OCD. Recently, a modified scale for ASD was developed, the *Children's Yale-Brown Obsessive Compulsive Scale-PDD* (Scahill et al., 2006). This modified scale's symptom checklist was expanded to include repetitive behaviors associated with autism, such as spinning objects, staring, twirling, and repeating words and phrases, which can help ascertain differential observation between repetitive behaviors associated with ASD or with OCD. Scahill et al. (2006) reported that the modified version was found to be reliable, distinct from other measures of repetitive behavior, and sensitive to change, but these outcomes were not yet specifically tested for HFASD.

To sum up, this section presented a list of psychiatric measures to assess comorbidity in HFASD that is not all-inclusive but does delineate some of the major general and specific self-report and other-report (parents, teachers) instruments that have been most commonly implemented in the study of individuals with HFASD. As seen, there is a great need for researchers in the field to establish "gold standard," reliable, valid diagnostic tools to assess comorbid conditions associated with ASD. Such assessment measures should take into account the possible overlaps in symptoms between HFASD and comorbid disorders, as well as the unique manifestations of psychiatric symptoms in the HFASD population.

## Summary and Conclusions

Overall, the co-occurrence of psychiatric conditions such as ADHD, mood disorders, and anxiety disorders with HFASD is high, probably higher than in LFA. Moreover, at least for depression and anxiety, risk seems to increase with age in HFASD. Reasons for the high rates of such comorbidities with one or more psychiatric disorders in HFASD are still speculative. The contribution of potential genetic, cognitive, and environmental risk factors should be studied further, as well as potential underlying neurobiological mechanisms involved in psychiatric disorders in HFASD. Despite some recent efforts, most of the instruments to evaluate comorbidity in HFASD were not specifically designed for ASD and definitely not for HFASD. Thus, the need exists to develop such assessment systems that are valid and reliable in children along the spectrum, and that take into consideration the possibly unique form, content, and function of symptoms in the high-functioning population, in order to enhance differential diagnoses between ASD and other psychiatric disorders.

Currently, diagnosis of comorbidity relies heavily upon clinicians' judgment, based on changes over time in symptom manifestations, deterioration in functioning, demonstration of

behaviors that are outside the spectrum, and lack of responsiveness to treatments targeting children with ASD. The self/other and observation scales that are available make it hard to achieve objective diagnoses of comorbidity in HFASD. Yet, having said all this, it is impossible to ignore the significant percentages of children with HFASD who exhibit significant comorbid syndromal or sub-syndromal psychiatric conditions. Furthermore, those characterized by such conditions clearly appear to be at greater risk for more severe impairment and for both social-emotional and cognitive-academic maladjustment. Consequently, specific intervention models should be developed to target these complex comorbidities. Specifically, instructional methods should be oriented toward helping children and adolescents overcome both their difficulties based on their ASD and those based on their comorbid conditions. For example, cognitive-behavioral models to reduce anxiety and depression are a recent important experimental trend as described in the following chapter on social intervention.