AD/HD and Autism Spectrum Disorders

by Sam Goldstein, PhD

THE PREVALENCE OF AD/HD in the U.S. population has been estimated to be between three and seven percent. At this time the dual diagnosis of AD/HD and any pervasive developmental disorder (PDD) is excluded in the DSM-IV-TR diagnostic rules. Despite this restriction, many studies have observed the significant presentation of AD/HD symptoms in children with autism spectrum disorder (ASD). This co-occurrence is nearly fifty percent in some large and/or epidemiological community-based studies.

Core features of AD/HD include inattention, hyperactivity, and impulsivity. Despite the DSM-IV-TR rules, comorbid diagnoses of ASD and AD/HD are commonly made in clinical practice. This is primarily because symptoms of AD/HD can be significantly impairing and are typically not improved by the behavioral interventions directed at ASD. Further, there is far more research demonstrating the benefits of AD/HD treatments for these symptomatic problems than there is for treatments for ASD.

Prominent features of AD/HD and ASD include difficulties in listening to and following instructions, keeping things organized, sitting still, taking turns, talking excessively, and interrupting others. Many of these symptoms are at times difficult to differentiate from ASD. In fact, in a recent large-scale epidemiologic sample, the problems with attention and self-regulation were found to be the strong factor of symptoms for youth ASD between the ages of six and sixteen (Goldstein and Naglieri, 2010, Autism Spectrum Rating Scales).

It has been suggested that hyperactivity may be more prominent in children with ASD at younger ages but diminishes as they grow older, while symptoms of inattention and distractibility remain into adulthood. This month's column will review a number of recent studies clearly demonstrating the need to change our conceptualization of the relationship between AD/HD and ASD.

► **Jahromi LB, Kasari CL, McCracken JT, et al. (2009). Positive effects of methylphenidate on social communication and self-regulation in children with pervasive developmental disorders and hyperactivity. *Journal of Autism and Developmental Disorders, 39*(3), 395-404.**
These authors examined the effect of methylphenidate on social communication and self-regulation in children with autism spectrum disorders and hyperactivity. In a population of over thirty children ages five to thirteen who participated in a four-week crossover trial of placebo and increasing doses of methylphenidate, observational measures of certain aspects of the children's social communication, self-regulation, and affective behavior were measured each week. A significant positive effect of the medication was seen on children's use of joint attention initiations, response to bids for joint attention, self-regulation, and regulated affect. These results go beyond other studies and clearly suggested that methylphenidate may have positive effects on social behaviors in children with autism and hyperactivity.

► **Anckarsater H, Stahlberg O, Larson T, Hakansson C, et al. (2006). The impact of ADHD in autism spectrum disorders on temperament, character and personality development. *American Journal of Psychiatry, 163*(7), 1239-1244.**
Over 200 consecutive adults referred for neuropsychiatric evaluation were assessed for current and lifetime AD/HD in autism spectrum disorders. In a subgroup of subjects, the presence of Axis II personality disorders was also evaluated. Individuals with AD/HD reported high novelty seeking and high harm avoidance. Individuals with ASD reported low novelty seeking, low reward dependence, and high harm avoidance. The overlap between DSM-IV personality disorders categories was high. The authors suggested they appeared less clinically useful in this context. The authors suggested that AD/HD and ASD are associated with specific temperament configurations, increased risk of personality disorders, as well as deficits in character maturation.

► **Arnold LE, Aman MG, Cook AM, Witwer AN, Hall KL, Thompson S, & Ramadan Y. (2006). Atomoxetine for hyperactivity in autism spectrum disorders: Placebo controlled crossover pilot trial. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*(10), 1196-1205.**
A small sample of children ages five to fifteen years with Asperger syndrome, full autism, or PDD—Not Otherwise Specified and AD/HD symptoms were treated for six weeks with atomoxetine and placebo with a one-week washout period in between. Symptoms were evaluated using parent and teacher questionnaires. Seven of the sixteen children were considered responders to the atomoxetine but not the placebo. One child discontinued the study due to adverse events. This child was rehospital-

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What Have We Learned?

- Core features of AD/HD overlap significantly with ASD.
- In some studies nearly 50 percent of youth with ASD meet diagnostic criteria for AD/HD.
- ASD symptoms are more common in children with AD/HD than in the general population.
- Medication treatments effective for AD/HD can also be effective for attention problems in youth with ASD and as well may improve some ASD symptoms. Genetic disorders such as Fragile X increase the risk of both AD/HD and ASD.
- Problems with attention and self-regulation appear to be common characteristics for youth with ASD. It is likely these symptoms will need to be included in future diagnostic considerations for ASD.

ized for violence while on atomoxetine; however, prior episodes predated treatment. The authors report that response rates were similar to a large study of methylphenidate treatment for AD/HD symptoms in autism with a lower rate of discontinuation due to side effects. They suggested further study is needed.

► **Farzin F, Perry H, Hessl D, Loesch D, Cohen J, Bacalman S, Gane L, et al. (2006). Autism spectrum disorders and attention-deficit/hyperactivity disorder in boys with Fragile X premutation. *Developmental and Behavioral Pediatrics, 27*(2 suppl), S137-44.**

Fragile X syndrome results when greater than 200 repeats of a CGG allele occur in the FMR1 gene. Individuals are considered premutation if they have 55-200 repeats. Although most are unaffected, some premutation individuals may display cognitive deficits and behavior problems. In an effort to test whether premutation in the Fragile X gene would increase risk for AD/HD in autism, researchers compared 14 clinic-referred permutation subjects to 13 boys tested and having the premutation but not displaying deficits leading to a referral. Both groups were compared to 16 male siblings of these group members who themselves were negative for premutation. Proportionally more boys in the subject group were being treated with stimulant medication. There was also a higher rate of ASD in subjects and nonsubjects with the premutation. The authors suggested that their study demonstrates that premutation carriers, even those who do not present to clinics, may be at increased risk for AD/HD and ASD. The authors also suggested that if children are identified with Fragile X premutation through testing, they should also be screened for these other disorders.

► **Gadow KD, DeVincent CJ, Pomeroy J, & Azizian A. (2005). Comparison of DSM-IV symptoms in elementary school-age children with PDD versus clinic and community samples. *Autism, 9*(4), 392-415.**

These authors compared DSM-IV symptoms in children between the ages of six and twelve years of age with PDD, clinic controls, and community-based samples. Parents and teachers completed a number of questionnaires. The PDD group received higher symptom severity ratings than the regular education group but was similar to the non-PDD clinic sample. Screening prevalence rates were highest for AD/HD, ODD, and generalized anxiety disorder. PDD subtypes exhibited differentially higher rates of psychiatric symptoms. The magnitude of rater and gender differences in symptom severity ratings was modest. It appears that clinic-referred children with PDD exhibit a pattern of psychiatric symptoms highly similar to non-PDD clinic referrals.

► **Gadow KD, Roohi J, DeVincent CJ, & Hatchwell E. (2008). Association of ADHD, tics, and anxiety with dopamine transporter (DAT1) genotype in autism spectrum disorder (2008). *Journal of Child Psychology and Psychiatry, 49*(12), 1331-1338.**

Parents and teachers completed a DSM-IV-referenced rating scale for 67 children with ASD. According to parent ratings, children with a 10-10 repeat allele versus a combined group of all other genotypes exhibited less severe symptoms of hyperactivity and impulsivity as well as less severe language deficits. Teacher ratings indicated that social anxiety and tic symptoms were more severe for children with a 10-10 genotype versus all others. There was no association of tic severity found with DAT1 polymorphism. The authors suggest that there is an extraordinary variability in ASD clinical phenotypes that can be explained in part by the same genes that are implicated in a host of other psychiatric disorders in non-autistic populations.

► **Ghuman JK, Aman MG, Lecavalier L, et al. (2009). Randomized, placebo-controlled, crossover study of methylphenidate for attention-deficit/hyperactivity disorder symptoms in preschoolers with developmental disorders. *Child and Adolescent Psychopharmacology, 19*(4), 329-339.**

These authors investigated the short-term efficacy and safety of methylphenidate to treat AD/HD symptoms in a population of preschoolers with ASD symptoms as well as intellectual disability. A small study of 14 preschoolers with methylphenidate titration was examined

in a single-blind manner followed by a four-week double-blind crossover phase. Methylphenidate improved parent rated AD/HD symptoms in these preschoolers. Fifty percent were rated as responders. This was particularly true for the children with autistic symptoms. Half of the preschoolers, however, experienced side effects with methylphenidate, including reports of increased stereotypic behavior, stomach discomfort, sleep-related difficulty, and emotional lability. The authors concluded that the predominant direction of response in these children favored methylphenidate even though the response was more subtle and variable than in older and typically developing children.

► **Gillberg C & de Souza L. (2002). Head circumference in autism, Asperger syndrome, and ADHD: A comparative study. *Developmental Medicine and Child Neurology, 44*(5), 296-300.**

Although there has been a long history of interest in minor congenital anomalies as predictive of developmental impairments such as AD/HD, this is only the second article to address this issue with the first in 1999 (Ghaziuddin M, et al., Is megalencephaly specific to autism? *Journal of Intellectual Disability Research, 43*(8), 279-82). These authors were interested in testing the hypothesis that children with ASD without comorbid learning disability demonstrated the highest rate of macrocephalus (abnormally large skull). Children with ASD were compared with a population of fifty children who met criteria for AD/HD. The group with Asperger syndrome included a subset of individuals with macrocephalus, recorded both at birth and at follow-up after the first year of life. Another subgroup developed macrocephalus during childhood. New cases of macrocephalus tended to emerge particularly in the AD/HD group from birth to follow-up. The authors concluded that macrocephalus appears to be associated with AD/HD and not just ASD. In the AD/HD group, four children met the diagnosis for macrocephalus. It is important to note, however, that the majority of those with Asperger syndrome, ASD, and AD/HD did not differ from unaffected individuals in regards to head size.

► **Lecavalier L. (2006). Behavioral and emotional problems in young people with pervasive developmental disorders: Relative prevalence, effects of subject characteristics, and empirical classification. *Journal of Autism and Developmental Disorders, 36*(8), 1101-1114.**

Parents and teachers rated nearly 500 non-clinically referred children with ASD on a child behavior rating scale. The authors sought to examine the relative prevalence of specific behavior problems to derive empirical classifications of behavior and emotional problems for this population. Results found that children with ASD experienced high rates of behavioral and emotional problems. Cluster analysis suggested that six and eight cluster solutions best fit the ratings provided by parents and teachers respectively. Parent and teacher cluster solutions contained groups of children characterized as problem-free, hyperactive, anxious, and with undifferentiated behavior disturbances.

► **Mulligan A, Anney RJ, O'Regan M, Chen W, Butler L, Fitzgerald M, Buitelaar J, & Steinhausen HC. (2009). Autism symptoms in Attention-Deficit/Hyperactivity Disorder: A familial trait which correlates with conduct, oppositional defiant, language and motor disorders. *Journal of Autism and Developmental Disorders, 39*(2), 197-209.**

Autism symptoms were compared in 821 children with AD/HD, their siblings, and controls. Shared familiarity of autism symptoms in AD/HD was calculated. Autism symptoms were higher in subjects than siblings or controls and higher in male siblings than male controls. Autism symptoms were familial, partly shared with familiality of AD/HD in males. Latent class analysis demonstrated that autism symptoms and AD/HD represent a familial trait associated with increased neurodevelopmental and oppositional/conduct disorders.

► **Nijmeijer JS, Hoekstra PJ, Minderaa RB, et al. (2009). PDD symptoms and ADHD: An independent familial trait? *Journal of Abnormal Child Psychology, 37*(3), 443-453.**

These authors sought to determine whether subtle symptoms of autism within the context of AD/HD are transmitted in families independent of AD/HD as well as whether autism symptom familiarity is influenced by gender and age. Two hundred and fifty-six sibling pairs with at least one child with AD/HD and a 147 controls ages five to nineteen years were investigated. Children fulfilling full diagnostic criteria for ASD were excluded. Children with AD/HD and their siblings had higher levels of reported ASD symptoms than healthy controls. Sibling correlations remain similar in strength even after controlling for intelligence and AD/HD and when not confounded by comorbid anxiety. Sibling correlations were higher in females than in males. Social symptoms demonstrated the strongest sibling correlations in older versus younger sibling pairs. These results confirm that children with AD/HD demonstrated higher levels of ASD symptoms than observed in the general population. The data further suggest that the familiarity of subtle ASD symptoms in the context of AD/HD is largely independent from AD/HD familiarity.

► **Goldstein S & Schwebach AJ. (2004). The comorbidity of Pervasive Developmental Disorder and Attention Deficit Hyperactivity Disorder: Results of a retrospective chart review. *Journal of Autism and Developmental Disorders, 34*(3), 329-339.**

These authors sought to determine if a sample of children meeting diagnostic criteria for ASD display symptoms and impairments related to AD/HD sufficient to warrant a comorbid diagnosis of AD/HD. Introspective chart review was conducted with 57 children diagnosed with the PDDs of autism or PDD–Not Otherwise Specified or AD/HD. In a pool of subjects having PDD with sufficient data (nearly 30), 7 or 26 percent met DSM-IV criteria for AD/HD—Combined Type. Nine or 33 percent met diagnostic criteria for AD/HD—Inattentive Type, and 11 or 41 percent did not demonstrate a significant number of AD/HD symptoms to warrant a comorbid diagnosis. The authors concluded their findings reinforced clinical observations indicating that a significant group of children with a PDD may also experience an independent comorbid condition of AD/HD. ●