

Attention Deficit-/Hyperactivity Disorder (AD/HD) in Autism Spectrum Disorder.

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Abstract

The purpose of this review is to provide an overview of the research on Attention-Deficit/Hyperactivity (AD/HD) in individuals with autism spectrum disorder (ASD). Topics explored are the prevalence of AD/HD, the importance of studying AD/HD, as well as the questionnaire measures used to measure AD/HD in individuals with ASD. Research on the relationship between AD/HD in ASD and parental stress and psychological distress, developmental regression, language and communication, adaptive behavior, social skills, autism severity, challenging behavior, comorbid psychopathology, gastrointestinal symptoms, sleep problems, epilepsy, sensory issues, motor difficulties, and quality of life are also discussed. Research on cardiac reactivity and executive functioning are also explored. Finally, recommendations for treatment are given as well as areas where future research is needed.

Key words: Autism spectrum disorders, Attention-deficit/hyperactivity disorder (AD/HD), Comorbidity, Treatment

1. Introduction

Recent research has demonstrated how Attention-deficit/hyperactivity disorder (AD/HD) in autism spectrum disorder (ASD) is becoming a highly researched area in the field of comorbidity research (Matson & Williams, in press; Mannion & Leader, 2013). Matson, Rieske, and Williams (2013) provided a thorough review on the relationship between autism spectrum disorders (ASD) and AD/HD. They discussed comorbidity with other conditions such as comorbid psychopathology and sleep problems. The aim of the current paper is to expand on Matson et al.'s (2013) review by exploring the relationship between AD/HD in autism spectrum disorder and other comorbid conditions, such as gastrointestinal symptoms and epilepsy. We will also review this topic in relation to parental stress and psychological distress, language, adaptive behavior, challenging behavior, and quality of life. Taurines et al. (2012) conducted a review on AD/HD and autism, and included research on neuropsychological findings and therapeutic options. To expand on Taurines et al. (2012), and Matson et al. (2013), topics including executive functioning, cardiac reactivity, and a thorough review of treatment options will be explored.

2. Attention-Deficit/ Hyperactivity Disorder (AD/HD) and ASD

2.1. Prevalence

Matson et al. (2013) discussed prevalence rates in their recent review, and reported prevalence rates ranging from 20 to 70%. Turygin, Matson, and Tureck (2013) found that the prevalence of AD/HD symptoms was 4.5% in toddlers with ASD or at risk for developmental delay. Hanson et al. (2013) found that less than 16% of children and adolescents with ASD met clinically significant levels of AD/HD symptoms as measured by parent report. When teacher and parent report was combined, a comorbidity rate of 2% was found.

While much of the research focuses on the prevalence of AD/HD in individuals with ASD, some studies have focused on the prevalence of ASD in individuals with AD/HD. Russell, Rodgers, Ukoumunne, and Ford (in press) investigated the prevalence of AD/HD in children with a diagnosis of ASD. The authors also investigated the prevalence of ASD in children with a diagnosis of AD/HD. They reported that 19.9% of the children with ASD also had AD/HD, while 24.1% of the children with AD/HD had ASD. The researchers reported that 0.3% of children had both ASD and AD/HD. Mulligan et al. (2009) found that children with AD/HD display significantly more symptoms of autism than their siblings or typically developing controls.

2.2. Importance of studying AD/HD

The DSM-IV-TR (American Psychiatric Association, 2000) did not allow for the co-occurrence of AD/HD and ASD. That is, one could not receive both a diagnosis of ASD and AD/HD together. However, in the DSM-5 (American Psychiatric Association, 2013), the diagnoses of ASD and AD/HD will no longer be mutually exclusive. It is important to research the comorbidity of ASD and AD/HD as determining a diagnosis is often the first step in deciding treatment priority. When one has a diagnosis of either AD/HD, ASD, or combined AD/HD and ASD, then the best treatment modality can be delivered to the individual.

2.3. Subjective Measures to assess AD/HD

Matson et al. (2013) provided a thorough review of the assessment of AD/HD in ASD. The Conners' Rating Scales-Third Edition (Conners, 2008) is one featured measure that is used in the assessment of AD/HD. The Child Behavior Checklist (CBCL) (Achenbach & Rescorla, 2001) has been used to determine the prevalence of AD/HD symptoms in individuals with ASD. Skokauskas and Gallagher (2012) used the CBCL and found that

44.78% of children with ASD met criteria for clinically significant attention-deficit/hyperactivity disorder. Sikora, Vora, Coury, and Rosenberg (2012) also used the CBCL. The authors reported that approximately 40% had an elevated score on either the Attention Problem subscale or the Attention Deficit Hyperactivity Problem subscale, and 19% had elevated scores on both subscales. Turygin et al. (2013) used the inattention/hyperactivity subscale on the Baby and Infant Screen for Children with aUtism Traits (BISCUIT), Part II (Matson, Boisjoli & Wilkins, 2007). The Autism Spectrum Disorders-Comorbidity for Adults (ASD-CA) (Matson, Terlonge, & González, 2006) includes a subscale for Attention/Hyperactivity/Impulsivity. Future research should examine the prevalence of AD/HD symptoms in adults with ASD. The ASD-CA may be a suitable instrument for this research.

3. Relationships between AD/HD in ASD and other variables

3.1. Parental Stress and Psychological Distress

In the AD/HD literature, Takeda, Ambrosini, deBerardinis, and Elia (2012) investigated the relationship between parental psychiatric conditions and child comorbidity in children with AD/HD. It was found that AD/HD with internalizing disorder had a significant association with paternal psychiatric conditions. Kröger et al. (2011) found that current familial risk factors were predictors of autistic symptoms in children with AD/HD. The authors commented that higher familial risk factors may be due to the increased ASD symptoms of the child. The authors also commented on the need for longitudinal studies to replicate this association.

van Steijn, Oerlemans, van Aken, Buitelaar, and Rommelse (2013) found that higher paternal ASD and AD/HD symptoms were related to poorer scores of acceptance and conflict resolution in parent-child interactions. van Steijn, Oerlemans, van Aken, Buitelaar, and

Rommelse (in press) investigated parental stress and depression in parents of children with ASD and/or AD/HD. The researchers found that depressive symptoms were more pronounced in the parents of children with ASD alone, and ASD and AD/HD combined. Both fathers and mothers reported more stress parenting a child with ASD and/or AD/HD than when parenting their unaffected sibling. Kotte et al. (2013) found that children with AD/HD and autistic traits were more likely to have more problems with siblings than children with AD/HD alone. Kotte et al. (2013) also found that AD/HD children with autistic traits had a higher rate of pregnancy and infancy complications than other children with AD/HD alone. The authors commented that prenatal and perinatal complications alone, or in combination with genetic risk factors could account for the development of autistic traits in some children with AD/HD. This is an area where future research should be conducted.

3.2. Developmental Regression

Recent reviews have discussed the relationship between developmental regression and comorbidity in autism. Such areas of research include gastrointestinal symptoms (Mannion & Leader, in press-a), sleep problems (Mannion & Leader, in press-b), comorbid psychopathology (Mannion & Leader, under submission-a), and epilepsy (Mannion & Leader, under submission-b). However, this is an area of research where very little has been done in relation to AD/HD in autism spectrum disorder. Developmental regression is a potential area where future research could be conducted. Is there a relationship between language or skills regression and AD/HD in individuals with ASD?

3.3. Language and Communication

Mulligan et al. (2009) found that children who have the combined type of AD/HD who also have language disorder have higher autism symptom scores than those without language disorder. Scheirs and Timmers (2009) compared IQ in individuals with Pervasive

Developmental Disorder-Not Otherwise Specified (PDD-NOS) and AD/HD. It was found that PDD-NOS had higher verbal and performance IQs than AD/HD. The study attempted to distinguish between PDD-NOS, AD/HD and combined PDD-NOS and AD/HD. Based on intelligence scores, only PDD-NOS and AD/HD emerged as distinct categories, while comorbid PDD-NOS and AD/HD did not emerge as a distinct category. The authors commented that it can be debated whether a category exists of individuals with PDD-NOS and combined AD/HD diagnosis.

3.4. Adaptive Behavior

Sikora et al. (2012) found a greater impairment in adaptive functioning for children with ASD and clinically significant AD/HD symptoms in comparison with children with ASD and fewer AD/HD symptoms. In support, Rao and Landa (in press) reported that children with ASD and AD/HD had greater delays in adaptive functioning than children with ASD alone.

3.5. Social Skills

Demopoulos, Hopkins, and Davis (2013) compared individuals with AD/HD to those with ASD on tests of facial and vocal affect recognition, social judgment and problem solving, and parent- and teacher-report of social functioning. It was found that both AD/HD and ASD groups performed significantly worse than the control group. The authors suggested that social cognitive deficits may be similar in individuals with AD/HD as those with ASD. Kotte et al. (2013) found that children with AD/HD who showed autistic traits were more likely to fight with and be rejected by peers than children with AD/HD alone. Rao and Landa (in press) reported that children with both ASD and AD/HD had more severe social impairment than children with ASD alone.

3.6. Autism Severity

Sprenger et al. (2013) found that individuals with ASD and additional AD/HD showed a greater severity of autism symptoms than those with ASD alone. This was especially so in social interaction, where those with ASD and AD/HD showed more difficulties in social interaction than those with ASD alone.

3.7. Challenging behavior

Kotte et al. (2013) reported that children with AD/HD and autistic traits were more likely to have more school behavior problems. Gadow, DeVincent, and Pomeroy (2006) compared AD/HD subtypes in children with pervasive developmental disorder. The combined type of AD/HD had more severe aggressive and oppositional symptoms. They also had more symptoms of pervasive developmental disorders. It was reported that the Hyperactive-Impulsive type were the least impaired.

Goldin, Matson, Tureck, Cervantes, and Jang (2013) investigated tantrum behavior in children with ASD, AD/HD and comorbid ASD and AD/HD. Children with comorbid ASD and AD/HD showed the highest levels of tantrum behavior, followed by the ASD group. The researchers reported that children with comorbid ASD and AD/HD have a more similar symptom presentation to children with ASD than children with AD/HD. In support, Konst, Matson, and Turygin (2013) reported that children with ASD and comorbid AD/HD exhibited significantly greater tantrum behavior. Increases in ASD symptomatology were associated with increased tantrum behavior in those with ASD, AD/HD, and comorbid ASD and AD/HD.

Martin, Hamshere, O' Donovan, Rutter, and Thapar (in press) reported that hyperactive-impulsive traits may be linked to restricted and repetitive behavior in children

with AD/HD. Stratis and Lecavalier (2013) found that AD/HD symptoms were positively associated with stereotypic movement. Rao and Landa (in press) reported that parents rated children with ASD and comorbid AD/HD as presenting with more stereotypic and repetitive behavior than those with ASD alone.

3.8. Comorbid Psychopathology

Matson et al. (2013) provided an overview of comorbidity of ASD and AD/HD with other conditions, and discussed tic disorders, depression and Oppositional Defiant Disorder, among other comorbid psychopathology. Tureck, Matson, May, Davis, and Whiting (2013) investigated comorbid symptoms in children with ASD compared to children with AD/HD. It was found that children with ASD had more comorbid symptoms than children with AD/HD. However, both children with ASD and children with AD/HD showed more comorbid symptoms than children with no psychological diagnosis. Jang et al. (2013) found that children with ASD and AD/HD exhibited higher rates of comorbid symptoms than children with ASD alone or children with AD/HD alone. Children with comorbid ASD and AD/HD also showed more severe comorbid symptoms. Specifically, conduct behavior, worry/depressed symptoms, avoidant behavior and tantrum behaviors were more severe in children with ASD and comorbid AD/HD than those with ASD alone or AD/HD alone.

Kotte et al. (2013) found that children with AD/HD and autistic traits exhibited higher rates of comorbid psychiatric disorders than those with AD/HD alone. They were also more likely to have high rates of mood dysregulation. Mulligan et al. (2009) found that children with AD/HD and Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD) had more autism symptoms than children with AD/HD without these comorbid disorders. In support of this finding, Grzadzinski et al. (2011) found that oppositional behaviors were higher in children with AD/HD and autistic traits than children with AD/HD alone.

3.9. Gastrointestinal Symptoms

McKeown, Hisle-Gorman, Eide, Gorman, and Nylund (2013) investigated the association of constipation and fecal incontinence with AD/HD. Children with AD/HD had an increased prevalence of constipation (4.1% of children with AD/HD versus 1.5% of children without AD/HD) and fecal incontinence (0.9% of children with AD/HD versus 0.15% of children without AD/HD). The rate of constipation and fecal incontinence was the same for children with AD/HD who were prescribed medication, as those not prescribed medication. We know AD/HD and autism are comorbid conditions, and we know gastrointestinal symptoms are common in children with ASD. However, we do not yet know about the relationship between AD/HD and gastrointestinal symptoms in individuals with ASD.

3.10. Sleep Problems

Matson et al. (2013) discussed how sleep problems can co-occur in individuals with ASD and AD/HD. Tsai et al. (2012) examined sleep problems in children with AD/HD and ASD separately. Children with AD/HD alone and ASD alone had more sleep problems than children with epilepsy and typically developing children. Corkum, Davidson, and MacPherson (2011) provided a framework for the assessment and treatment of sleep problems in children with AD/HD. Similar guidelines would be useful for individuals with ASD and comorbid AD/HD. Much more research is needed on sleep problems in children with ASD comorbid AD/HD.

3.11. Epilepsy

Lo-Castro and Curatolo (in press) conducted a review on epilepsy associated with autism and AD/HD and questioned if there is a genetic link between the disorders. The

authors commented that future research is needed on examine the relationship between conditions. They also commented on the need for longitudinal studies to determine how genetic-environmental risk factors may disrupt developmental trajectories in the brain.

Gonzalez-Heydrich et al. (2007) commented that AD/HD coexisting with epilepsy is poorly understood. Gonzalez-Heydrich et al. (2007) reported that comorbidity of psychiatric disorders in AD/HD with epilepsy is similar to that in AD/HD without epilepsy. Previous research has focused on identifying the prevalence of epilepsy in those with ASD, and identifying the prevalence of AD/HD in those with epilepsy. Socanski, Aurlien, Herigstad, Thomsen, and Larsen (2013) investigated the prevalence of epilepsy in children with AD/HD. A significantly higher rate of epilepsy was found that of those in the general population. The epilepsy diagnosis preceded the AD/HD diagnosis, with patients being diagnosed with epilepsy on average 1.8 years before receiving an AD/HD diagnosis. Tanabe, Kashiwagi, Shimakawa, Tamai, and Wakamiya (in press) found that 32.4% of children with epilepsy were diagnosed as having AD/HD.

Torres, Whitney, and Gonzalez-Heydrich (2008) conducted a review of pharmacological treatment of AD/HD in patients with epilepsy. Though not ASD specific, this may be useful for clinicians who are treating individuals with a comorbid AD/HD and epilepsy diagnosis along with ASD.

3.12. Sensory Issues

The relationship between sensory issues and comorbidity has been explored in recent studies, including comorbidities such as sleep problems (Mannion & Leader, in press-b), gastrointestinal symptoms (Mannion & Leader, in press-a), epilepsy (Mannion & Leader, under submission-b), and comorbid psychopathology (Mannion & Leader, under submission-a). Very little research has been conducted into the relationship between AD/HD and sensory

issues. Lin, Yang, and Su (2013) found correlations between sensory modulation problems and hyperactivity in children with AD/HD. Future research should examine the relationship between sensory issues in individuals with ASD and comorbid AD/HD.

3.13. Motor Difficulties

Mulligan et al. (2009) found that children who have the combined type of AD/HD who have motor disorder have higher autism symptom scores than those without motor disorder. This is supported by Papadopoulos, Rinehart, Bradshaw, and McGinley (2013) reported that children with AD/HD without comorbid autism do not have impaired motor proficiency. The authors commented that motor difficulties may be seen as possible markers for identifying autism symptoms in individuals with AD/HD.

3.14. Quality of Life

Sikora et al. (2012) reported poorer health-related quality of life for children with ASD and clinically significant AD/HD symptoms than children with ASD and fewer AD/HD symptoms. The authors commented that by reducing AD/HD symptoms in children with ASD, as well as treating core ASD symptoms, families may see greater improvement in quality of life. Quality of life in comorbid ASD and AD/HD is an area where future research is necessary.

4. Cardiac Reactivity

Bink et al. (in press) investigated cardiac reactivity and attention task performance. They compared cardiac reactivity in adolescents with ASD and comorbid AD/HD to those with AD/HD alone. Cardiac reactivity was similar for both groups. Adolescents who were on stimulant medication did not have higher heart rates than those who were not on stimulant

medication. Bink et al. (in press) recommended that future studies include additional physiological measures such as electroencephalogram (EEG).

5. Executive Functioning

It is well documented that individuals with ASD have deficits in executive functioning (Ozonoff, Pennington, & Rogers, 1991). Research has been conducted comparing executive functioning in individuals with ASD, AD/HD and comorbid ASD and AD/HD. Semrud-Clikeman, Walkowiak, Wilkinson, and Butcher (2010) compared executive functioning in children with Asperger Syndrome compared to children with AD/HD and typically developing children. Those with Asperger Syndrome and those with AD/HD showed more difficulty with executive functioning than controls. Children with Asperger Syndrome showed the most difficulty in emotional control, behavioral regulation, fluid reasoning and planning, compared to those with AD/HD.

Sanderson and Allen (2013) investigated the role of symptoms of inattention and/or hyperactivity/impulsivity in predicting inhibitory impairments in children with autism. Symptoms of inattention and/or hyperactivity/impulsivity were more common in children with autism than typically developing controls. One third of children with autism scored above the clinical cut-off for AD/HD inattentive type, and one quarter of children with autism scored above cut-off for hyperactive/impulsive type. However, Sanderson and Allen (2013) found no link between symptoms of hyperactivity/impulsivity and inhibitory performance in children with autism. The authors found that symptoms of inattention were related to conflict task performance. Sinzig, Morsch, Bruning, Schmidt, and Lehmkuhl (2008) compared executive functioning profiles in children with AD/HD, and in children with ASD with and without comorbid AD/HD. Children with ASD and comorbid AD/HD showed more problems in inhibitory performance, but not in the working memory task. The research found

that AD/HD symptoms seemed to worsen inhibition performance in children with comorbid ASD and AD/HD, as children with ASD alone performed well in comparison to children with AD/HD alone.

Nydén et al. (2010) investigated neuropsychological functioning in adults with ASD, AD/HD and combined ASD and AD/HD. The dysfunctions shown in the combined ASD and AD/HD group were distinct from those in the ASD and AD/HD groups. Those with comorbid ASD and AD/HD were not just showing a summary of the dysfunctions found in the ASD and AD/HD groups. The AD/HD group showed the most severe neuropsychological impairments.

6. Recommendations for treatment

Matson et al. (2013) commented that little has been done with respect to treatment approaches and methods as the topic of ASD and AD/HD is only a recent area of study. Mahajan et al. (2012) designed clinical practice pathways for evaluation and medication choice for AD/HD symptoms in children and adolescents with ASD. For evaluation, it is recommended that medical problems, sleep problems, and comorbid psychiatric conditions are considered in the evaluation of AD/HD symptoms. If medication is necessary, the authors recommended that stimulant medications be considered first, as they have a well-documented safety record and less side effects. The AD/HD symptom evaluation pathway and AD/HD symptom medication choice practice pathway are included in the Mahajan et al. (2012) paper.

6.1. Medication

Reichow, Volkmar, and Bloch (2013) conducted a systematic review and meta-analysis of pharmacological treatment of the symptoms of AD/HD in children with pervasive

developmental disorders (PDD). The authors reported on the efficacy of methylphenidate treatment, but noted that there were increased side effects such as depression, irritability, and social withdrawal side effects that were more common in children with pervasive developmental disorders. The research also found that clonidine and atomoxetine may be effective in treating AD/HD symptoms children with PDD.

6.2. Behavioral treatment of AD/HD

DeWitt, Aman, and Rojahn (1997) compared the effects of reinforcement contingencies in children with and without AD/HD. No difference was found between groups in how they respond to reinforcement schedules. Fabiano et al. (2009) conducted a meta-analysis of behavioral treatments for AD/HD. Results indicated that behavioral treatments were highly effective for those with AD/HD. Lee, Niew, Yang, Chen, and Lin (2012) conducted a meta-analysis of behavioral parent training for children with AD/HD. The researchers found that behavioral parent training was an effective treatment. However, children with AD/HD and other comorbid behavioral problems benefited less from behavioral parent training than children with AD/HD alone.

7. Future research

In line with recent revisions to the DSM-5 (American Psychiatric Association, 2013), the prevalence of combined ASD and ADHD diagnosis is set to increase. This review has explored several avenues for future research, such as quality of life, sensory issues and motor issues. Research is needed on the relationship between AD/HD in ASD and other comorbid conditions, such as sleep problems and epilepsy. The relationship between gastrointestinal symptoms in ASD and comorbid AD/HD is an area where future research is necessary. Research is needed on executive functioning in ASD and comorbid AD/HD. Gargaro, Rinehart, Bradshaw, Tonge, and Sheppard (2011) recommended that future research should

investigate executive functioning in individuals with autism with and without significant symptoms of AD/HD. Future research should examine AD/HD in ASD across the lifespan from children to adolescents to younger adults and older adults. Nydén et al. (2010) recommended that children with neuropsychiatric developmental disorders be re-examined in adulthood, as criteria for diagnosis may have not been fulfilled, and neurocognitive functions may have changed over time. Finally, longitudinal research is needed to determine if AD/HD symptoms change over time. AD/HD in childhood may present as different symptoms in adulthood. Future research needs to determine how comorbid AD/HD symptoms change as an individual with ASD ages.

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