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Adaptive Behavior in Young Autistic Children: Associations with Irritability and ADHD symptoms

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) symptoms affect 40–60% of autistic children and have been linked to differences in adaptive behavior. It is unclear whether adaptive behavior in autistic youth are directly impacted by co-occurring ADHD symptoms or by another associated feature of both autism and ADHD, such as increased irritability. The current study examined relationships between irritability, ADHD symptoms, and adaptive behavior in 3- to 7-year-old autistic children. Results suggest that, after adjusting for co-occurring ADHD symptoms, higher levels of irritability are associated with differences in social adaptive behavior specifically. Understanding relationships between irritability, ADHD, and adaptive behavior in autistic children is critical because measures of adaptive behavior, such as the Vineland Scales of Adaptive

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Functioning, are often used as a proxy for global functioning, as well as for developing treatment plans and measuring outcomes as primary endpoints in clinical trials.

Introduction

Co-occurring psychiatric disorders occur commonly in autistic individuals and can impact a range of functional outcomes. Attention-deficit/hyperactivity disorder (ADHD) symptoms affect up to 40–60% of autistic children (de Bruin et al. 2007; Hawks and Constantino 2020; Lai et al. 2019; Simonoff et al. 2008). Although some evidence suggests that co-occurring autism and ADHD symptoms are associated with differences in adaptive behavior (Avni et al. 2018; Scandurra et al. 2019; Yerys et al. 2019), this relationship has not always been consistently reported (Ashwood et al. 2015; Craig et al. 2015). Because of these inconsistent findings, it is unclear whether lower levels of adaptive behavior are associated with the presence of ADHD symptoms or with other features that are shared by autism and ADHD.

Adaptive behavior is generally understood as an individual's ability to independently perform skills that are considered necessary for personal and social sufficiency in real-world, daily life (Sparrow et al. 2005). Given its association with both autism-related behaviors and overall developmental level, adaptive behavior is often used as an index of global functioning in autistic individuals (Chatham et al. 2018). Understanding the range of factors that are associated with adaptive behavior can help clinicians target treatments and best support autistic individuals. This is particularly true for young autistic children for whom adaptive behavior is often targeted through early intensive behavioral intervention.

Both autism and ADHD share several non-diagnostic specific features that could potentially be associated with lower levels of adaptive behavior, including higher rates of negative emotionality, irritability, and agitation. Irritability/Agitation commonly refers to both difficult behaviors, such as aggression and self-injury, as well as mood features, such as a quick temper and frequently changing mood (Owen et al. 2009). Early research suggests that irritability occurs in approximately 20% of autistic individuals (Lecavalier 2006). Irritability in autism has been linked to greater internalizing and attention problems (Hill et al. 2014), increased parent stress (Davis and Carter 2008; Lecavalier et al. 2006; Valicenti-McDermott et al. 2015), and lower levels of adaptive functioning (Davico et al. 2022; Williams et al. 2018). Similarly, emotional dysregulation, including increased levels of irritability, have also been commonly reported in ADHD (Fernandez de la Cruz et al. 2015; Overgaard et al. 2015; Shaw et al. 2014) and have been linked to increased impairment, including higher risk of functional impairment (Anastopoulos et al. 2011) and greater social difficulties (Bunford et al. 2018; Lee et al. 2018).

Despite evidence that (1) irritability commonly co-occurs with both autism and ADHD (2) irritability is associated with increased differences in adaptive behavior in autism and ADHD, independently, and (3) co-occurring autism and ADHD symptoms are associated with differences in adaptive behavior (Avni et al. 2018; Scandurra et al. 2019; Yerys et al. 2019), the relationship between irritability and adaptive behavior in autistic children with co-occurring ADHD symptoms is poorly understood. As such, the current study aimed to evaluate the associations between irritability and symptoms of ADHD on autistic children's

early adaptive behavior. Specifically, this study sought to understand whether irritability and ADHD symptoms are each associated with levels of adaptive behavior independently, or whether there is a compounding effect such that the presence of one factor (i.e. irritability) increases the influence of the other factor (i.e. ADHD symptoms). We predicted that, while both ADHD and irritability would each independently be related to children's adaptive behavior, irritability would be related to increased differences in adaptive behavior over-and-above the relationship with ADHD symptoms alone. Understanding the relationships among these behavioral domains can be particularly useful when establishing treatment plans.

Methods

Study Design and Participants

This study was a secondary analysis of data combined from three separate studies of autistic children who were between 3- and 7-years-old and whose parents completed the same set of parent-report measures (n=185). For participants who were in more than one study (n=6), only the most recent data were used for analyses. Participant demographics from each study are reported in Table 1. Details for each of these studies are provided below. Inclusion criteria in all studies included, (1) DSM-5 diagnosis of Autism Spectrum Disorder (ASD), which was established or confirmed using the Autism Diagnostic Observation Schedule-2 (ADOS-2; Lord et al. 2000) and the Autism Diagnostic Interview-Revised (ADI-R; Lord et al. 1994); (2) Have a guardian who is able to provide informed consent; and (3) If cognitively able, participant must provide informed assent/consent. All studies were approved by the appropriate university Institutional Review Boards.

Study 1—Study 1 included 63 autistic children between 3- and <6-years-old who were recruited from the community through flyers and brochures, emails, social media posts, and the research center's registry between May 2015 and May 2017. Children were eligible if they were between the age of 36 and < 72 months. Exclusion criteria included (1) Having a genetic disorder (e.g., Fragile X syndrome); (2) Vision or hearing problems; (3) Significant motor impairment (e.g. cerebral palsy); (4) Chronic or acute medical illness; and (5) History of epilepsy or seizure disorder, being on medication for seizures, or any seizure in the last year.

Study 2—Study 2 included 82 autistic children between the ages of 3- and <8-years-old recruited from the community through flyers and brochures, emails, social media posts, and the research center's registry between July 2018 and March 2020. Enrollment and data collection for Study 2 was still underway at the time of the current analyses. Children were eligible if they were between the age of 36 and < 96 months at initial assessment visit. Exclusion criteria included (1) A known genetic or neurological syndrome or condition with established link to autism (e.g., Fragile X syndrome, CHD8 mutations); (2) Child had a seizure in the past year; (3) Motor or sensory impairment that would interfere with the valid completion of study measures including significant hearing or vision impairment not correctable by a hearing aid or glasses/contact lenses; (4) History of neonatal brain damage (e.g., with diagnoses of hypoxic or ischemic event); (5) Any known environmental circumstances that were likely to account for the autism diagnosis

(e.g. severe nutritional or psychological deprivation etc.); and (6) No more than two comorbid psychiatric diagnoses including ADHD, Oppositional Defiant Disorder (ODD), Anxiety, or Disruptive Mood Dysregulation Disorder (DMDD). Participants on stimulants (e.g. Amphetamine, Dexmethylphenidate, Methylphenidate) were asked to washout on their medication for the 24 hours prior to their study visits.

Study 3—Study 3 included 290 autistic children between 3- and 17-years-old recruited into a clinical trial examining the efficacy of oxytocin to improve reciprocal social behaviors in autistic children (Sikich et al. 2021; Spanos et al. 2020). Children were recruited from clinical programs, research registries, and community referrals at one of seven collaborating sites between August 2014 and November 2017. Children were eligible if they were between 3 years 0 months to 17 years 11 months at baseline. For participants who did not meet criteria on either the ADOS or the ADI, but still had a clinical diagnosis of ASD, the Steering Committee was required to review and approve inclusion. Exclusion criteria included (1) a known diagnosis of Rett Syndrome or Childhood Disintegrative Disorder or marked sensory impairment such as deafness or blindness; (2) Active cardiovascular disease or renal disease that is not controlled by medication; (3) Pregnancy, lactation, or refusal to practice contraception if sexually active; (4) Changes in allied health therapies, behavioral, or educational interventions within the two months prior to randomization other than those associated with school holidays; (5) Changes in psychiatric medications within 4 weeks of randomization; (6) Previous treatment with chronic intranasal oxytocin (daily dosing more than 1 month); (7) Caretakers who were unable to speak English, be consistently present at visits to report on symptoms, or were otherwise judged as unable to comply with the protocol by the data collection site team; and (8) Active seizures within the 6 months preceding screening or baseline. For the current analyses, we included only data collected at the baseline (pre-treatment) visit and restricted the sample to participants who were between 3- and <8-years old at that time point (n=40).

Measures

Cognitive Ability—Cognitive ability was measured using the *Stanford–Binet Intelligence Scales of Intelligence Fifth Edition (SB5)* Abbreviated Battery IQ (ABIQ; Roid 2003), the *Differential Abilities Scales-II* (DAS-II; Elliott 1990), or the *Mullen Scales of Early Learning: AGS Edition* (MSEL; Mullen 1995). The SB5 or DAS-II were used for children ages 3:6–7:11, while the MSEL was used for children <3:6 years of age. In all studies, if the DAS-II or SB5 were not believed to yield a valid score (e.g., inability to achieve a basal due to limited expressive/receptive language), then the child was administered the MSEL. For each measure, a full scale IQ (FSIQ) was calculated based on that measure's available scoring; specifically, the Early Learning Composite (ELC) Standard Score from the MSEL, the General Conceptual Ability (GCA) composite score from the DAS-II, and the ABIQ from the SB5.

Adaptive behavior—The *Vineland Adaptive Behavior Scales (VABS)* Parent/Caregiver Rating Form was used in all studies to assess adaptive behavior. Studies 1 and 3 utilized the VABS - second edition (VABS-II; Sparrow et al. 2005) whereas Study 2 used the VABS – third edition (VABS-3; Sparrow et al. 2016). The VABS is a well-standardized

measure for assessing adaptive behavior in the domains of communication, daily living, socialization, motor, and maladaptive behaviors. Norms are available from birth to 90 years. The VABS has been shown to discriminate clinical samples, such as those with autism, from nonclinical samples. Because the Adaptive Behavior Composite (ABC) score is comprised of different subscales in the VABS-II compared to the VABS-3 (Sparrow et al. 2016), the current study focused only on individual domain scores, specifically the domain scores for Communication, Socialization, and Daily Living Skills. The test-retest reliability for these three individual domain scores was high in both versions of the VABS. The VABS-II test-retest reliability (all reported as adjusted R-values for ages 3–6/ages 7–12) for Communication was r = .92/.88, for Socialization was r = .88/.84, and for Daily Living Skills was r = .91/.93 (Sparrow et al. 2005). In the VABS-3, test-retest reliability for Communication was r = .87/.88, for Socialization was r = .83/.94, and for Daily Living Skills was r = .86/.87 (Sparrow et al. 2016). Concordance correlation coefficients (CCC) for these three individual domain scores between the two versions was moderate (Farmer et al. 2020): Communication CCC = .78, Socialization CCC = .84, and Daily Living Skills CCC = .79.

Irritability and ADHD Symptoms—Irritability and ADHD symptoms were assessed with the Aberrant Behavior Checklist-Community (ABC; Aman and Singh 1986; Kaat et al. 2014). The ABC is a caregiver-report scale originally developed to assess drug and other treatment effects in studies of individuals with developmental disabilities and is commonly used in descriptive and treatment studies of autistic individuals. This inventory has five subscales consisting of (1) Irritability/Agitation; (2) Lethargy and social withdrawal; (3) Stereotypic behavior; (4) Hyperactivity and non-compliance (hereafter referred to as ‘Hyperactivity’); and (5) Inappropriate Speech. Each question is rated on a 0–3 severity scale, with 0 indicating the absence of a behavior, and 3 indicating a high severity level. Irritability was reflected in the ABC Irritability/Agitation subscale, while ADHD symptoms were reflected in the ABC Hyperactivity subscale. Test-retest reliability of both the Irritability/Agitation and Hyperactivity subscales is high (r = .98; Aman and Singh 1986). Additionally, good internal consistency, as well as convergent validity between the Irritability/Agitation and hyperactivity subscales and similar subscales on the Child Behavior Checklist (CBCL) have been reported in a large sample of autistic youth (Kaat et al. 2014).

Data Analysis

All analyses were run in SAS version 9.4 (SAS Institute Inc.) and results with $p < .05$ were considered significant. We first tested the normality of our data using the Kolmogorov-Smirnov (K-S) test. Because not all of our variables were normally distributed we tested our hypothesis that differences in adaptive behavior will be associated with higher levels of both irritability and ADHD symptoms by employing a series of Spearman partial correlations. Age and IQ were included as covariates in these models by adding them to the partial statement in SAS. Additionally, we also included a variable accounting for which study the data was derived in the partial statement of the model. The study covariate was added in order to ensure that the results were not driven by study-specific effects and to account for the use of the VABS-3 in Study 2 compared to the VABS-II used in Studies

1 and 3. Finally, to test the hypothesis that irritability is associated with lower levels of adaptive behavior when accounting for the relationship between irritability, adaptive behavior, and co-occurring symptoms of ADHD, we ran three general linear models (GLM) with ABC Irritability/Agitation predicting the Socialization, Communication, and Daily Living Skills subdomains on the VABS, respectively. ABC Hyperactivity, age, IQ, and study were included as covariates in each of the GLM models. Additionally, the VABS Daily Living Skills standard scores were transformed using a cubed function in order to ensure that all dependent variables were normally distributed (VABS Communication and VABS Socialization were both normally distributed without being transformed).

Results

Irritability, as reflected in the ABC Irritability/Agitation subscale score, was negatively correlated with each of the domain scores on the VABS (Table 2, Column 1). Similarly, ADHD symptoms as reflected in the ABC Hyperactivity subscale, were negatively correlated with each of the domain scores on the VABS (Table 2, Column 2). When covarying for ADHD symptoms (as well as age, IQ, and study), higher levels of irritability were associated with lower scores on the VABS Socialization subdomain ($F = 4.25$ (6, 178), $p < .05$, partial eta^2 [95% CIs] = .02 [.00 - .08]), but not the VABS Communication ($F = 1.05$ (6, 178), $p > .05$, partial eta^2 [95% CIs] = .006 [.00 - .05]) or Daily Living Skills ($F = 2.02$ (6, 178), $p > .05$, partial eta^2 [95% CIs] = .01 [.00 - .06]) subdomains. The relationship between ABC Irritability and VABS Socialization was equivalent to a Cohen's d of .31.

Discussion

Adaptive behavior is a key indicator of overall functioning among autistic individuals and informs treatment planning and long-term prognosis (Meyer et al. 2018). Measures of adaptive behavior are also commonly used to determine efficacy in treatment outcome studies (Chatham et al. 2018). As such, understanding factors that contribute to differences in adaptive behavior among autistic individuals is important. Notably, the focus on preschool and early school-age autistic children is of particular importance given the availability of empirically-validated interventions that can be delivered during the early childhood period when the brain is rapidly developing (Dawson et al. 2012). The current study explored two sets of behavioral characteristics that commonly occur in autism that we predicted would be related to adaptive behavior in autistic children: symptoms of ADHD and of Irritability/Agitation.

Previous research on the relationship between co-occurring ADHD symptoms and adaptive behavior in autistic individuals has been mixed. We hypothesized that the heterogeneity in previous findings was driven by co-occurring factors, namely irritability (Mayes et al. 2011). Thus, we predicted that, while both ADHD and irritability would be related to differences in adaptive behavior among young autistic children, irritability would be associated with greater difficulties in adaptive behavior over-and-above the association found for ADHD symptoms alone. In line with this hypothesis, our results showed that both ADHD symptoms and irritability symptoms independently were associated with adaptive behavior in 3- to 7-year-old autistic children. Interestingly, although ADHD symptoms and irritability

symptoms were independently associated with each domain of adaptive behavior explored (i.e., socialization, daily living skills, and communication), a compounding effect whereby irritability was associated with increased differences in adaptive behavior over-and-above ADHD symptoms was only found for the socialization subscale on the VABS.

Symptoms of ADHD and irritability can both cause social difficulties (Bunford et al. 2018; Harkins et al. 2021; Leibenluft and Stoddard 2013), given that many of these symptoms often occur in a social context. For example, irritability symptoms can include negative emotionality, aggressive behavior toward others and yelling at others, while ADHD symptoms include disturbing others and disrupting group activities. Our findings suggest that autistic children who have high levels of both irritability and ADHD symptoms are likely to have more difficulty in the domain of socialization than autistic children with either ADHD or irritability alone. As such, helping autistic children learn to self-regulate symptoms of irritability and negative emotionality and to communicate their needs in more adaptive ways could have a positive influence on their social skill development.

These findings are particularly salient given that our sample focuses on young children during a stage that is associated with tremendous growth in self-regulatory capacities (Rothbart et al. 2006). Learning to regulate one's attention, activity level, impulses, and emotions is a process that unfolds during the preschool years, and successful development of self-regulation is predictive of kindergarten and later school success (Duckworth and Carlson 2013). Our findings provide an opportunity to closely examine these features in this age range in order to support and enhance clinical approaches. Few treatment studies account for differences in emotion regulation in autistic children, and those that have been published typically focus on older school-age children and adolescents (Sofronoff et al. 2007; Weiss et al. 2018). Further research is needed to understand if incorporating specific strategies for addressing irritability in young children would increase the benefits of existing early behavioral intervention approaches for autism.

Our results need to be considered in light of several limitations. First, we combined data from three separate studies that had different inclusion and exclusion criteria. Furthermore, there was variability in the version of the VABS that was used across studies. Comparison of scores between the VABS-II and VABS-3 has suggested that the VABS-3 produces lower scores, particularly in those with lower levels of ability, as compared to the VABS-2 (Farmer et al. 2020). Furthermore, as noted in the methods, the concordance between the individual domain scores between the two versions was moderate. That said, our results remained the same when covarying for study in our analyses. Despite this, there is still a chance that study specific effects may have impacted our outcomes. Second, this study relied solely on caregiver reported measures of adaptive behavior and irritability. It is possible that multi-modal assessment of adaptive behavior and irritability would uncover additional relationships not discovered in the current analyses. Third, most of our findings were small effect sizes, with our primary analysis resulting in Cohen's d = .31. As noted by Cohen, while d = .31 is considered a small effect, it is still larger than a "trivial" effect (Cohen 1988). Additionally, reporting small effect sizes is critical to combat known issues in publication biases (Schäfer and Schwarz 2019). Finally, it is worth noting that other factors, such as sensory challenges, anxiety, and sleep deficits, can be associated

with both ADHD symptoms and irritability in autism. As such, it is possible that there are additional factors that can be contributing to our findings. Future studies should explore the interrelationship between these factors, ADHD symptoms, irritability, and adaptive behavior in autistic children.

In summary, our current study suggests that both symptoms of irritability and ADHD are separately correlated with adaptive behavior in young autistic children. After adjusting for the effect of co-occurring ADHD symptoms, we found irritability continued to be moderately negatively correlated with socialization skills. Understanding the relationships among irritability, ADHD, and adaptive behavior in young autistic children is critical given that adaptive behaviors often provide an estimate of global functional impairment and are commonly used to measure autism treatment outcomes. Furthermore, understanding how different co-occurring symptom profiles influence functioning in autism may help clinicians to develop individualized treatment approaches that will improve long-term outcomes in particular subgroups of autistic children.

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Table 1.

Demographics

	Overall (N=185)	Study 1 (N=63)	Study 2 (N=82)	Study 3 (N=40)
Sample Characteristics				
Age – Years [Mean (SD)]	4.8 (1.2)	4.2 (0.9)	5.3 (1.3)	5.0 (1.1)
Sex – Male [N (%)]	149 (80.5%)	49 (77.8%)	62 (75.6%)	38 (95%)
Full Scale IQ [Mean (SD)]	80.1 (25.6)	77.8 (25.6)	80.4 (25.1)	83.0 (26.7)
ADOS Comparison Scores [Mean (SD)]	7.74 (1.6)	7.32 (1.7)	8.1 (1.3)	7.7 (1.8)
Vineland Adaptive Behavior Scales [Mean (SD)]				
Socialization	74.7 (17.0)	78.4 (16.5)	72.4 (15.4)	73.5 (20.0)
Communication	80.5 (18.6)	81.0 (19.6)	77.1 (15.5)	86.5 (21.7)
Daily Living Skills	77.6 (17.4)	79.4 (20.0)	75.5 (11.6)	78.9 (22.2)
Aberrant Behavior Checklist [Mean (SD)]				
Irritability (max range 0–45)	12.7 (8.8)	10.9 (7.5)	12.5 (9.1)	15.8 (9.4)
Hyperactivity (max range 0–48)	20.3 (11.3)	18.8 (11.9)	20.1 (10.9)	23.3 (11.1)

Notes. Higher standard scores on the Vineland Adaptive Behavior Scales are associated with higher levels of adaptive behavior, while higher total scores on the Aberrant Behavior Checklist are associated with more difficulties with Irritability/Agitation or hyperactivity. Study 1 was a Department of Defense sponsored study of anxiety in preschool autistic children (Award# W81XWH-14–1-0526). Study 2 was a sub-study of the 2017–2022 Duke Autism Centers of Excellence (ACE) Center (NICHD P50-HD093074) exploring characteristics of neurotypical children, autistic children, children with ADHD, and autistic children with co-occurring ADHD. Only the subset of autistic children (with or without ADHD) are included in this study's sample. Study 3 was baseline data from a clinical trial of Oxytocin in Autism to enhance Reciprocal Social Behaviors (2012–2017 ACE Network Study; NICHD U01-HD073984) and included only autistic participants.

Table 2.

Spearman Partial correlations Between VABS and ABC Scales in full sample (N=185)

	Aberrant Behavior Checklist	
	Irritability	**Hyperactivity**
Vineland Adaptive Behavior Scales		
Socialization	r = −.30, p < .0001	r = −.30, p < .0001
Communication	r = −.21, p < .01	r = −.29, p < .0001
Daily Living Skills	r = −.20, p < .01	r = −.26, p < .001

Notes: All correlations covaried for the effects of age, IQ, and study. VABS=Vineland Adaptive Behavior Scales. ABC=Aberrant Behavior Checklist.