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# Attention deficit/hyperactivity disorder symptoms moderate cognition and behavior in children with autism spectrum disorders

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## Abstract

Recent estimates suggest that over 30% of children with autism spectrum disorders (ASD) meet diagnostic criteria for attention deficit/hyperactivity disorder (ADHD), and another 20% of children with ASD exhibit subthreshold clinical ADHD symptoms. Presence of ADHD symptoms in the context of ASD could have a variety of effects on cognition, autistic traits, and adaptive/maladaptive behaviors including: exacerbating core ASD impairments; adding unique impairments specific to ADHD; producing new problems unreported in ASD or ADHD; having no clear impact; or producing some combination of these scenarios. Children with ASD and co-morbid ADHD symptoms (ASD+ADHD; n=21), children with ASD without ADHD (ASD; n=28), and a typically developing control group (n=21) were included in the study; all groups were matched on age, gender-ratio, IQ, and socioeconomic status. Data were collected on verbal and spatial working memory, response inhibition, global executive control, autistic traits, adaptive functioning, and maladaptive behavior problems. In this sample**,** the presence of ADHD symptoms in ASD exacerbated impairments in executive control and adaptive behavior and resulted in higher autistic trait, and externalizing behavior ratings. ADHD symptoms were also associated with greater impairments on a lab measure of verbal working memory. These findings suggest that children with ASD+ADHD symptoms present with exacerbated impairments in some but not all domains of functioning relative to children with ASD, most notably in adaptive behavior and working memory. Therefore, ADHD may moderate the expression of components of the ASD cognitive and behavioral phenotype, but ASD+ADHD may not represent an etiologically distinct phenotype from ASD alone.

Autism spectrum disorders (ASD) and attention deficit hyperactivity disorders (ADHD) are diagnosed based upon behavioral symptoms (APA, 2000). ASD is characterized by impairments in social functioning, communication, and restricted, repetitive behaviors/interests, while ADHD is characterized by inattention and hyperactivity/impulsivity.

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[2]When spatial working memory data is combined for the ASD and ASD+ADHD groups and then compared to the TYP group we find a significant difference in total between errors, $t(56)=2.81$, $p<0.05$, Cohen's $d=0.61$).

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Although the Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition Text Revision (DSM-IV-TR; APA, 2000) precludes a co-morbid diagnosis of ASD and ADHD, a recent study examining co-morbidity revealed that over 30% of children with high-functioning ASD met diagnostic criteria for ADHD and an additional 25% of them exhibited elevated ADHD symptoms (Leyfer et al., 2006; see Bradley & Isaacs, 2006 for descriptions in a low-functioning adolescent sample). Additionally, research at the genetic (e.g., Smalley et al., 2002; Ogdie et al., 2003; Reiersen et al., 2007; Gadow, Roohi, DeVincent, & Hatchwell, 2008; Ronald et al., 2008), structural (Brieber et al., 2007) and functional (e.g., Durston et al., 2003; Schmitz et al., 2006) neuroanatomic levels of analysis suggest shared genetic risk loci and brain regions impacted in individuals with ASD and ADHD. Furthermore, similar associated behavioral features (e.g., executive control (EC) and aggression; Clark et al., 1999; Leyfer et al., 2006; Matsushima et al., 2008) indicate shared variance at the behavioral level.

This overlap raises the larger question of whether behavioral and cognitive phenotypes for children with ASD and clinically significant ADHD symptoms (hereafter referred to as ASD +ADHD) differ from children with ASD without significant ADHD symptoms. Several studies have probed EC, autistic symptoms and traits, or other (non-social) maladaptive behaviors in low- and high-functioning children with ASD+ADHD and children with ASD alone (Luteijn et al., 2000; Matsushima et al., 2008; Sinzig et al., 2008a; 2008b; Gomarus et al., 2009). Adaptive functioning (i.e., independent skills in everyday settings) has not been investigated in an ASD+ADHD group. It remains unclear whether a homogeneous sample of high-functioning children with ASD+ADHD shares similar impairments (and to the same degree) as an ASD sample across multiple domains of functioning. In what follows, we summarize the current literature on EC, autistic symptoms and behaviors, adaptive, and other maladaptive behavior in children with ASD, ADHD, and ASD+ADHD.

Current evidence suggests EC impairments in ASD, ADHD, and ASD+ADHD groups, although meaningful differences may exist between the groups regarding the affected EC processes. Consistent findings in ASD include weaknesses on parent ratings of cognitive flexibility (with moderate support in performance measures; for review see, Geurts, Corbett, & Solomon, 2009), as well as planning, organization, and to a lesser extent spatial working memory, whereas inhibition and verbal working memory task performance are relatively intact (for review, see Hill, 2004; Kenworthy et al., 2008). Consistent findings for ADHD include impaired performance on tasks of response inhibition, vigilance, verbal and spatial working memory, and planning (for review, see Willcutt et al., 2005).

Studies directly comparing EC in ASD and ADHD (Ozonoff & Jensen, 1999; Gioia et al., 2002; Geurts et al., 2004; Goldberg et al., 2005; Tsuchyia et al., 2005; Happé et al., 2006; Johnson et al., 2007; Geurts et al., 2008; Gomarus et al., 2009; Corbett et al., 2009) reveal a fairly consistent ADHD-specific weakness in response inhibition (but see Johnson et al., 2007; Corbett et al., 2009) and spatial working memory deficits (but see Goldberg et al., 2005), and an ASD-specific EC weakness in flexibility (but see Goldberg et al., 2005; Tsuchyia et al., 2005). Two of three studies directly comparing EC processes in an ASD +ADHD group versus an ASD group reveal a unique deficit in inhibitory control in ASD +ADHD, but no differences in cognitive flexibility or working memory (Sinzig et al., 2008b; Goramus et al., 2009; but see Sinzig et al., 2008a).

Recent studies have examined the presence of autistic symptoms, defined as social and communicative impairments as well as restricted/repetitive behaviors and autistic traits in ADHD populations. We focus on autistic traits as measured dimensionally using the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005). While several studies have validated the SRS as a measure of autistic traits in ASD samples (Constantino et al., 2000;

Constantino et al., 2003; Constantino et al., 2004), studies with ADHD samples have documented greater autistic traits than found in neurotypical populations (e.g., Reiersen et al., 2007). A handful of studies used the Childhood Social Behavior Questionnaire (CSBQ; Luteijn et al., 1998) to compare autistic symptoms measured dimensionally in ASD and ADHD samples. One study reported greater social and communication impairments for the ASD group based on broad domain CSBQ scores (Luteijn et al., 2000); while another reported group differences only on ASD-specific subscales (e.g., Reduced Social Contacts and Resistance to Change; Geurts et al., 2008). Taken together, these studies suggest that while individuals with ADHD do not meet diagnostic criteria for ASD, they exhibit elevated ASD traits/symptoms when using these dimensional measures. However, the symptoms may not be additive; similar ASD symptom (CSBQ) ratings were found for ASD+ADHD and ASD samples (Luteijn et al., 2000; Goramus et al., 2009).

Adaptive functioning is generally impaired in both ASD and ADHD, but individuals with ASD show more severe impairments. The large discrepancy between adaptive functioning and IQ is one of the most well established impairments in individuals with ASD (Volkmar et al., 1987; 1993; Carter et al., 1998; Constantino et al., 2004; Saulnier & Klin, 2008). Several cross-sectional studies in children and adults demonstrate impairments in all three domains of the Vineland Adaptive Behavior Scale (VABS) for high- and low-functioning individuals on the autism spectrum (Volkmar et al., 1987; 1993; Saulnier & Klin, 2008). In one study, VABS profiles correctly identified over 90% of individuals with ASD versus a developmentally-delayed group matched on age and IQ (Volkmar et al., 1993). Individuals with ADHD also exhibit reduced adaptive functioning relative to their own IQ and to typically developing matched controls (Barkley et al., 1990; Roizen et al., 1994; Stein et al., 1995; Happé et al., 2006; Stavro et al., 2007). The few studies examining both groups together show greater impairments for the ASD group (Stein et al., 1995; Happé et al., 2006). To date, no published study has examined adaptive functioning in an ASD+ADHD group relative to an ASD group.

Maladaptive behaviors are increased in high-functioning individuals with ASD and those with ADHD, but more often include internalizing behavior problems in ASD and externalizing behavior problems in ADHD. There are increased internalizing problems, and to a lesser degree, externalizing behavior problems, such as withdrawal, social problems, anxiety/depression, and thought disorders in high-functioning ASD groups (Sturm et al., 2004; Matsushima et al., 2008). Parent reports reveal significant externalizing, and to a lesser degree, internalizing, behavior problems, such as aggression, hyperactivity, and inattention in ADHD groups (Stein et al., 1995; Hudziak et al., 2004; Matsushima et al., 2008); however, many ADHD symptoms overlap with externalizing maladaptive behaviors, as well as symptoms of commonly associated co-morbid disorders (e.g., oppositional defiant disorder and conduct disorder) (Hudziak et al., 2004). The one study that examined a high-functioning group of children with ASD+ADHD[1] reported increased externalizing behavior problems, aggression, delinquent behaviors, and thought problems in the ASD+ADHD group relative to an ASD group which exhibited subthreshold externalizing problems (Matsushima et al., 2008), suggesting that ADHD symptoms exacerbated externalizing problems in ASD. This study was limited, however, by a relatively small number of children in the ASD group (n=9).

[1]Matsushima and colleagues refer to their sample as “PDD” for Pervasive Developmental Disorders, however upon closer inspection of the sample (49/54 children recruited for the study received a diagnosis of autism) it appears that the PDD reference is akin to our use of “ASD” and not a specific diagnosis of pervasive developmental disorder – not otherwise specified. Therefore, we will refer to their sample as an ASD sample to reduce confusion.

In light of the evidence reported above for both continuities and discontinuities in the cognitive and behavioral profiles in ASD and ADHD, we examined whether the co-occurrence of ASD and ADHD symptoms marks a meaningful phenotype within ASD at the cognitive and behavioral levels. While some previous investigations are limited by small samples (e.g., Matsushima et al., 2008) or no information on cognitive functioning (Luteijn et al., 2000), the current study compares cognitive and behavioral profiles across several domains among children with ASD+ADHD, children with ASD, and typically developing controls (TYP) matched on age, IQ, gender ratio, and socioeconomic status. Based on the reviewed literature, we predict that in comparison to TYP, both ASD groups will exhibit similar difficulties in spatial working memory, cognitive flexibility, and internalizing behavior. We further expect that ASD+ADHD will exacerbate global EC deficits, autistic traits and symptoms, adaptive functioning deficits, and externalizing behavior, and produce new deficits in inhibition and verbal working memory.

## Method

### Participants

Twenty-eight children with an ASD without elevated symptoms of ADHD (ASD); 21 children with an ASD and elevated symptoms of ADHD (ASD+ADHD); and 21 typically developing (TYP) children participated in the study. The first two groups were recruited through a hospital clinic specializing in ASD and neuropsychological assessment. Both clinical groups were diagnosed with a high-functioning ASD (ASD group: Autism n=13, Asperger's Syndrome n=11, Pervasive Developmental Disorder-Not Otherwise Specified [PDD-NOS] n=4; ASD+ADHD: Autism n=9, Asperger's Syndrome n=6, PDD-NOS n=6) using DSM-IV criteria (APA, 1994). All participants in the two clinical groups also qualified for a 'broad ASD' on the ADI/ADI-R (LeCouteur et al., 1989; Lord et al., 1994) and/or the ADOS (Lord et al., 1999) following the criteria established by the NICHD/NIDCD Collaborative Programs for Excellence in Autism (Lainhart et al., 2006); all but four children received both diagnostic instruments. The broad ASD criteria include meeting the ADI cutoff for autism in the social domain and at least one other domain or meeting the ADOS cutoff for the combined social and communication score. In addition, all children in the ASD+ADHD group met criteria for either ADHD Combined Type or Predominantly Inattentive Type on the DSM-IV ADHD parent rating scale. Given their relevance to the domains assessed here, stimulant medications were withheld 36 hours prior to testing (ASD group n=5; ASD+ADHD group n=5). Children in the ASD group were taking the following other medications: selective serotonin reuptake inhibitors (n=2); antipsychotics (n=1) while children in the ASD+ADHD group were taking the following medications: selective serotonin reuptake inhibitors (n=2); antipsychotics (n=2). The TYP group was recruited from the community via advertisements. All participants were required to have a Full Scale IQ≥80 as measured by one of three Wechsler Intelligence scales (Wechsler Intelligence Scale for Children–3rd Edition, Wechsler Intelligence Scale for Children–4th Edition, Wechsler Abbreviated Scale of Intelligence; Wechsler 1991; 1999; 2003), which resulted in excluding four participants from the ASD+ADHD group (original n=25). We excluded participants in the clinical groups if they had any parent reported history of comorbid genetic or neurological disorders (e.g., Fragile X syndrome, Tourette's syndrome). TYP participants were screened and excluded if they or a first-degree relative were found to have developmental, language, learning, neurological, or psychiatric disorders or psychiatric medication usage, which resulted in the exclusion of three participants (original n=24). Groups did not differ in terms of age ($F(2,67)=0.83$, $p=0.44$), Hollingshead's (1975) Four-Factor index for socioeconomic status ($F(2,63)=0.39$, $p=0.68$), gender ratio ($\chi^2(n=70)=3.06$, $p=0.22$), or IQ ($F(2,66)=1.14$, $p=0.33$; See Table 1).

## Diagnostic Measures

**Autism Diagnostic Interview/Autism Diagnostic Interview-Revised and Autism Diagnostic Observation Schedule (ADI/ADI-R; ADOS)—**The ADI/ADI-R (LeCouteur et al., 1989; Lord et al., 1994) is a detailed parent or primary caregiver interview of developmental history and autism symptoms. Scores are aggregated into symptom clusters that correspond to DSM-IV criteria for a diagnosis of autism. The ADOS (Lord, et al., 1999) is a structured play and conversational interview that includes a series of social presses and other opportunities to elicit symptoms of an ASD.

**Diagnostic and Statistical Manual of Mental Disorders-IV Attention Deficit Hyperactivity Disorder Rating Scale-Parent Edition (DSM-IV; ADHD rating scale)—**The ADHD Rating Scale (DuPaul, Power, Anastopoulos, & Reid, 1998) assesses severity in inattention and hyperactivity/impulsivity symptoms. This 18-question scale yields two domains: inattention and hyperactivity/impulsivity. For each question, parents use a 0-3 scale to rate the participant. A higher score indicates more symptom severity, and a score of 2 or 3 is considered a significant symptom; six or more significant symptoms in either the inattention or hyperactivity/impulsivity domains meet criteria for an ADHD diagnosis.

## Executive Control (EC)

**Behavior Rating Inventory of Executive Functions–Parent Form (BRIEF)—**The BRIEF (Gioia et al., 2000) is an informant report of EC in everyday situations comprised of eight scales which are collapsed into two broad indices: the Behavioral Regulation Index (BRI) and the Metacognition Index (MCI). Results are reported as T-scores. Higher scores indicate greater impairment; T-scores≥65 (i.e., 1.5 SDs≥the mean) indicate clinically significant ratings. Dependent variables include the two broad indices, as well as the Inhibition and Shift sub-scales.

**Wechsler Intelligence Scale for Children-IV–Digit Span (DS)—**DS (Wechsler, 2003) measures auditory attention and verbal working memory. Participants must repeat number sets back to the administrator in both forward and reverse order (i.e., backwards). Number sequences increase from two to nine digits as the task advances. Dependent variables include a standard score (mean=10, SD=3) of the child's accuracy during forward administration, backwards administration, and a total score; however, the current study used the backwards standard scores as this allows isolation of manipulation (i.e., working memory) from short-term storage of information.

**Spatial Working Memory–Cambridge Neuropsychological Tests Automated Battery—**For Spatial Working Memory (Cambridge Cognition, 1996), children are initially presented with three boxes displayed on the computer screen. Children are then instructed to find a target (i.e., a blue token) hidden inside one of an array of boxes by using a touch-screen to search the boxes. The boxes are baited with a target one at a time, and once the target is found it does not appear in that location again. The task begins with three boxes and increases up to eight boxes, and the target is hidden in every location. The task does not move to the next level until all targets are found. Dependent variables include between errors, which are the total number of times a child returns to a previously baited location.

**Walk Don't Walk-Test of Everyday Attention for Children—**Walk Don't Walk (Manly et al., 1999) is a measure of sustained attention and pre-potent response inhibition. Respondents must attend to two auditory stimuli (i.e., beeps and beeps plus crashing noise); the former prompts respondents to mark the corresponding tile of a path, while the latter cues them to stop marking the corresponding tile of the path. To receive credit, children must correctly mark the number of beeps heard. The temporal interval between the auditory stimuli decreases as the task proceeds. The dependent variable is a scaled score (mean=10, SD=3) of accuracy across 20 trials.

### Autistic Traits

**Social Responsiveness Scale (SRS):** The SRS (Constantino & Gruber, 2005) is a 65-item informant report of autistic traits rated on a 4-point Likert Scale (0 to 3 points). Higher scores indicate more autistic traits; T-scores≥65 (i.e., 1.5 SDs≥the mean) suggest clinically significant autistic traits. Based on factor analysis, these traits fall on a single dimension (Constantino & Gruber, 2005), so the SRS Total T-score was the dependent variable of interest.

### Adaptive Functioning

**Vineland Adaptive Behavior Scales–Interview Edition (VABS):** The VABS–Interview Edition (Sparrow et al., 1984) is a standardized, structured parent interview of adaptive behaviors across the following domains: Communication, Daily Living Skills, and Socialization using standard scores (mean=100; SD=15), and the domains can be combined into an Adaptive Behavior Composite. Dependent variables include the three domain standard scores.

### Maladaptive Behavior

**Behavior Assessment System for Children (BASC):** The BASC (Reynolds & Kamphaus, 1992) is an informant measure of both adaptive and problematic behaviors in everyday settings. It is comprised of 14 clinical scales and two broad domains: Externalizing Problems, Internalizing Problems. T-scores≥65 (i.e., 1.5 SDs≥the mean) indicate clinically significant symptoms. Dependent variables include the two broad domains and the following clinical scales: Attention Problems, Hyperactivity, Withdrawal, and Atypicality.

**Procedures:** This battery of tests and informant measures was administered over two sessions lasting two to three hours as part of a larger, study examining the neuropsychological profile of children with ASD. Parental or legal guardian consent and child assent were obtained prior to testing, families were compensated for their time, and the protocol was approved by the institutional review board.

**Analyses:** To compare the EC, autistic traits, adaptive functioning, and maladaptive behaviors of all three groups, group by task univariate (ANOVA) and multivariate analyses of variance (MANOVA) were completed. MANOVAs were used when a measure provided more than one dependent variable of interest. A False Discovery Rate of $q<.05$ (Benjamini & Hochberg, 1995) was used to control for the number of ANOVAs and MANOVAs conducted (i.e., 19 F-tests). When ANOVA and/or MANOVA analyses survived the False Discovery Rate then a Tukey's hsd of $p<0.05$ was used for post-hoc comparisons.

## Results

### Executive Control

Parent ratings of EC on the BRIEF's broad indices (BRI; MCI) and two selected subscales (Inhibition; Shift) revealed a consistent pattern: the ASD+ADHD group received higher (more impaired) ratings than the ASD and TYP groups, Wilk's Lambda: $F(8,122)=13.86$, $p<0.001$ (Tukey's hsd $p<0.05$ for ASD+ADHD vs. ASD and ASD+ADHD vs. TYP for all four measures) and the ASD group was rated higher than the TYP group (Tukey's hsd $p<0.05$ for ASD vs. TYP for all four measures; see Table 2). Lab measures of verbal working memory, $F(2,62)=5.56$, $p<0.05$, revealed the ASD+ADHD group scoring significantly lower than the TYP group (Tukey's hsd $p<0.05$) but not the ASD group, even though there was a medium effect size for the latter comparison. No significant differences were found between groups on spatial working memory, $F(2,56)=1.85$, $p=0.17$, and response inhibition measures, $F(2,56)=1.51$, $p=0.23$; although, as shown in Table 2, there were medium effect sizes for worse performance by the ASD+ADHD group relative to the other groups.

### Autistic Traits and Symptoms and ADHD Symptoms

Overall, the ASD and ASD+ADHD groups received significantly higher autistic trait ratings on the SRS relative to the TYP group, $F(2,64)=91.09$, $p<0.001$ (Tukey's hsd $p<0.05$ for ASD vs. TYP and ASD+ADHD vs. TYP; see Table 3), and the ASD+ADHD group received higher autistic trait ratings on the SRS compared to the ASD group (Tukey's hsd $p<0.05$). However, the ASD and ASD+ADHD groups did not differ in the number of autism symptoms as reported on the ADI Social, ADI Communication, ADI Repetitive Behavior, and the ADOS Social+Communication scales (all $ts(43)\leq1.58$, all $ps\geq0.12$). For ADHD symptoms, the ASD+ADHD group was rated as having more Total symptoms, Inattention symptoms, and Hyperactivity/Impulsivity symptoms compared to the ASD and TYP groups, $F(2,67)=36.80$, $p<0.001$ (Tukey's hsd $p<0.05$ for all comparisons). The ASD group was rated as having more Total and Inattention symptoms, but not Hyperactivity/Impulsivity symptoms, compared to the TYP group. The differences between the ASD+ADHD group and the ASD group were expected as the ADHD Rating scale was the measure used to distinguish the ASD from the ASD+ADHD group.

### Adaptive Functioning

Overall, both ASD and ASD+ADHD groups received significantly lower adaptive functioning ratings on the Communication, Daily Living Skills, and Socialization domains relative to the TYP group, $F(6,100)=10.26$, $p<0.001$ (Tukey's hsd $p<0.05$ for ASD vs. TYP and ASD+ADHD vs. TYP for all three measures), but the ASD+ADHD group exhibited a more severe impairment in Daily Living Skills compared to the ASD group, $F(2,52)=23.76$, $p<0.001$ (Tukey's hsd $p<0.05$; see Table 4).

### Maladaptive Behaviors

Overall, both ASD and ASD+ADHD groups received higher maladaptive behavior ratings on the broad indices of Externalizing Problems and Internalizing Problems, as well as the clinical scales of Atypicality, Attention Problems, Hyperactivity, and Withdrawal compared to the TYP group, $F(12,102)=8.67$, $p<0.001$ (Tukey's hsd $p<0.05$ for ASD vs. TYP and ASD+ADHD vs. TYP for all six measures; see Table 3). Furthermore, the ASD+ADHD group received significantly higher ratings for Externalizing Problems, Attention Problems, and Hyperactivity, than the ASD group (Tukey's hsd $p<0.05$).

### Age and Gender Effects

As a secondary analysis, age and gender effects were examined. As a first pass analysis for age, all dependent variables were correlated with age, and an FDR ($q<.05$) was applied. Not one of the correlations survived this correction and further analyses were not conducted. To examine gender effects, all females were removed and analyses were re-run. The pattern of results remained the same save one finding: group differences between Controls and ASD on the Communication Domain of the Vineland were no longer significant (Control: mean=102.75, SD=7.38; ASD mean=98.8 SD=14.33, Tukey's HSD $p=.83$).

## Discussion

The current study probed the impact of ADHD symptoms on the ASD phenotype relative to children with ASD without significantly elevated ADHD symptoms and TYP children. Consistent with our predictions, we found that children with ASD+ADHD exhibited significantly exacerbated problems in verbal working memory, global EC, autistic traits, adaptive function, and externalizing behaviors. Contrary to our predictions, the ASD +ADHD group also exhibited exacerbated cognitive flexibility deficits in everyday settings, but no significant inhibition deficits on our lab measure, and we failed to find spatial working memory impairments in either clinical group. Of note, both EC lab measures showed a pattern in which Controls scored higher than the ASD group which in turn scored higher than the ASD+ADHD group.

### Executive Control

Our finding of exacerbated global EC deficits in children with ASD+ADHD compared to both TYP and ASD groups is consistent with our hypothesis that combining two disorders with distinct EC deficit profiles would have an additive effect overall. Past research on the BRIEF has shown unique EC profiles for ASD and ADHD samples (Gioia et al., 2002), but no previous study has examined profiles for an ASD+ADHD sample. Our findings of impaired EC behaviors in the ASD group are consistent with several previous BRIEF studies (Gilotty et al., 2002; Gioia et al., 2002; Kenworthy et al., 2009) and other informant-based measures of cognitive flexibility (Green et al., 2006; Didden et al., 2008; Peters-Scheffer et al., 2008). The current study's findings of greater impairments in EC for the ASD+ADHD group are consistent with prior findings of greater global impairments in ADHD (Gioia et al., 2002); however, our finding of greater cognitive flexibility impairments in the ASD +ADHD group was unexpected. One potential interpretation is that the ASD+ADHD group has greater EC impairments (as suggested from the verbal working memory lab measure and a prior report of inhibitory control: Sinzig et al., 2008b) and these processes produce an additive effect, increasing global EC deficits.

Our reported verbal working memory deficit in the ASD+ADHD group relative to TYP (and a medium effect size compared to the ASD group) is in contrast with a previous study showing similar levels of impairment in ASD and ASD+ADHD samples during a verbal working memory task (Goramus et al., 2009). Differences in task design may explain the discrepant findings. The task used here, backwards Digit Span, required manipulation of stored information, while the task from the earlier study required only storage of verbal stimuli across a delay. This suggests that manipulation of verbal information in working memory may be a unique deficit for the ASD+ADHD sample. A recent meta-analysis (Willcutt et al., 2005) examined verbal working memory manipulation in ADHD and found evidence for an impairment with a medium weighted effect size (Cohen's $d$=.55). A significant impairment in working memory was found in 55% of studies. While this was not the largest effect reported for ADHD, the working memory manipulation does appear to be an area of weakness in ADHD and our findings for the ASD+ADHD group converge with the ADHD literature. Our failure to find spatial working memory deficits in the ASD +ADHD group relative to the TYP or ASD groups is consistent with a prior study (Sinzig et al, 2008b); however, this conflicts with the emerging literature of a subtle ASD-related impairment in spatial working memory that requires larger sample sizes to reach statistical significance (see Kenworthy et al., 2008 for review). Our results also highlight a potential distinction between spatial and non-spatial working memory weaknesses in these children, although the findings in this area remain complex and somewhat contradictory; future studies should examine these potential working memory distinctions in children with ASD +ADHD.

Our finding of no group differences in the response inhibition measure corroborates one previous study (Sinzig et al., 2008a), but conflicts with another (Sinzig et al., 2008b). However, recent theoretical arguments suggest that the response inhibition task used here, Walk Don't Walk, may be confounded with processing speed demands (Bishop & Norbury, 2005). In addition, the mean of the TYP group was slightly below average relative to the Walk Don't Walk standardization sample and out of line with the TYP group's high average IQ and minimal ADHD symptoms. This raises the broader question of Walk Don't Walk's sensitivity to accurately tap attention/impulsivity in this sample. Therefore, this measure may not have been the most sensitive for detecting response inhibition impairments prototypically associated with ADHD; future studies should focus on well-replicated and purer measures of inhibition, such as the Go/No-Go and Stop-Signal tasks (Willcutt et al., 2005).

Of note, many of the ASD and even the ASD+ADHD groups' EC means fall within 1 SD of the published norms, and this may lead to some concern regarding the meaningfulness of the group differences. However, the age-, IQ-, gender-ratio-, socioeconomic-matched Control group performs better than either of the ASD or ASD+ADHD groups on the BRIEF and Digit Span, demonstrating that these EC areas are a relative weakness for high-functioning children with ASD and ASD+ADHD. Indeed, a significant portion of children with ASD (19%-50% across the subscales and indices) score in the borderline or clinical range on the BRIEF (T-score ≥65).

### Autistic Traits and Symptoms

We found exacerbated autistic traits in the ASD+ADHD group, although findings in this and previous reports diverge depending on whether traits or symptoms were measured. We found the ASD+ADHD group received higher autistic trait ratings on the SRS, but not significantly more autism symptoms on the ADI and ADOS. Prior investigations also did not find differences when using another symptom based measure, the CSBQ (Luteijn et al., 2000; Goramus et al., 2009). One potential explanation for the divergent findings is that the SRS was designed to measure autistic traits on a broad spectrum from typical to clinically significant; whereas the CSBQ (Luteijn et al., 2000) and ADI/ADOS are designed to measure clinically elevated ASD symptoms (Gotham, Risi, Pickles, & Lord, 2006). Thus, the CSBQ may have been insensitive to differences between ASD and ASD+ADHD groups, consistent with our lack of group differences on ADI and ADOS scales. Another explanation may be that the SRS assesses more than autism-specific traits, and therefore ratings of broader social problems may explain the higher ratings in our ASD+ADHD sample as well as previous ADHD samples (e.g., Reiersen et al., 2007). Placed within this context, the present study indicates that ADHD exacerbates the social disabilities of children with ASD.

### Adaptive Functioning

Our finding of significant impairments across various adaptive function domains in both ASD groups relative to TYP controls is in line with past studies (e.g., Volkmar et al., 1987; 1993; Saulnier & Klin, 2008); however, the finding of greater impairments in Daily Living Skills for the ASD+ADHD group relative to the ASD group is novel. The exacerbated impairments in the Daily Living Skills domain may result from increased global EC deficits in the ASD+ADHD group and associated difficulties in organization and planning, which are key cognitive skills that aid codification of everyday routines, such as eating, dressing, showering, and brushing one's teeth. Disorganization is one of the inattention symptoms for an ADHD diagnosis (APA, 2000), and previous research has documented impaired organization and planning in ASD (Kenworthy et al., 2005) and in ADHD (Willcutt et al., 2005). Regardless, the presence of ADHD exacerbates daily living skills in ASD.

Although adaptive Communication scores are depressed in both ASD groups compared to the TYP group, the difference between the pure ASD and TYP group scores becomes non-significant when girls (n=8) are removed from the sample, a finding that converges with recent evidence of more severe communication deficits in females with ASD than males at an early age (Hartley & Sikora, 2009). Further work is needed to map out potential gender differences in the behavioral presentation of ASD.

### Maladaptive Behaviors

Our findings that the ASD+ADHD group has significantly elevated externalizing maladaptive behaviors, Hyperactivity and Attention Problems, relative to the ASD and TYP groups, but has similar Withdrawal and Atypicality scores to the ASD group, supports several prior studies (Luteijn et al., 2000; Matsushima et al., 2008; but see Goramus et al., 2009), and confirms our hypothesis that ADHD exacerbates the externalizing behavior problems in the ASD profile. Many of the items in the clinical scales and the Externalizing Problems index rated higher in the ASD+ADHD group overlap with core ADHD symptoms. While to some degree this may reflect intra-rater reliability across similar questions on these measures, it is also notable that the two clinical groups were rated similarly for Internalizing Problems. Indeed, this finding suggests that parents of children with ASD+ADHD were not simply biased in their ratings, but targeted specific domains affected by ADHD symptoms. Although it may be tempting to conclude that our both of our ASD groups' functioning in maladaptive internalizing behaviors is not of clinical concern (T-scores are <1 SD from published norms), it is important to note that relative to their cognitive functioning level and to matched Controls they are exhibiting significantly greater Internalizing problems, and this supports recent findings that internalizing disorders such as specific phobias, OCD and depression are some of the more common comorbid psychiatric conditions in high-functioning ASD (Leyfer et al., 2006).

### Implications for Our Understanding of ASD and ASD+ADHD Phenotypes

The current study has implications for the: conceptualization of the ASD+ADHD phenotype; interpretation of past ASD studies of EC; and clinical assessment and treatment of children presenting with ASD and ADHD symptoms. Pennington (2002) outlines six general criteria that must be met to identify a distinct phenotype. There must be differences in: 1) in treatment response; 2) clinical profiles (i.e., discriminates ASD from ASD+ADHD); 3) differences on performance measures that are independent from measures defining the diagnosis, such as neuropsychological or neuroimaging measures; 4) etiology; 5) pathogenesis; and 6) developmental trajectories. The current study is best equipped to address Pennington's (2002) second and third criteria. Using established cut-offs for children with ADHD (DuPaul et al., 1998) we were able to identify two dissociable groups for the purpose of the current study, but future studies employing multiple methods of diagnosis in both discrete and dimensional fashions will confirm whether this distinction is clinically meaningful. Moreover, our neuropsychological and adaptive behavior findings, which are independent of measures used to define ASD and ADHD, do not support categorically different performance. While speculative, we would suggest that the observation of exacerbation of ASD impairments in some but not all domains of functioning for the ASD+ADHD group is most consistent with a "moderating" hypothesis (Mundy, Henderson, Inge, & Coman, 2007; Gadow et al., 2008). This hypothesis proposes that the presence of ADHD (and associated risk genes and behaviors) affects the expression of the ASD phenotype, but does not constitute a separate phenotype. Consistent with our hypothesis are previous findings of overlapping risk genes (Reiersen et al., 2007; Gadow et al., 2008; Ronald et al., 2008) and brain structure anomalies (Brieber et al., 2007). Future research in the ASD+ADHD phenotype, with a particular focus on treatment response, pathogenesis, and developmental trajectory, will rigorously test this hypothesis and as well as other models (e.g., for detailed models of comorbidity see Neale & Kendler, 1995).

This study also has implications for the interpretation of EC data collected in previous research that has not routinely screened for ADHD in ASD (but see Goldberg et al., 2005; Corbett et al., 2009). If the presence of ADHD symptoms in the context of ASD creates an exacerbated or moderated profile, as discussed above, past studies should be interpreted with caution when considering the severity (or the effect size) of EC impairment. As the field's understanding of ASD is refined, specificity regarding its associated features, including EC, will also improve. Finally with respect to clinical implications, the notable findings of increased difficulties with daily living skills make them a primary target in the assessment and intervention of children with ASD and ADHD symptoms.

## Limitations

Several potential factors may limit the generalization of our findings. Many of the key findings are based on informant ratings of child behavior across a variety of domains. While informant ratings are subject to bias, this concern should be mollified by the observation that caregivers in the ASD+ADHD group did not rate their children as more severely impaired across all domains (e.g., VABS Social and Communication Skills, BASC Internalizing Problems). This enhances confidence that group differences are not solely related to informant bias. Another concern regarding the informant ratings is the potential overlap between measures used to create the groups (e.g., ADI and ADHD rating scale) and dependent measures (SRS and BRIEF). The ADI and ADHD rating scale were created to count the number of symptoms for diagnostic purposes, and, particularly in the case of the ADI, are not intended for use as a continuous measure of severity (Gotham et al., 2006). In contrast, the BRIEF (Gioia et al., 2000) and SRS (Constantino & Gruber, 2005) are both well-normed, continuous measures, designed to assess a wide array of neurotypical and clinical populations. Nevertheless, the Inhibition and Working Memory subscales from the BRIEF have a high correlation with ADHD diagnostic measures (Gioia & Isquith, 2001), and therefore findings may reflect group assignment. Somewhat small samples are also a concern particularly when examining performance on the spatial working memory and response inhibition measures; we generally found a trend toward increasing impairment across the TYP, ASD, and ASD+ADHD group, supported by medium effect sizes despite non-significant $p$ values. Another limiting factor is that the ASD+ADHD group was defined through the use of a single parent measure, and this would not suffice using DSM-IV TR criteria for securing significant impairments in two contexts (APA, 2000) or standards applied in the ADHD literature (e.g., Lahey et al., 2004). Another limiting factor is that our sample is considerably high-functioning with a mean IQ in the High Average range, and therefore our findings in the ASD+ADHD group relative to the ASD group may not apply to lower functioning samples. Moreover, establishing a lower bound Full Scale IQ of 80 in all groups during matching reduced differences for the ASD+ADHD group, from which four excluded children were excluded.

## Conclusions

The current study examined cognitive, social, and adaptive profiles of children with ASD +ADHD symptoms relative to children with ASD symptoms. It provides novel findings for a potential ASD+ADHD phenotype that has exacerbated impairments in autistic traits, daily living skills, and maladaptive behaviors, and potentially unique impairments in verbal working memory. The ASD+ADHD phenotype may inform novel treatment targets, as well as provide a potential method for parsing heterogeneity within the autism spectrum.

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**Table 1**

Participant demographics

| N | TYP<br>21 | ASD<br>28 | ASD+ADHD<br>21 |
|---|---|---|---|
| Chronological Age (Years) | | | |
| M (SD) | 10.30 (1.76) | 9.70 (2.12) | 9.65 (1.62) |
| Range | 7.34-13.81 | 6.61-13.66 | 7.50-12.88 |
| Full Scale IQ | | | |
| M (SD) | 116.24 (11.53) | 117.39 (18.68) | 111.24 (13.56) |
| Range | 100-140 | 85-159 | 88-136 |
| Gender (male/female) | 13/8 | 20/8 | 18/3 |
| Race | | | |
| AI/AN* | 0 | 0 | 1 |
| Asian | 0 | 0 | 0 |
| Black/African American | 0 | 3 | 1 |
| Caucasian | 19 | 19 | 13 |
| Indian/Southeast Asian | 0 | 2 | 0 |
| Other | 2 | 3 | 4 |
| Missing | 0 | 1 | 2 |
| Family Socioeconomic Status | | | |
| M (SD) | 23.71 (8.64) | 23.13 (11.36) | 26.16 (14.93) |

*AI/AN= American Indian/Alaskan Native

## Table 2

Group Differences in Executive Control Scores

| | TYP M (SD) | ASD M (SD) | ASD+ADHD M (SD) | Group Differences* |
|---|---|---|---|---|
| Behavior Rating Inventory of Executive Function (BRIEF) | | | | |
| BRI (T-Score) | 41.62 (6.55) | 59.92 (11.89) | 71.60 (10.78) | TD<ASD<ASD+ADHD |
| MCI (T-Score) | 43.29 (5.55) | 58.19 (10.57) | 73.65 (6.75) | TD<ASD<ASD+ADHD |
| Inhibit (T-Score) | 44.10 (6.88) | 57.31 (11.81) | 69.65 (13.28) | TD<ASD<ASD+ADHD |
| Shift (T-Score) | 43.71 (10.25) | 63.62 (13.30) | 72.50 (11.55) | TD<ASD<ASD+ADHD |
| Digit Span (DS) | | | | |
| Backwards (Scaled Score) | 11.80 (2.80) | 10.80 (3.08) | 9.10 (2.63) | TD>ASD+ADHD; ASD=TD, ASD=ASD+ADHD[a] |
| Spatial Working Memory | | | | |
| BE (Raw Score) | 38.59 (14.09) | 43.88 (16.33) | 49.65 (19.59) | None[b] |
| Walk Don't Walk | | | | |
| Total (Scaled Score) | 7.43 (2.60) | 6.18 (3.29) | 5.56 (4.27) | None[c] |

BE= Between Errors

*These differences are significant after controlling for multiple comparisons with the False Discovery Rate ($q<0.05$), and then using Tukey's hsd ($p<0.05$) for post-hoc analyses.

[a]Effect size for the difference between ASD and ASD+ADHD was medium (Cohen's $d=0.59$)

[b]Effect sizes for the difference between ASD+ADHD vs. TYP and ASD+ADHD vs. ASD were medium-to-large (Cohen's $d=0.65$ and 0.42, respectively)

[c]Effect sizes for the difference between ASD+ADHD and TYP and ASD vs. TYP were medium (Cohen's $d=0.53$ and 0.42, respectively)

**Table 3**

Group Differences in Autistic Traits and Symptoms, and ADHD Symptoms

| | TYP M (SD) | ASD M (SD) | ASD+ADHD M (SD) | Group Differences** |
|---|---|---|---|---|
| *Social Responsiveness Scale (SRS)* * | | | | |
| Total | 41.30 (5.64) | 69.88 (13.01) | 81.29 (18.89) | TD<ASD<ASD+ADHD |
| *ADOS* | | | | |
| *Social + Communication Score* | | | | |
| M (SD) | -------- | 11.81 (4.13) | 11.05 (4.68) | N.S. |
| Range | -------- | 6-20 | 1-21 | |
| *ADI/ADI-R* | | | | |
| *Social Score* | | | | |
| M (SD) | -------- | 16.68 (7.06) | 19.60 (4.84) | N.S. |
| Range | -------- | 1-27 | 10-28 | |
| *Verbal Communication Score**** | | | | |
| Total Score M (SD) | -------- | 14.52 (5.47) | 16.65 (4.42) | N.S. |
| Range | -------- | 2-24 | 8-24 | |
| *Repetitive Behaviors Score* | | | | |
| M (SD) | -------- | 6.28 (2.64) | 6.35 (2.35) | N.S. |
| Range | -------- | 1-10 | 2-10 | |
| *ADHD Rating Scale* | | | | |
| *Inattention Symptoms* | | | | |
| M (SD) | 0.10 (0.30) | 1.89 (1.81) | 7.52 (1.50) | TYP<ASD<ASD+ADHD |
| Range | 0-1 | 0-5 | 3-9 | |
| *Hyperactivity/Impulsivity Symptoms* | | | | |
| M (SD) | 0.10 (0.30) | 1.64 (1.77) | 5.19 (2.98) | TYP<ASD<ASD+ADHD |
| Range | 0-1 | 0-5 | 0-9 | |
| *Total ADHD Symptoms* | | | | |
| M (SD) | 0.19 (0.51) | 3.54 (3.02) | 12.71 (3.77) | TYP<ASD<ASD+ADHD |
| Range | 0-2 | 0-9 | 6-18 | |

* SRS scores are T-Scores (mean=50, SD=10). ADOS, ADI, and ADHD Rating Scale scores are raw scores.

** These differences are significant after controlling for multiple ANOVA or MANOVA comparisons with the False Discovery Rate ($q<0.05$), and using Tukey's hsd ($p<0.05$) for post-hoc analyses.

**Table 4**

Group Differences in Adaptive Functioning, and Maladaptive behaviors

| | TYP M* (SD) | ASD M (SD) | ASD+ADHD M (SD) | Group Differences** |
|---|---|---|---|---|
| *Vineland Adaptive Behavior Scales (VABS)* | | | | |
| Communication | 106.63 (10.65) | 94.86 (15.67) | 85.41 (19.58) | TD>ASD=ASD+ADHD |
| Daily Living Skills | 104.25 (14.24) | 79.45 (15.34) | 66.82 (17.84) | TD>ASD>ASD+ADHD |
| Social Skills | 103.37 (10.57) | 79.59 (11.84) | 73.41 (16.87) | TD>ASD=ASD+ADHD |
| *Behavior Assessment System for Children (BASC) Domains* | | | | |
| Externalizing Problems | 42.45 (5.88) | 49.57 (9.86) | 62.50 (15.14) | TD<ASD<ASD+ADHD |
| Internalizing Problems | 41.60 (7.79) | 51.71 (12.47) | 52.33 (11.93) | TD<ASD=ASD+ADHD |
| *Subscales* | | | | |
| Atypicality | 43.25 (8.45) | 58.57 (14.66) | 67.33 (17.70) | TD<ASD=ASD+ADHD |
| Attention Problems | 44.90 (6.17) | 56.48 (8.29) | 68.22 (5.34) | TD<ASD<ASD+ADHD |
| Hyperactivity | 41.55 (7.98) | 55.81 (10.47) | 67.78 (17.41) | TD<ASD<ASD+ADHD |
| Withdrawal | 44.75 (8.54) | 57.48 (11.77) | 59.28 (13.88) | TD<ASD=ASD+ADHD |

* All scores except for those from the VABS are T-Scores (mean=50, SD=10). VABS scores are Standard Scores (mean=100, SD=15).

** These differences are significant after controlling for multiple ANOVA or MANOVA comparisons with the False Discovery Rate ($q<0.05$), and using Tukey's hsd ($p<0.05$) for post-hoc analyses.