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Identifying comorbid ADHD in autism: Attending to the inattentive presentation

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ABSTRACT

Background: There are high rates of comorbidity between ADHD and ASD; however, there has been limited work parsing rates by ADHD presentation. In addition, commonly used questionnaires have demonstrated reduced utility in capturing ADHD symptoms in individuals with ASD. We examined the prevalence of comorbid Attention-Deficit/Hyperactivity Disorder (ADHD) parsed by DSM-5 presentation in clinic-referred youth with Autism Spectrum Disorder (ASD) without intellectual disability (ID). We compared common rating scales to determine which most effectively identified comorbid ADHD.

Method: We examined comorbid ADHD diagnoses from archival assessment data for 419 youth with ASD without ID. We examined diagnostic discriminability of the parent and teacher ADHD Rating Scale (ADHD R-S), and Attention and ADH Problems Scales of the Child Behavior Checklist and Teacher Report Form using receiver operating characteristic (ROC) curves. Hierarchical logistic regression was used to examine measures' unique contribution to ADHD diagnosis.

Results: Sixty-one percent of the study sample met DSM-5 criteria for an attention disorder. ADHD, Combined (ADHD-C) represented the largest proportion of ADHD diagnoses (76.8%), followed by Inattentive (ADHD-I;19.7%), Hyperactive/Impulsive (.02%), and Un-/Other Specified (.02%). Measures provided greater diagnostic discriminability in identifying ADHD-C relative to ADHD-I. The ADHD R-S inattentive symptom count provided the greatest discriminability for both subtypes and was the only scale that provided clinically meaningful differentiation between those with ASD only and ASD + ADHD-I.

Conclusions: These results support using the ADHD R-S to capture comorbid ADHD symptoms in ASD. The findings underscore the need for more thorough examination of inattentive symptoms to rule out ADHD-I.

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1. Introduction

Attention-Deficit/ Hyperactivity Disorder (ADHD) is one of the most common comorbid disorders diagnosed in children with Autism Spectrum Disorder (ASD) with rates of co-occurrence ranging from 30 to 70% (Antshel, Zhang-James, Wagner, Ledesma, & Faraone, 2016; Joshi et al., 2017; Lee & Ousley, 2006; Leitner, 2014; Leyfer et al., 2006; Simonoff et al., 2008; Sinzig, Walter, & Doepfner, 2009; Taurines et al., 2012). Joshi et al. (2017) report that the clinical presentation of ADHD in youth with ASD is similar to its presentation outside the context of ASD with respect to age of onset, distribution of diagnostic presentations, symptom profile, and symptom severity. In their psychiatrically referred sample of 140 youth with ASD without intellectual disability (ID), 76% also met diagnostic criteria for ADHD per the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV;* American Psychiatric Association, 1994). Moreover, 41% of youth with ASD with comorbid ADHD had not been identified as having an attention disorder until their participation in the study, and thereby were less likely to have received appropriate treatment. Evidence suggests that individuals with comorbid ASD and ADHD benefit from pharmacological interventions that address symptoms of ADHD (Santosh, Baird, Pityaratstian, Tavare, & Gringras, 2006; Taurines et al., 2012); thus, failing to appropriately identify a comorbid ADHD diagnosis may preclude these children from receiving evidence-based treatments and contribute to greater adaptive and/or behavioral challenges (Jang et al., 2013; Joshi et al., 2017; Posserud, Hysing, Helland, Gillberg, & Lundervold, 2018; Yerys et al., 2009). In fact, the growing awareness of, and evidence for, the presence of functionally impairing co-occurring ADHD symptoms in youth with ASD led to the removal of the exclusivity clause between the diagnoses with the most recent iteration of the *DSM* (5th ed.; *DSM-5;* American Psychiatric ssociation, 2013; Antshel et al., 2016; Colombi & Ghaziuddin, 2017; Goldstein & Schwebach, 2004; Russell, Rodgers, & Ford, 2013; Sprenger et al., 2013; Yoshida & Uchiyama, 2004).

The majority of studies examining ASD and ADHD comorbidity do not parse the different presentations of ADHD, and existing studies were completed prior to the publication of *DSM-5* (2013). Joshi et al. (2017) reported the following breakdown of *DSM-IV* (1994) ADHD subtypes in their sample with ASD (lifetime diagnosis): 33% with Hyperactive/ Impulsive subtype (ADHD-H/I), 8% with Inattentive subtype (ADHD-I), and 59% with Combined subtype (ADHD-C). This distribution was comparable to the researchers' ADHD only comparison sample (N = 74) and consistent with a prior study that reported similar proportions of ADHD subtypes in youth with ASD (i.e., the inattentive subtype being the most prevalent in a sample of 109; Leyfer et al., 2006). However a prior study that examined the prevalence of *DSM-III-R* (3rd ed., rev.; American Psychiatric ssociation, 1987)/ *DSM-IV* (1994) ADHD subtypes using a larger sample of clinically referred youth (N = 301) reported a different distribution of subtype prevalence rates: 9% ADHD-H/I; 30% ADHD-I; and 61% ADHD-C (Faraone, Biederman, Weber, & Russell, 1998).

Previous studies outside the context of ASD have demonstrated differences in comorbid symptomatology between groups with different ADHD presentations. Groups with ADHD-I are reported to have greater prevalence of internalizing disorders, learning disability, and to be more likely to be referred for speech-language evaluation and intervention, while those with ADHD-C have greater prevalence of externalizing disorders (Carlson & Mann, 2000; Weiss, Worling, & Wasdell, 2003). These relationships were corroborated by Gadow, DeVincent, and Pomeroy (2006) in a sample of preschool and school age children with Pervasive Developmental Disorder (PDD).

Fair et al. (2013) provide additional support for brain based differences between those with ADHD-C and ADHD-I using resting-state functional connectivity MRI in a sample of 7–14 year olds without ASD. The authors noted that in youth with ADHD-C, atypical connectivity was prominent in midline default network components, as well as insular cortex; in contrast, the ADHD-I group exhibited atypical patterns within the dorsolateral prefrontal cortex and cerebellum.

In a comprehensive research review examining ADHD without ASD, Milich, Balentine, and Lynam (2002) also suggest differences in how inattentive symptoms manifest in youth with ADHD-I ("sluggish cognitive tempo" [SCT], consisting of behaviors such as drowsiness, lethargy, and hypoactivity) versus ADHD-C (characterized by distractibility). Furthermore, in a small sample comparing children without ASD but with ADHD-C (N = 16), ADHD-I (N = 14), and controls (N = 17), Maedgen and Carlson (2000) reported differences in social functioning and behavior/ ability across the presentations, which are especially important to recognize and address in a sample with comorbid ASD. Parents and teachers rated children with ADHD-C as being more aggressive, emotionally dysregulated and demonstrating high intensity of both positive and negative behavior. In contrast, children with ADHD-I were rated as showing social passivity, but were not characterized as emotionally dysregulated. The ADHD-I group also self-reported deficits in social knowledge. Thus research indicates accurately identifying ADHD presentation, even within children already diagnosed with autism, has important implications for treatment planning.

We acknowledge that a more recent review of the literature (Willcutt et al., 2012) questions the utility of ADHD presentations given they are unstable over time, and may offer limited predictive power over and above ADHD symptom dimensions (i.e., inattention, hyperactivity/ impulsivity) in explaining academic and cognitive functioning, social/emotional and behavioral functioning, and treatment response. In addition, several studies have also shown few differences in performance across ADHD presentations on neuropsychological tests measuring aspects of attention, executive functioning, and academic skills (Nigg, Blaskey, Huang-Pollock, & Rappley, 2002; Riccio, Homack, Jarratt, & Wolfe, 2006). While these findings provide compelling evidence for shifting towards a dimensional conceptualization of ADHD, the *current* diagnostic system (i.e., *DSM-5* [2013]) continues to be based on categories of diagnoses, which are also most easily understood by mental health providers, educators, and parents. Moreover, Gadow et al. (2006) reported ADHD-C and ADHD-I were well differentiated (i.e., differentiated to the same extent as a non-PDD sample) in their sample of youth with PDD. Thus, an examination of ADHD prevalence rates in a clinical sample with comorbid ASD is valuable since the publication of *DSM-5* (2013) permits dual diagnosis of ASD and ADHD, which may have resulted in changes in patterns of diagnosis.

Rosen, Mazefsky, Vasa, and Lerner (2018) note that while there has been considerable research on the phenomenology of co-occurring ADHD and ASD, less work has been done in the area of assessment, thereby underscoring the importance of this research. However, identifying comorbid ADHD symptoms in individuals with ASD may be challenging using existing measures of symptomatology. Findings from Yerys et al. (2017) suggest the ADHD Rating Scale, Fourth Edition (ADHD-RS-IV; DuPaul, Power, Anastopoulos, & Reid, 1998) does not adequately separate the constructs of inattention and hyperactivity/impulsivity in individuals with comorbid ASD. Parent reported symptoms on the scale did not demonstrate factor structures comparable to a sample without comorbid ASD (i.e., one-, two-, and three-factor models revealed unsatisfactory fits). Despite Joshi et al.'s (2017) findings that ADHD symptoms present similarly in youth with comorbid ASD, findings from Yerys et al. suggest the tools used to measure those symptoms may not identify them in the same way as they do for ADHD outside the context of ASD. It was recommended that while the ADHD-RS-IV remains a useful clinical tool, it should be used in combination with extra clinical interviewing to more accurately parse symptoms of inattention and hyperactivity/impulsivity from symptoms of ASD (e.g., poor eye contact, repetitive behaviors).

The Achenbach scales, including the Children's Behavioral Checklist (CBCL) and Teacher Report Form (TRF; Achenbach & Rescorla, 2001) contain subscales screening for symptoms of attention and ADHD problems in addition to multiple supplementary scales measuring psychiatric symptoms. Prior research examining the utility of the CBCL in identifying ADHD symptoms outside the context of ASD among youth with other comorbid diagnoses (e.g., Conduct Disorder, Anxiety, Major Depressive Disorder) indicated that the measure had good convergent validity with a diagnosis made based on structured interview (Biederman et al., 1993). In a study of the CBCL and ADHD-RS-IV in a Korean sample (Kim et al., 2005), researchers reported that both measures together (T score > 60 on the Attention problems subscale of the CBCL; 90th percentile cutoff points on the ADHD-RS-IV) had the greatest sensitivity and positive predictive value in identifying the presence of an ADHD diagnosis when compared to the Kiddie Schedule for Affective Disorders and Schizophrenia interview (K-SADS; Kaufman et al., 1997). Studies examining the occurrence of comorbid psychiatric problems in children with ASD using the CBCL have reported that almost a quarter of their samples had clinically significant concerns on the Attention-Deficit/ Hyperactivity (ADH) and/or Attention Problems subscale per parent report (i.e., T-score ≥ 70; Kanne, Abbacchi, & Constantino, 2009; Sikora, Vora, Coury, & Rosenberg, 2012). However, the co-occurrence of clinically significant ADHD problems in ASD as measured by the CBCL subscale remains below the range of comorbidity across the two disorders (i.e., 30–70%) suggesting this measure may not be sufficiently sensitive to ADHD symptoms in ASD. Moreover, as is the case for the ADHD-RS-IV, Medeiros, Mazurek, and Kanne (2017) reported that the established eight-factor structure of the CBCL was not a good fit in a sample of youth with ASD, and that an exploratory factor analysis proposing a three-factor structure was a better fit for this sample.

There are a number of additional behavioral screening measures that provide information regarding the presence of clinically significant symptoms of ADHD including the Behavior Assessment System for Children, Second edition (BASC-2; Reynolds & Kamphaus, 2004) and Conners' Rating Scale, Revised (Conners, Sitarenios, Parker, & Epstein, 1998). The focus on the ADHD-RS and Achenbach for this paper is due in part to convenience given our clinic's testing batteries. However, prior research suggests the Achenbach scales have good construct validity when compared to other screening tools, such as the BASC, and more focused rating scales such as the Conners' Rating Scale (Achenbach & Rescorla, 2001). However it is worth nothing that a few studies have identified the BASC has greater diagnostic discriminability, particularly for ADHD-I, when compared to the Achenbach scales (Doyle, Ostrander, Skare, Crosby, & August, 1997; Ostrander, Weinfurt, Yarnold, & August, 1998; Vaughn, Riccio, Hynd, & Hall, 1997).

Taken together, previous research has documented high rates of comorbidity between ADHD and ASD; however, there has been limited work parsing comorbidity rates by ADHD presentation since the publication of *DSM-5* (2013). In addition, commonly used rating scales have demonstrated reduced utility in capturing symptoms of ADHD in samples of individuals with ASD. The current study aimed to fill gaps by fulfilling several objectives. We first aimed to examine the prevalence of comorbid *DSM-5* (2013) ADHD presentations in a clinically referred sample. We hypothesized that overall ADHD-ASD prevalence rates would be comparable to those reported in previous studies of ADHD presentations in samples with and without comorbid ASD, with ADHD-C representing the largest proportion of attention disorder diagnosis (Faraone et al., 1998; Joshi et al., 2017).

A second aim of the study was to compare the diagnostic discriminability of the parent and teacher ADHD-RS-IV, as well as the CBCL and TRF Attention and ADH Problems Scales, in identifying ADHD symptoms in comorbid ASD. Preliminary findings from our group (Rau et al., 2017) showed the parent ADHD-RS-IV and CBCL provided greater diagnostic discriminability in predicting ADHD-C than ADHD-I when diagnoses were comorbid with ASD without ID, and the parent ADHD-RS-IV Inattentive symptom count provided the greatest level of diagnostic discriminability for both presentations. Thus, in our current study, which incorporated teacher report, we predicted the inattentive symptom count of the parent and teacher ADHD-RS-IV would provide the greatest diagnostic discriminability in identifying ADHD symptoms in a sample of ASD without ID, given ADHD diagnosis requires symptoms to be present across settings. Moreover, the items on the ADHD-RS-IV are more consistent with *DSM-5* (2013) diagnostic criteria for ADHD. We also predicted that the measures found to have the greatest diagnostic discriminability in the analyses above would explain variance between diagnostic groups over and above demographic variables.

2. Methods

2.1. Participants

This project used archival neuropsychological assessment data from 419 clinically referred youth with Autism Spectrum Disorder (ASD), 259 of whom were also diagnosed with a comorbid attention disorder. Data were originally collected from patients who presented to the Division of Pediatric Neuropsychology Center for Autism Spectrum Disorders at Children's National (several clinic locations in Maryland, Virginia, and Washington, DC) for clinical or research-based evaluation. Following an IRB approved protocol, participants' parents consented to storage of their assessment data in research databases and granted access to the de-identified data for future studies. Doctorate-level clinicians, which included licensed clinical psychologists, neuropsychologists, psychiatrists, and postdoctoral fellows practicing under the supervision of licensed psychologists/neuropsychologists, integrated quantitative and qualitative data from parent and teacher questionnaires, clinical interview, and performance-based neuropsychological assessments/observations to determine whether youth met DSM criteria for ADHD. Clinicians examined for presence of symptoms across settings (e.g., home, school, evaluation room), developmental course of symptoms, level of associated functional impairment, and ruled out whether the symptoms might better be explained by other diagnoses (e.g., depressive or anxiety disorders, language disorder). Clinicians employed neuropsychological measures to assess brief, sustained, and divided attention (visual and/or auditory), inhibition, working memory, and incorporated behavioral observations in conjunction with test scores to determine for presence of symptoms during the evaluation. Several commonly used measures included continuous performance tasks, digit span forwards and backwards, and subtests from the Test of Everyday Attention for Children ([TEA-Ch]; Manly, Robertson, Anderson, & Nimmo-Smith, 1999). We acknowledge that recent literature indicates neuropsychological measures do not provide useful diagnostic value in ruling an attention disorder in or out (Barkley, 2019). However, these aforementioned measures, as well as additional neuropsychological tests that are not directly designed to assess attention and executive functioning nonetheless provide valuable data about comorbid diagnoses that may be contributing to ADHD-like symptoms (e.g., language disorder).

A number of clinicians also employ a semi-structured interview of ADHD symptoms, which provides a more in depth assessment of ADHD symptomatology beyond the ADHD-RS-IV by eliciting specific examples of dysfunction and incrementally guides clinicians through DSM-5 criteria to determine whether the child meets criteria for an attention disorder. Information on the frequency with which clinicians employed the semi-structured ADHD interview was not available in our dataset. In addition, Information on whether clinicians used the 'AND' (6 symptoms required by a single rater in either symptom domain) or the 'OR' rule (6 symptoms required across raters/ settings; Bird, Gould, & Staghezza, 1992) when examining symptoms of ADHD to inform ADHD diagnoses was also not available. Thus, use of the 'OR' rule may have resulted in some children being diagnosed with ADHD even if they did not present with 6 symptoms in a domain in *each* setting, but did demonstrate 6 symptoms across settings.

Inclusion criteria for the sample included: evaluation occurred after June 2013 to increase the likelihood that clinicians used *DSM-5* (2013) diagnostic criteria when making ADHD diagnoses, age 6–18 years old, IQ > 70, and a clinical *DSM-5* (2013) ASD diagnosis as well as meeting criteria for 'broad autism spectrum disorder' in accordance with criteria established by the NICHD/NIDCD Collaborative Programs for Excellence in Autism (see Lainhart et al., 2006), and based on expert clinical judgment as well as Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) and/or the Autism Diagnostic Observation Schedule first or second edition (ADOS; Lord et al., 2000; ADOS-2; Lord et al., 2012). Youth with intellectual disability (ID) were excluded for the purpose of removing confounding factors of global delays that can moderate presentation of ADHD symptoms (Lerner et al., 2018; Witwer & Lecavalier, 2010), and also to improve the generalizability of these findings to the fastest growing subset of individuals with ASD (i.e., those without ID; Idring et al., 2015). Exclusionary criteria for the study included any known co-morbid neurogenetic conditions, such as fragile X syndrome, psychosis, or neurological disorders (e.g., hydrocephalus) that could affect cognitive functioning. The final sample consistent of 419 youth (76% male) with mean age of 11.12 years and overall IQ in the average range (mean FSIQ = 99.18). See Table 1 for additional demographics of the sample.

Table 1
Descriptive statistics for demographic variables for the study sample.

Variable	Total (N = 419)	ASD only (N = 160)	ASD + ADHD (N = 259)	Test statistic	Effect size
Gender (% male)	76	78	76	$\chi 2$ (1df) = .33	.03^^
Age at testing (6-18 years; M[SD])	11.12 [3.51]	11.28 [3.46]	11.02 [3.54]	*t* (417) = .76	.08^
FSIQ (range = 70-143; M[SD])	99.18 [17.11]	102.94 [18.70]	96.86 [15.65]	*t* (290.66) = 3.34*	.36^
Comorbid Diagnoses (N[%])					
Depressive/mood disorder	34 [8.11]	7 [4.38]	27 [10.42]	$\chi 2$ (1df) = 4.86*	.11^^
Bipolar disorder	2 [.48]	0	2 [.77]	$\chi 2$ (1df) = 1.24	.05^^
Anxiety disorder	122 [29.12]	42 [26.25]	80 [30.89]	$\chi 2$ (1df) = 1.03	.05^^
Obsessive compulsive disorder	4 [.95]	3 [1.88]	1 [.39]	$\chi 2$ (1df) = 2.32	.07^^
Trauma disorder	2 [.48]	1 [.63]	1 [.39]	$\chi 2$ (1df) = .12	.02^^
Gender dysphoria	3 [.71]	0	3 [1.16]	$\chi 2$ (1df) = 1.87	.07^^
Disruptive Behavior Disorder	1 [.24]	1 [.63]	0	$\chi 2$ (1df) = 1.62	.06^^
Neurodevelopmental disorder other than ASD or ADHD	84 [20.05]	40 [25]	44 [16.99]	$\chi 2$ (1df) = 3.96*	.10^^
Race/ Ethnicity[$] (N [%])	*N = 317*	*N = 118*	*N = 199*		
Caucasian	209 [65.93]	87 [73.73]	122 [61.31]	$\chi 2$ (1df) = 5.09*	.13^^
African American	44 [13.88]	12 [10.17]	32 [16.08]	$\chi 2$ (1df) = 2.17	.08^^
Asian/Pacific Islander	20 [6.31]	7 [5.93]	13 [6.53]	$\chi 2$ (1df) = .05	.01^^
Mixed/Other	24 [7.57]	7 [5.93]	17 [8.54]	$\chi 2$ (1df) = .72	.05^^
Hispanic (*N = 93, 40, 53*)	26 [27.96]	6 [15]	20 [37.74]	$\chi 2$ (1df) = 5.85*	.25^^

* Denotes significant comparisons (two-sided $p \leq .05$).
^ Cohen's d.
^^ Phi coefficient.
$ race/ethnicity data were not available for the entire study sample; the N's for the number of participants in each diagnostic group for whom these data were available are provided.

Table 2
Descriptive statistics for variables of interest.

Variable*	ASD	ASD + ADHD-C	ASD + ADHD-I	ASD vs. ASD + ADHD-C			ASD vs. ASD + ADHD-I		
Full Sample Subsample@	(N = 160) (N = 61)	(N = 199) (N = 121)	(N = 51) (N = 28)	Test Statistic	*p*-value	Effect Size	Test Statistic	*p*-value	Effect Size
% male									
Full Sample	78	75	81	χ2 (1 *df*) = .60	0.439	.04^^	χ2 (1*df*) = .28	0.598	.04^^
Subsample@	80	74	82	χ2 (1 *df*) = .51	0.477	.05^^	χ2 (1*df*) = .30	0.586	.06^^
Age									
Full Sample	11.28 (3.46)	10.64 (3.41)	12.79 (3.54)	*t* (407 *df*) = 1.75	0.08	.01^	*t* (407*df*) = -2.70	0.007	.03^
Subsample@	10.43 (3.27)	10.69 (3.54)	12.54 (3.98)	*t* (207 *df*) = -.46	0.86	-.07^	*t* (207*df*) = -2.95	0.018	-.60^
FSIQ									
Full Sample	102.94 (18.70)	96.12 (15.95)	99.41 (13.78)	*t* (311.31 *df*) = 3.66	< .001	.35^	*t* (116.70*df*) = 1.47	0.144	.03^
Subsample@	94.62 (17.34)	97.58 (15.54)	103.43 (16.80)	*t* (204 *df*) = -1.15	0.413	-.18^	*t* (204*df*) = -2.37	0.035	-.54^
Rating Scales (Subsample only)@									
Parent ADHD-RS-IV[a]									
Inattn SC[b]	3.28 (2.96)	6.18 (2.56)	5.54 (2.90)	*t* (207 *df*) = -6.78	< .001	−1.06^	*t* (207*df*) = -3.63	0.001	-.83^
Hyp/Imp SC[c]	2.38 (2.38)	4.66 (2.70)	2.25 (2.58)	*t* (207 *df*) = -5.61	< .001	-.88^	*t* (207*df*) = .22	0.968	.05^
Teacher ADHD-RS-IV[a]									
Inattn SC[b]	2.66 (3.13)	4.00 (3.00)	3.46 (3.28)	*t* (207 *df*) = -2.78	0.011	-.44^	*t* (207*df*) = -.1.15	0.414	-.26^
Hyp/Imp SC[c]	1.56 (2.40)	2.74 (2.54)	.89 (1.60)	*t* (126.59 *df*) = -3.07	0.004	-.48^	*t* (75.52*df*) = 1.54	0.376	.35^
CBCL[d]									
Attn Prob T[e]	63.11 (10.47)	69.71 (9.99)	65.11 (9.19)	*t* (207 *df*) = -4.19	< .001	-.66^	*t* (207*df*) = -.87	0.596	-.20^
ADH Prob T[f]	59.74 (8.85)	67.29 (8.18)	62.39 (7.34)	*t* (207 *df*) = -5.81	< .001	-.91^	*t* (207*df*) = -1.41	0.278	.32^
TRF[g]									
Attn Prob T[e]	56.77 (8.38)	61.91 (7.77)	56.93 (5.48)	*t* (207 *df*) = -4.25	< .001	.67^	*t* (207*df*) = -.09	0.994	-.02^
ADH Prob T[f]	56.70 (7.63)	62.06 (7.26)	57.04 (5.36)	*t* (115.34 *df*) = -4.54	< .001	-.71^	*t* (72.39*df*) = -.24	0.971	-.05^

Note: A 2-sided Dunnett correction was applied to account for multiple comparisons; *Statistics are Mean(SD) unless otherwise noted; @refers to the subset of patients for whom behavioral ratings were available; all 210 of the participants in the subsample had completed ADHD-RS, CBCL and TRF data. ^Cohen's d; ^^Phi coefficient.

[a] ADHD Rating Scale.
[b] Inattention Symptom count.
[c] Hyperactive/Impulsive Symptom count.
[d] Child Behavioral Checklist.
[e] Attention Problems T-score.
[f] ADH Problems T-score.
[g] Teacher Report Form.

A subset of this sample (N = 210) for whom parent and teacher questionnaire data were available were further analyzed to address the question of the measures' diagnostic discriminability in identifying ADHD symptoms in comorbid ASD. Specifically, three diagnostic groups were compared: ASD only, ASD + ADHD-C, and ASD + ADHD-I. Descriptive statistics for this sample are presented in Table 2. The diagnostic discriminability of the measures of interest in identifying symptoms of ADHD-H/I and Other or Unspecified ADHD could not be completed due to the low rates of these diagnoses in our overall sample.

2.2. Measures

2.2.1. ADHD-Rating Scale, Fourth Edition (ADHD-RS-IV)

The ADHD-RS-IV is a brief behavioral questionnaire designed to screen for symptoms of inattention and hyperactivity/ impulsivity in children ages 5–18 through parent or teacher report. The inattention and hyperactivity/impulsivity subscales each have nine questions that match *DSM-IV* (American Psychiatric ssociation, 1994) symptoms of ADHD, and symptom frequency is measured on a 4-point Likert scale, with those occurring often or very often being considered clinically symptomatic. The ADHD-RS-IV as opposed to the ADHD-RS, 5th edition (DuPaul, Power, Anastopoulos, & Reid, 2016) was used because the latter was not published until 2016, several years after *DSM-5's* (2013) publication, and symptoms listed in the rating scale did not change across versions.

2.2.2. Achenbach System of Empirically Based Assessment (ASEBA)

The ASEBA includes the Child Behavior Checklist (CBCL) and the Teacher Report Form (TRF), which are widely used questionnaires to screen for the presence of psychiatric symptoms in children ages 6–18 years (Achenbach & Rescorla, 2001). Parents and teachers rate the frequency of behaviors within the past six months on a 0 to 2 point scale and responses are compared to a standardization sample stratified by age and gender to produce T-scores for eight empirically based scales and six DSM oriented scales. T-Scores from the Attention Problems and ADH Problems subscales of these measures were used in analyses.

2.2.3. Intellectual assessment

Intellectual functioning was assessed using the following measures: Wechsler Abbreviated Scale of Intelligence, Second edition (WASI-II; Wechsler, 2011), Wechsler Adult Intelligence Scale, Fourth edition (WAIS-IV; Wechsler, 2008), Wechsler Intelligence Scale for Children, Fourth edition (WISC-IV; Wechsler, 2003), Wechsler Intelligence Scale for Children, Fifth edition (WISC-V; Wechsler, 2014), Wechsler Preschool and Primary Scale of Intelligence, Fourth edition (WPPSI-IV; Wechsler, 2012), Differential Abilities Scales, Second edition (DAS-II; Elliot, 2007), or the Reynolds Intellectual Assessment Scales (RIAS; Reynolds & Kamphaus, 2003).

2.2.4. Autism diagnosis

All participants met DSM-5 criteria for ASD by expert clinical judgement and also met diagnostic cutoffs for autism spectrum disorder on the ADOS (Lord et al., 2000)/ ADOS-2 (Lord et al., 2012) and/or the ADI-R. (Lord et al., 1994). The ADOS is a semi-structured, observational assessment that scores a participant's response to social presses for communication, reciprocal social behavior, and repetitive behaviors and stereotyped interest patterns. The ADI-R is a structured parent interview about the child's developmental history with an emphasis on communication, social development, and repetitive and restricted behaviors.

2.3. Data analyses

Data analyses were performed using SPSS Statistics Version 24 (IBM Corp., 2016) and R 3.2 (R Core Team, 2013). Data were cleaned and inspected for outliers and data points that were 3.29 or more standard deviations above the sample mean were removed.

Prevalence of ADHD presentations were derived through descriptive statistics (i.e., frequencies) of the entire sample (N = 419). Receiver operating characteristic (ROC) curve analyses were used to compare the diagnostic specificity and sensitivity of the parent and teacher report using the ADHD-RS-IV (symptom counts [SC]) and the Attention Problems and ADH Problems subscales (T-scores) from the CBCL and TRF that were available for the subsample (N = 210). To determine measures' diagnostic discriminability in predicting ADHD diagnoses, the area under the curve (AUC) was approximated. Researchers have described that AUCs in the mid .50 s lack clinical utility, those in the mid .60 s are medium in size but are insufficient in isolation, AUC values in the .70–.80 s are clinically valid, and AUCs that exceed .90 likely suggest problems rather than superior specificity and sensitivity since they are rarely achieved in social science research (Rice & Harris, 2005; Youngstrom, Meyers, Youngstrom, Calabrese, & Findling, 2006; Youngstrom, 2014). Significance tests (e.g., Venkatraman analyses [Venkatraman & Begg, 1996]) were conducted to compare the clinically meaningful AUCs for the variables of interest. Hierarchical logistic regression was employed to determine how much unique variance was explained by measures with meaningful AUCs.

3. Results

More than half of the study sample met *DSM-5* (2013) diagnostic criteria for an attention disorder (N = 259; 61.81%). The distribution of ADHD presentations among those with an attention disorder included: 199 (76.8%) diagnosed with ADHD, Combined Presentation (ADHD-C), 51 (19.7%) diagnosed with ADHD, Predominantly Inattentive Presentation (ADHD-I), 5 (.02%) diagnosed with ADHD, Predominantly Hyperactive/ Impulsive Presentation (ADHD-H/I), and 4 (.02%) diagnosed with Unspecified or Other Specified ADHD. Participants with ASD without a comorbid attention disorder had significantly higher IQs than those with ASD and a comorbid attention disorder. The ASD + ADHD-I group was significantly older than the ASD group. Demographics and groups comparisons for the ASD only, ASD + ADHD-C, and ASD + ADHD-I groups are presented in Table 2. A comparison between ASD and ASD + ADHD-H/I was not possible given the low prevalence of the diagnosis in our sample.

Parent and teacher report of ADHD symptoms was compared across participants with ASD, ASD + ADHD-C, or ASD + ADHD-I for a subset of the sample for whom data on behavioral rating scales/ questionnaires were available (N = 210). Of note, the characteristics of this subsample differed from that of the entire study sample. Namely, in the full sample, the ASD group had significantly higher mean IQ than the ASD + ADHD-C group; however in the subsample, the ASD + ADHD-I group had significantly higher IQ than the ASD group. There were no significant differences in age or IQ between the ASD and ASD + ADHD-C groups, and no significant differences in gender across all three diagnostic groups (See Table 2). Correlations amongst the demographic variables and measures of interest are presented in supplementary Table 1.

Values of AUCs for variables of interest completed through ROC curve analyses can be found in Table 3. All measures provided medium or greater levels of diagnostic discriminability for identifying symptoms of ADHD-C with comorbid ASD. In contrast, only the ADHD-RS-IV Inattentive SC provided clinically meaningful diagnostic accuracy for comorbid ADHD-I symptoms. Comparisons of all possible pairs of AUCs were completed for the variables of interest comparing ASD vs. ASD + ADHD-C using Venkatraman tests. The only comparison that was significant following correction for multiple comparisons was that between the parent ADHD-RS-IV Inattentive SC (AUC = .768) and CBCL Attention Problems T-score (AUC = .687; FDR corrected p = .042). In other words, the parent ADHD-RS Inattentive SC was significantly better at discriminating those with comorbid ADHD-C from those without the diagnosis when compared with the CBCL Attention Problems T-score. None of the other comparisons were significant following FDR correction.

Hierarchical logistic regressions were used to examine the unique contribution of variables with medium to clinically meaningful AUCs. Results from these analyses are summarized in Table 4. Age was entered as the first step when examining predictors of comorbid ADHD-I and results indicated that age significantly predicted diagnostic group (χ^2 = 6.52; p = .011). Older age was predictive of greater likelihood of ADHD-I diagnosis, such that a child who was one year older than another would be about 1.2 times more likely to have a comorbid ADHD-I diagnosis. The parent ADHD-RS-IV Inattentive SC was entered in a second block and further improved the predictive power of the model as evidenced by a clinically significant reduction in log likelihood ratios (χ^2 = 11.01,

Table 3
Area under the curve (AUC) calculated from ROC curves for variables of interest.

	ASD vs. ASD + ADHD-C					ASD vs. ASD + ADHD-I				
				95% Conf. Interval					95% Conf. Interval	
Index test	AUC[@]	Standard Error	*p*-value	Lower	Upper	AUC[a]	Standard Error	*p*- value	Lower	Upper
Parent ADHD-RS-IV[a] Inattn SC[b]	.77	.04	< .001	.69	.84	.71	.06	.002	.59	.83
Parent ADHD-RS-IV[a] Hyp/Imp SC[c]	.74	.04	< .001	.66	.81	.47	.07	.678	.34	.60
Teacher ADHD-RS-IV[a] Inattn SC[b]	.63	.05	.005	.54	.72	.57	.07	.267	.45	.70
Teacher ADHD-RS-IV[a] Hyp/Imp SC[c]	.66	.04	.001	.57	.74	.47	.06	.605	.34	.59
CBCL[d] Attn Prob T[e]	.69	.04	< .001	.60	.77	.58	.06	.254	.45	.70
CBCL[d] ADH Prob T[f]	.73	.04	< .001	.65	.81	.60	.06	.116	.49	.72
TRF[g] Attn Prob T[e]	.70	.04	< .001	.62	.79	.57	.06	.291	.45	.69
TRF[g] ADH Prob T[f]	.71	.04	< .001	.63	.80	.57	.06	.295	.45	.69

Note: AUC Benchmarks: .70-.80 = large, clinically informative; mid .60 = medium, insufficient in isolation; ≤ mid .50 = small, not useful (Rice & Harris, 2005; Youngstrom et al., 2006; Youngstrom, 2014); [@]Area under the curve; [a]ADHD Rating Scale; [b]Inattention Symptom count; [c]Hyperactive/Impulsive Symptom count; [d]Child Behavioral Checklist; [e]Attention Problems T-score; [f]ADH Problems T-score [g]Teacher Report Form.

Table 4
Logistic regression models predicting comorbid ADHD diagnosis by presentation.

ASD versus ASD + ADHD-I	B	Standard Error	*p*-value	Odds ratio (OR)	OR 95% Confidence Interval Lower	Upper
Block 0						
Constant	−.78	0.23	.001	0.46		
Block 1: $\chi2 = 6.52$, $p = .011$, $R^2 = .099$[$]						
Constant	−2.64	.80	.001	.071		
Age (years)	**.16**	**.07**	**.013**	**1.18**	**1.04**	**1.34**
Block 2: $\chi2 = 11.01$, $p = .001$, $R^2 = .251$[$]						
Constant	−4.01	1.01	< .001	.018		
Age (years)	.18	.07	.010	1.20	1.04	1.37
Parent ADHD-RS-IV[a] Inattn SC[b]	**.27**	**.09**	**.002**	**1.31**	**1.10**	**1.54**

ASD versus ASD + ADHD-C	Lower	Upper	B	Standard Error	*p*-value	Odds ratio (OR)	OR 95% Confidence Interval Lower	Upper
Block 0								
Constant			.69	.16	< .001	1.98		
Block 1: $\chi2 = .23$, $p = .634$, $R^2 = .002$$								
Constant			.45	.51	.373	1.58		
Age (years)			**.02**	**.05**	**.635**	**1.02**	**.93**	**1.12**
Block 2: $\chi2 = 44.08$, $p < .001$, $R^2 = .300$[$]								
Constant			−1.81	.71	.011	.16		
Age			.06	.06	.292	1.06	.95	1.18
Parent ADHD-RS-IV[a] Inattn SC[b]			**.25**	**.08**	**.001**	**1.29**	**1.11**	**1.49**
Parent ADHD-RS-IV[a] Hyp/Imp SC[c]			**.20**	**.09**	**.028**	**1.22**	**1.02**	**1.45**
Block 3: $\chi2 = 7.18$, $p = .028$, $R^2 = .342$[$]								
Constant			−7.10	2.56	.005	.001		
Age			.09	.06	.138	1.10	.97	1.24
Parent ADHD-RS-IV[a] Inattn SC[b]			.22	.09	.010	1.25	1.05	1.47
Parent ADHD-RS-IV[a] Hyp/Imp SC[c]			.11	.11	.317	1.12	.90	1.39
CBCL[d] ADH Prob T[f]			**.02**	**.03**	**.646**	**1.02**	**.95**	**1.08**
TRF[g] ADH Prob T[f]			**.08**	**.03**	**.013**	**1.08**	**1.02**	**1.14**

[$] Nagelkerke R Square.
[a] ADHD Rating Scale.
[b] Inattention Symptom count.
[c] Hyperactive/Impulsive Symptom count.
[d] Child Behavioral Checklist.
[f] ADH Problems T-score.
[g] Teacher Report Form.

$p = .001$). Moreover, the ADHD-RS-IV Inattentive SC significantly predicted comorbid ADHD-I even after controlling for the effects of age ($B = .27$, $p = .002$). Higher endorsement of inattentive symptoms was predictive of greater likelihood of ADHD-I diagnosis, and each additional symptom increased the likelihood of diagnosis 1.3 fold.

Examination of predictors of comorbid ADHD-C diagnosis indicated that age was not a significant predictor. Variables with clinically meaningful AUCs (i.e., > .70) were entered in the regression model. The parent ADHD-RS-IV Inattentive and Hyperactive/Impulsive SC were entered in the first block and together significantly predicted ADHD-C diagnosis ($\chi^2 = 44.08$; $p < .001$). An increase of one symptom on each of these scales increased the odds of receiving an ADHD-C diagnosis about 1.2 fold. The CBCL and TRF ADH Problems T-Scores were entered in the next block and further improved the predictive power of the model ($\chi^2 = 7.18$; $p = .028$). When all 4 variables were present in the model, parent ADHD-RS-IV Inattentive SC ($B = .22$, $p = .010$) and TRF ADH Problems T-score ($B = .08$, $p = .013$) significantly predicted diagnostic group after controlling for the other variables in the model.

4. Discussion

Attention-Deficit/Hyperactivity Disorder (ADHD) is a commonly co-occurring diagnosis in youth with ASD. However, due to variability in the identification of ADHD symptoms in the context of ASD, ADHD diagnoses are missed in a significant proportion of youth with ASD, who subsequently do not receive treatment, which can impede functional outcomes (Joshi et al., 2017; Rosen, Mazefsky, Vasa, & Lerner, 2018). The present study aimed to identify *DSM-5* (2013) ADHD presentation prevalence rates in a clinic-referred sample of youth with ASD without ID. This goal was important given *DSM-5* (2013) permits dual diagnosis of ASD and ADHD, which may have impacted patterns of diagnosis documented in prior publications. A second aim was to determine the diagnostic discriminability of several commonly used measures to establish which were most effective in identifying symptoms of comorbid ADHD as well as determining the incremental validity of these measures in contributing to an ADHD diagnosis.

Consistent with previous work that reported comorbidity rates for ASD and ADHD ranging from 30 to 70%, 61.8% of our sample met *DSM-5* (2013) criteria for an attention disorder. This finding confirms the high co-occurrence of ADHD in ASD, but does not suggest increased rates of diagnosis since the publication of *DSM-5*. The distribution of ADHD presentations in comorbid ASD was not consistent with that of prior studies examining ADHD in ASD (Joshi et al., 2017; Leyfer et al., 2006), which may be due in part to difference in sample sizes across the studies (419 in our study and 107 and 109 in Joshi et al. and Leyfer et al.'s, respectively). However, our distribution was consistent with that of a non-ASD sample of comparable size (Faraone et al., 1998). As predicted, ADHD-C (76.8%) comprised the greatest proportion of attention diagnoses, followed by ADHD-I (19.7%), and ADHD-H/I (.02%) was the least prevalent of the presentations. Prior epidemiological studies of ADHD presentations outside the context of ASD have reported similarly low prevalence of ADHD-H/I in community and clinically referred samples (Baumgaertel, Wolraich, & Dietrich, 1995; Gaub & Carlson, 1997; Lahey, Pelham, Loney, Lee, & Willcutt, 2005; Wolraich, Hannah, Pinnock, Baumgaertel, & Brown, 1996). Thus, our study's focus on ADHD-C and ADHD-I is consistent with the existing body of ADHD presentation literature, which primarily directs attention to the ADHD-C and ADHD-I groups (Derefinko et al., 2008).

To address the second aim of the study, ROC curve and Venkatraman analyses were used to examine diagnostic discriminability of the parent and teacher ADHD-RS-IV, as well as the Attention and ADH Problems subscales of the CBCL and TRF for a subset of the sample for whom these data were available. Our results indicate that all measures had greater diagnostic discriminability in identifying symptoms of comorbid ADHD-C relative to ADHD-I. This discrepancy may be driven by the more "positive" (i.e., observable) symptoms seen in ADHD-C, including hyperactivity, talking excessively, that also lead to the identification of these children at younger ages. In contrast, symptoms of ADHD-I are less obvious (e.g., daydreaming, organization difficulties, working memory problems) and identified later in development when demands for these skills increase and impairment becomes more evident (Faraone et al., 1998). In our data as well, the ASD + ADHD-I group was the oldest amongst the three diagnostic groups.

When examining differences in functioning across ADHD presentations in non-ASD samples, prior research has consistently reported that the ADHD-C group is the most impaired on assessment measures relative to those with ADHD-I or ADHD-H/I (Colombi & Ghaziuddin, 2017; Gadow et al., 2004), which may also have driven the greater degree of diagnostic discriminability and earlier identification of participants within this presentation. Furthermore, deficits in attention and metacognitive aspects of executive functioning are not unique to youth with ADHD or ASD, but seen in both diagnoses even in the absence of comorbidity (Pinto, Rijsdijk, Ronald, Asherson, & Kuntsi, 2016; Sinzig, Morsch, Bruning, Schmidt, & Lehmkuhl, 2008), thereby making diagnosis of ADHD-I more challenging than ADHD-C in comorbid ASD. Thus given, attention is often disrupted in ASD due to deficits in social and executive functioning (Rosenthal et al., 2013), inattentive ADHD symptoms may not be as readily identified when inhibition is intact.

The parent ADHD-RS-IV Inattentive and Hyperactive/Impulsive SC, and the ADH Problems subscales of the CBCL and TRF provided the greatest diagnostic discriminability between ASD and ASD + ADHD-C, and the ADHD-RS-IV Inattentive SC was the only measure to provide clinically meaningful differentiation of comorbid ADHD-I from ASD alone. These findings indicate that despite the limitations of using the ADHD-RS-IV in youth with ASD (Yerys et al., 2017), the rating scale continues to provide diagnostic value in identifying comorbid ADHD in ASD. It is also important to note that the ADHD-RS-IV Inattentive subscale provided the greatest diagnostic discriminability for both ADHD-C and ADHD-I as opposed to measures assessing symptoms of hyperactivity/impulsivity. This finding may be explained by Chhabildas, Pennington, and Willcutt (2001)) work, which demonstrated that symptoms of inattention were significantly related to the performance of children with ADHD-I and ADHD-C on neuropsychological measures of vigilance, processing speed, and inhibition. In contrast symptoms of hyperactivity/impulsivity were not related to performance in any of these domains.

Teacher report did not provide discriminatory value for comorbid ADHD-I and only the TRF ADH Problems T-score provided clinically meaningful discriminability for comorbid ADHD-C. This finding suggests that in the context of multiple methods of information gathering/assessment (e.g., clinician's observation of the child, child's performance on attention and inhibition measures, parent report), teacher report on questionnaires is not capturing ADHD symptoms as consistently as other sources of information, which is consistent with prior research documenting teachers report lesser degree of symptomatology across psychiatric difficulties than parents in samples of children with ASD (Kanne et al., 2009).

The finding that all but one of the measures examined in this study provided poor diagnostic discriminability for ADHD-I symptoms indicates clinicians cannot rely as heavily on these rating scales/questionnaires when making diagnostic decisions. Rather, they will need to more closely examine symptoms of inattention that occur above and beyond what would be expected for mental age through clinical interview with the patient and parent (e.g., aforementioned semi-structured interview inquiring about DSM-5 ADHD symptoms), seeking collateral report via interview from teachers/ therapists, and review of medical and academic records (Barkley, 2015; Rosen et al., 2018). In addition observations and scores from performance based measures are valuable to rule in/out co-occurring symptoms/ diagnoses other than ADHD-I that could be presenting as an attention disorder (e.g., language disorder, sleep dysregulation) and avoiding mis-diagnosis of an attention disorder.

In examining the incremental validity of measures that were found to have clinically meaningful diagnostic discriminability, we highlighted the clinical utility of the parent ADHD-RS-IV Inattentive SC in identifying ADHD-I symptoms over and above the variance explained by age. Moreover, the parent ADHD-RS-IV Inattention and Hyperactive/Impulsive SC together significantly predicted ADHD-C diagnosis, and the CBCL and TRF ADH Problems subscales together provided additional incremental value above and beyond that explained by the parent ADHD-RS-IV. These findings suggest that the parent ADHD-RS-IV should be included in a battery assessing for comorbid ADHD and the CBCL and TRF ADH Problems subscales have additional diagnostic value in identifying ADHD-C symptoms.

Criterion contamination (i.e., clinicians used the measures of interest, among many additional variables when making comorbid ADHD diagnoses) is a limitation of the current study. Thus, ROC curve analyses may represent reliance of clinicians on particular measures rather than true diagnostic discriminability. Nonetheless, these results contribute in a meaningful way to the literature given that, to our knowledge, this study is the first of its kind to compare the diagnostic specificity and sensitivity of common measures to parse ADHD presentations in comorbid ASD without ID. Future work can attempt to replicate these findings using methodology to avoid criterion contamination (i.e., using different measures/sources of data to inform diagnosis than those being entered into the ROC curve analysis).

An additional limitation of our study is that we leveraged available data collected from a clinical sample, which may be biased as parents are bringing their children for assessment because of observed challenges at home or school and also may limit how representative our sample is to a community sample. Moreover, the subsample (N = 210) we used for our analyses assessing diagnostic discriminability of measures differed from our full clinical sample (N = 419) in regard to group mean IQs. Given these limitations, it will be important for future research in this area to use community or population based samples to examine whether the results can be replicated. Moreover, while we only included data from assessments completed after the publication of DSM-5, it is possible clinicians had not fully made changes in clinical practice, which may account for comparable rates of ADHD diagnosis in our sample with ASD as those reported in previous research prior to the publication of DSM-5.

A third limitation of the study is that we only analyzed two commonly used measures that attempt to capture ADHD symptomatology, as we were limited by the measures utilized by our clinic and availability of test data in our database. Moving forward, it will be important to examine additional measures specifically the Attention subscale from the BASC-2 (Reynolds & Kamphaus, 2004), considering prior studies have indicated this scale demonstrated greater accuracy in identifying ADHD-I than the CBCL and TRF in a sample without ASD (Vaughn et al., 1997). Additional measures to include in subsequent research are the Conners' Parent Rating Scale, Revised (Conners et al., 1998), Behavior Rating Inventory of Executive Function, Second edition (Gioia, Isquith, Guy, & Kenworthy, 2015), and neuropsychological assessments of attention and impulsivity (i.e., continuous performance tasks, Test of Everyday Attention for Children; Manly et al., 1999). In addition, given previous work has established differences in factor structure of the ADHD-RS-IV and CBCL in samples with ASD, completing item level analyses of different measures to determine which items are poor predictors of an ADHD diagnosis in comorbid ASD is an important undertaking. Items that are poor predictors can be modified and re-assessed.

4.1. Implications

The data presented herein provide a strong endorsement for the use of the ADHD-RS-IV in both clinical and research settings to capture ADHD symptoms in children with ASD. The parent and teacher Achenbach ADH scales also provide additional clinical utility to identify ADHD-C symptoms. These findings also highlight the need for increased and more thorough examination of symptoms of inattention in children with ASD to rule out ADHD-I, as rating scales/questionnaires provide limited diagnostic discriminability relative to comorbid ADHD-C.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Declaration of Competing Interest

All authors declare no conflict of interest

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.rasd.2019.101468.

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