Overlapping symptoms in Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorders: more similarities than differences

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Abstract

Background: While Autism Spectrum Disorder (ASD) and Attention Deficit/Hyperactivity Disorder (ADHD) may intuitively seem to be on the extremes of a single spectrum (ranging from impulsive to rigid), symptoms of ASD and ADHD often co-occur in the same children. This study aimed to provide an in-depth characterization of ADHD and ASD symptoms in children with and without ASD and/or ADHD using questionnaire data.

Methods: In total, we included 702 symptom measurements from 484 children aged between 6 and 18 years with ADHD (N=155), ASD (N=141), or typically developing (N=188) and analyzed these using linear mixed-effects models. We used latent-profile analysis (LPA) to investigate patterns of comorbid ADHD and ASD symptoms.

Results: The present study investigated restricted and repetitive behavior and symptoms of ADHD across a large sample of children with ASD and/or ADHD, compared to typically developing peers. We found that children with comorbid ASD and ADHD had the most severe symptoms that persisted over development. Children with a primary ADHD diagnosis had elevated levels of restricted and repetitive behavior, and children with ASD also had symptoms of ADHD. Latent profile analysis (LPA) further suggested that patterns of symptom comorbidity are not specific to diagnostic categories.

Conclusions: We found severe and persistent ASD and ADHD symptoms in children with comorbid ASD and ADHD. Children with a single diagnosis of ASD or ADHD had more moderate symptoms that improved with age. Furthermore, children with ASD had elevated ADHD symptoms, and vice versa, suggesting that symptoms are not specific to diagnostic categories.

Keywords: ADHD, autism, comorbidity, repetitive behaviors, attention problems

Introduction

Autism Spectrum Disorder (ASD) and Attention Deficit/Hyperactivity Disorder are the two most frequently diagnosed developmental disorders in childhood (Elsabbagh et al., 2012; Polanczyk, Willcutt, Salum, Kieling, & Rohde, 2014). While intuitively these disorders seem to be on the extremes of one spectrum - ADHD is inherently associated with behavior that appears *too* flexible, i.e. impulsivity, and ASD is associated with behavioral rigidity (American Psychiatric Association, 2013) - symptoms of both disorders often co-occur in the same children: an estimated 30-80% of children with ASD qualifies for a full DSM-diagnosis of ADHD (Gadow, DeVincent, & Schneider, 2009; Grzadzinski, Dick, Lord, & Bishop, 2016; Joshi et al., 2017; Mayes, Calhoun, Mayes, & Molitoris, 2012; Simonoff et al., 2008). Moreover, 20-60% of individuals with a primary diagnosis of ADHD show autistic traits (Grzadzinski et al., 2011, 2016; Kotte et al., 2013). In addition to deficits in social behavior and communication, and perhaps counterintuitively to the impulsivity associated with ADHD, children with ADHD also show elevated restricted and repetitive behavior that are more typical to ASD (Clark, Feehan, & Tinline, 1999; Grzadzinski et al., 2011, 2016; Martin, Hamshere, O'Donovan, Rutter, & Thapar, 2014), Obsessive-Compulsive Disorder (OCD) and Tourette Syndrome (TS) (Hirschtritt et al., 2015; Mohr Jensen & Steinhausen, 2015; Reale et al., 2017; Taurines et al., 2010). The frequent comorbidity of ASD and ADHD is not surprising per se, given the genetic overlap that has been reported between ASD and ADHD (Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010). In a large community twin sample, the highest genetic correlations were reported for restricted and repetitive behavior and inattention and hyperactivity (Polderman, Hoekstra, Posthuma, & Larsson, 2014; Ronald, Larsson, Anckarsäter, & Lichtenstein, 2014). This suggests that neurodevelopmental disorders such as ASD and ADHD may be on overlapping behavioral dimensions, perhaps also originating from overlapping

etiologies (Huisman-van Dijk, Schoot, Rijkeboer, Mathews, & Cath, 2016). Yet, not much is known about the relation between inattention and hyperactivity, and behavioral flexibility in children with developmental disorders.

We set out to perform an in-depth characterization of restricted and repetitive behavior and ADHD symptoms in a large sample of children with and without ASD and ADHD using questionnaire data from participants who took part in our studies between 2006 and 2016. We hypothesized that children with ASD would have the most severe restricted and repetitive behavior, with children with ADHD intermediate between children with autism and typically developing children (TDC). We further hypothesized that children with ADHD would have the most symptoms of ADHD, with children with autism intermediate between ADHD and TDC. Finally, we hypothesized that children with comorbid ASD and ADHD would have the most restricted and repetitive behavior and greatest symptom severity.

Method

Participants

A total of 296 children and adolescents, aged 6 – 18 years, with a primary diagnosis of ADHD (N = 155) or ASD (N = 141) were recruited for studies of the NICHE-lab at the Department of Psychiatry, the University Medical Center in Utrecht, and through advertising. The clinical diagnosis of ADHD was confirmed as a research diagnosis by a qualified researcher using the Diagnostic Interview Schedule for Children – Parent Version (DISC-P): (Costello, Edelbrock, & Costello, 1985). In the majority children with ASD (N = 100), the clinical diagnosis of ASD was confirmed by a qualified researcher using the Autism Diagnostic Interview – Revised (ADI-R: (Lord et al. 1994)).

188 Typically developing subjects, aged 6-18 years, were included from the pool of volunteers who had participated in studies by our lab between 2006-2016. All subjects

were screened by phone interview, to confirm the absence of major neurological or psychiatric disorders, as well as the absence of psychiatric conditions in their first-degree relatives. None of the control subjects were using any form of psychoactive medication. Parents of the typically developing subjects also participated in a DISC-P interview session to confirm the absence of any psychiatric condition in the subject.

Demographic characteristics of the sample are shown in Table 1. IQ was assessed for all participants using the (abbreviated version of the) Wechsler Intelligence Scale for Children (WISC-III (Kort et al., 2005)). Differences in demographic variables were assessed using the appropriate Students' T- or Chi-square tests.

Due to the longitudinal nature of many studies in our lab, a subset of participants returned one or more times with an average interval of two years. If available, follow-up assessments were included in the present study (Table 1).

The studies were approved by the Ethics Committee of the University Medical Centre Utrecht, The Netherlands, and took into account the ethical principles for medical research involving human subjects as stated in the declaration of Helsinki (amendment of Fortaleza, 2013). Written and oral information was provided, after which written informed consent was obtained from all parents. All children and adolescents provided written and/or verbal assent.

Questionnaires

Caregivers of all participants were asked to complete the Child Behavior Checklist (CBCL: (F. Verhulst, Van Der Ende, & Koot, 1996)) and the Repetitive Behavior Scale – Revised (Bodfish, Symons, & Lewis, 1999). Subjects were included in this analysis if they had complete CBCL and RBS-R data. When available, data from the Teacher Report Form (TRF: N TD = 123, N ADHD = 123, N ASD = 118 (F. C. Verhulst, van der Ende, & Koot, 1997)) and Youth Self Report (YSR: N TD = 122, N ADHD = 71, N ASD

= 60 (F. C. Verhulst, Van Der Ende, & Koot, 1997), for children between 11-18 only) were also included in the analyses.

As a measure of quality control, difference-scores between measurements were computed if participants had two or more measurements (Table 1). If the difference between two measurements deviated more than two standard deviations (SD) from the average difference between measurements, the two measurements were not considered reliable and were consequently removed from the analyses (N = 17).

Statistical Analyses

Group comparisons. First, for each CBCL subscale of interest, a Linear Mixed-Effects (LME) model was fit with diagnostic status as a fixed factor and subject as a repeated measures random factor. Diagnostic status was based on clinical records, resulting in four groups: 1) TDC, 2) ADHD, 3) ASD, and 4) ASD and ADHD (ASD/ADHD). As T-scores were used for these models, age and gender were not included in the design. When significant main effects were found, we performed post-hoc pairwise comparisons using least-squares means to test differences between diagnostic groups. Follow up analyses were also performed on raw CBCL scores, to investigate the longitudinal development of symptoms. If interaction effects between diagnostic status and age were present, these were further investigated using Pearson's correlations.

A similar approach was used for the subscales of the RBS-r, where an LME model was fit with diagnostic status, age and gender as fixed factors and subject as a repeated measures random factor. In the presence of significant main and/or interaction effects, we again ran post-hoc pairwise comparisons performed using least-squares means. If interaction effects between diagnostic status and age were present, these were further investigated using Pearson's correlations.

As differences in cognitive ability may be considered part of the phenotype in ASD and ADHD, IQ was not entered as a covariate in any of the primary analyses (Dennis et al. 2009). However, secondary analyses included PIQ or VIQ as an additional fixed factor to control for the influence of cognitive abilities.

Additional analyses where ADHD comorbidity in ASD was based on symptom ratings rather than DSM diagnoses are reported in the Supplemental Materials.

Latent Profile Analysis. In order to investigate whether there were hidden subgroups based on symptom profiles in a data-driven manner, we ran a Latent Profile Analysis (LPA) using the *Mclust* package in R (Scrucca, Fop, Murphy, & Raftery, 2016). The number of classes was determined based on the Bayesian Information Criterion (BIC; (Schwartz, 1978)), the Integrated Complete-data Likelihood (ICL; which adds an entropy term through which BIC is penalized for potential overlap between clusters (Baudry, Raftery, Celeux, Lo, & Gottardo, 2010; Biernacki, Celeux, & Govaert, 2000)), and the results of the Bootstrap Likelihood Ratio Test (BLRT; (McLachlan, 1987)). It has been suggested that the output of the BLRT should be taken over BIC or ICL in order to determine the optimal number of classes. However, there were no discrepancies between BIC, ICL and BLRT statistics in our study (Supplemental Table S1). As the LPA identified four groups with distinct patterns of symptoms, differences between classes were investigated using ANOVAs with age, IQ and parental education as predictors specifically within these four groups.

Results

Diagnostic group differences in ADHD symptoms

There was a main effect for diagnostic status on T-scores on the Attention Problems ($F(3,534) = 174.0$, $p < .001$), Rule Breaking Behavior ($F(3,534) = 50.3$, $p <$

.001), Aggressive Behavior (F(3,548) = 70.3, p < .001), Internalizing (F(3,530) = 137.7, p < .001) and Externalizing Behavior (F(3,542) = 136.0, p < .001) subscales (Figure 1A, Supplemental Figures 1A-D). Statistics for all post-hoc pairwise comparisons are reported in Supplemental Table S1. For the Attention Problems subscale, all pairwise comparisons reached significance, except between the ADHD and ASD groups. For Internalizing Behavior, there was no difference between the ASD and ASD/ADHD group, whereas for Externalizing Behavior there was no difference between the ADHD and ASD/ADHD group. Pairwise comparisons on Rule Breaking and Aggressive Behavior showed a similar pattern of all diagnostic groups differing from the TD group, but not from each other.

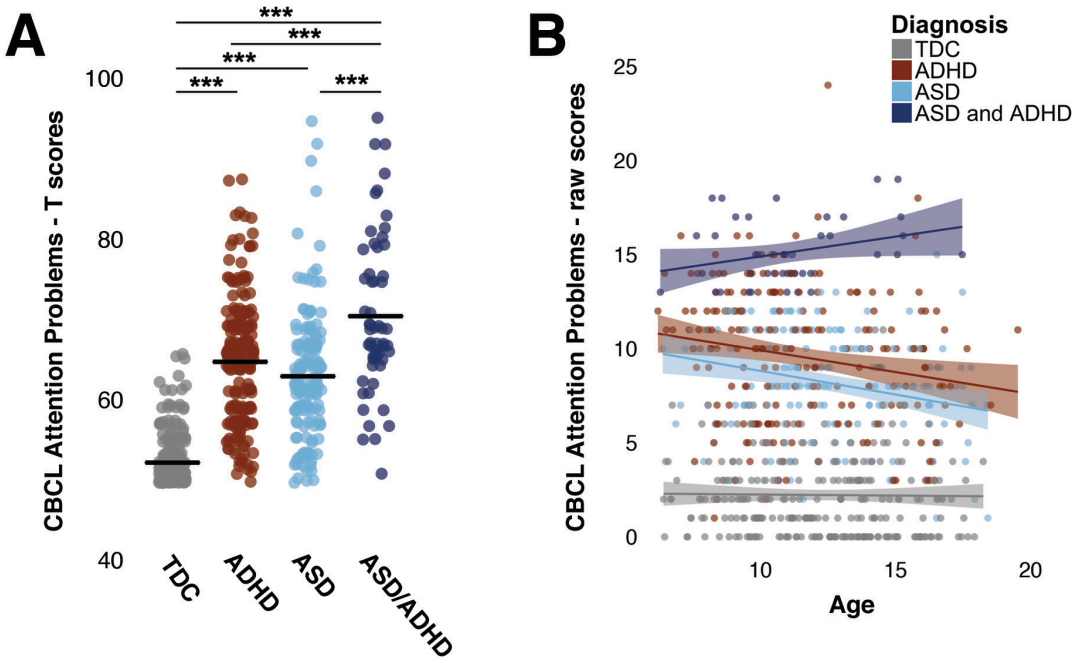

Figure 1. A) Parent-rated symptom severity (T-scores) on the Attention Problems subscale of the Child Behavior Checklist (CBCL). The ASD/ADHD group is defined by clinical diagnosis. Black horizontal bars denote the group mean. Asterisks display significance of pairwise comparisons: *** for p < .001, ** for p < .01. Panel B) shows raw scores on the Attention Problems subscale of the Child Behavior Checklist (CBCL) plotted against age, where attention problems decreased with age in children with ASD or ADHD, but not in children with comorbid ASD/ADHD.

Secondary analyses including VIQ or PIQ as covariates did not meaningfully alter the findings reported above. However, there were main effects of PIQ on Attention Problems ($F(1,661) = 8.4$, $p = .004$), Rule Breaking ($F(1,648) = 5.4$, $p = .020$) and Externalizing behaviors ($F(1,664) = 4.6$, $p = .032$).

Furthermore, when investigating symptom change over time, the raw CBCL scores showed an interaction between diagnostic status and age on attention as assessed by the Attention Problems subscale of the CBCL ($F(1,689) = 2.9$, $p = .034$). Post-hoc analyses showed a decline in attention problems in the ADHD ($t(198) = -2.5$, $p = .014$) and ASD ($t(143) = -2.8$, $p = .006$) groups, but no relation with age in the TD ($t(271) = -1.0$, $p = .339$) and ASD/ADHD ($t(46) = -1.4$, $p = 0.168$) groups (Figure 1B, Supplemental Figures 3A-D).

Diagnostic group differences in restricted and repetitive behavior

There was a main effect for diagnostic status (dx: $F(3,614) = 30.1$, $p < .001$) and age $F(1,613) = 10.8$, $p = .001$), and an interaction effect between dx and age ($F(3,605) = 6.3$, $p < .001$) for total RBS-r scores (Figure 2A). There was no main effect of gender ($p = .180$). Follow-up analyses showed reduction in RBS-r scores with age for children with ASD ($t(202) = 2.4$, $p = .016$) and ADHD ($t(120) = 2.8$, $p < .001$), but no change in TD children or those with ASD/ADHD (p's $> .132$) (Figure 2B).

Furthermore, there were main effects of diagnostic status (dx) and age for all five subscales of interest, respectively Stereotyped Behaviors (dx: $F(3,673) = 10.8$, $p < .001$, age: $F(1,674) = 12.8$, $p < .001$, gender: n.s., dx * age interaction: n.s.), Compulsive Behaviors (dx: $F(3,689) = 21.3$, $p < .001$, age: $F(1,690) = 8.4$, gender: n.s., $p = .004$, dx * age interaction: $F(3,691) = 8.0$, $p < .001$), Ritualistic Behaviors (dx: $F(3,688) = 27.0$, $p < .001$, age: $F(1,689) = 16.5$, $p < .001$, gender: n.s., interaction: $F(3,687) = 7.6$, $p < .001$), Insistence on Sameness (dx: $F(3,637) = 15.3$, p

< .001, age: F(1,636) = 4.1, p = .042, gender: F(1,526) = 3.9, p = .049, interaction: n.s.) and Restricted Behaviors (dx: F(3,674) = 22.6, p < .001, age: n.s., gender: n.s., interaction: F(3,677) = 9.0, p < .001). Pairwise comparisons and age-effects between diagnostic groups are shown in Supplemental Figures 2A-F and 4A-F and

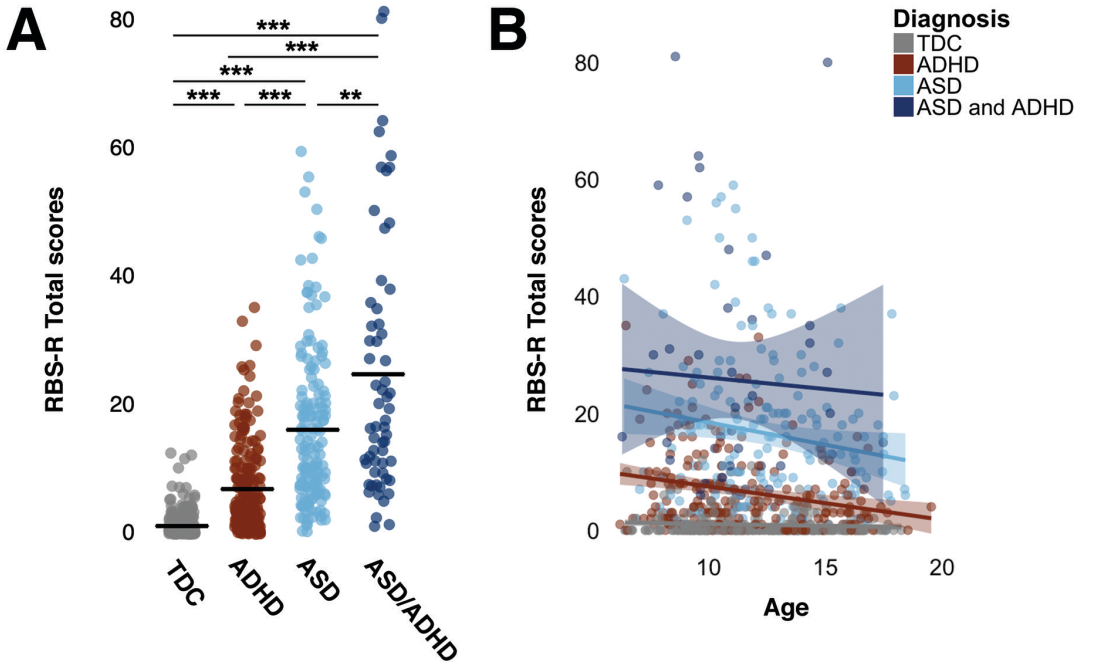

Figure 2. Parent-rated severity of restricted and repetitive behaviors measured by the Repetitive Behavior Scale – Revised (RBS-R). Black horizontal bars denote the group mean. Asterisks display significance of pairwise comparisons: *** for p < .001, ** for p < .01. Panel B shows total scores on the Repetitive Behavior Scale – Revised (RBS-R) against age, where Restricted and repetitive behavior decreased with age in children with ASD or ADHD, but not for TD children or children with comorbid ASD/ADHD.

Supplemental Table S2. In short, children with ASD and/or ADHD had increased Stereotyped Behaviors compared to typically developing children (all p's < .001). Yet there were no differences between children with developmental disorders (all p's > 0.091) on Stereotyped Behaviors. For Ritualistic behaviors , Compulsive Behaviors, Insistence on Sameness and Restricted Behaviors, all pairwise comparisons were significant (all p's < .048).

Latent Profile Analysis of attention problems and restricted and repetitive behavior

Table S1 shows that BIC- and ICL-values decreased with each class addition, and BLRT p-values remained significant for all comparisons, indicating a 9-class model was optimal (Figure 4). The 9-class model showed a number of classes with great similarity, which we therefore grouped together into four 'profiles': 'No symptoms', 'Symptoms of ADHD and ASD', 'Symptoms of ADHD and RSMs', and 'Symptoms of ADHD only'.

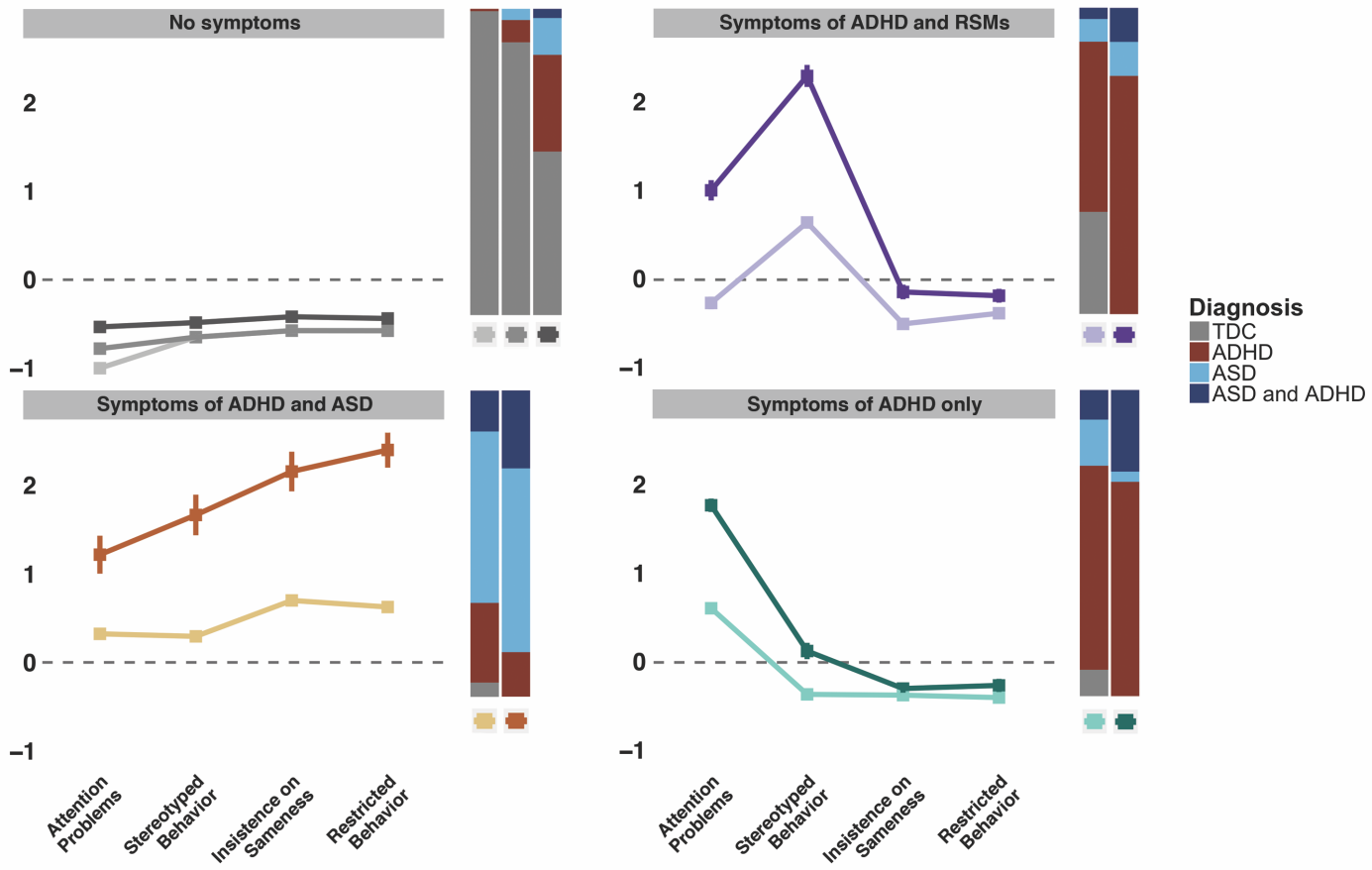

Figure 3. The latent-profile analysis yielded nine classes, that we have are organized into four profiles for purposes of visualization: 'No symptoms', 'Symptoms of ADHD and ASD' (where participants showed elevated scores on the CBCL and RBS-r), 'Symptoms of ADHD and RSM' (where participants showed elevated symptoms of ADHD and repetitive sensory-motor behavior, but no other restricted and repetitive behavior), and 'Symptoms of ADHD only' (where participants showed symptoms of ADHD, without elevated restricted and repetitive behavior). Directly adjacent to each of the four profiles the colored bars indicate the distribution (relative percentages) of primary diagnoses in each class.

The difference in symptom severity between the classes in the 'ADHD and ASD symptoms' and 'ADHD only' was associated with age ($F(1,37) = 4.5$, $p = .040$ and $F(1,224) = 6.1$, $p = .014$ respectively), where younger children showed more symptoms. Furthermore, for children with comorbid ADHD and ASD symptoms, symptoms severity was associated with full-scale IQ ($F(1,209) = 15.3$, $p < .001$). Finally, symptom severity was associated with maternal education level for all four profiles (No symptoms: $F(2,184) = 3.9$, $p = .022$, ASD and ADHD: $F(1,30) = 7.9$, $p = .008$, ADHD and RSM: $F(1,170) = 9.0$, $p = .003$, ADHD only: $F(1,169) = 6.15$, $p = .014$).

Discussion

The present study investigated restricted and repetitive behavior and symptoms of ADHD across a large sample of children with ASD and/or ADHD, compared to their typically developing peers. We found that children with comorbid ASD and ADHD had the most severe symptoms that persisted over development. Children with a primary ADHD diagnosis had elevated levels of restricted and repetitive behavior, and children with ASD also had symptoms of ADHD. Latent profile analysis (LPA) further suggested that patterns of symptom comorbidity are not specific to diagnostic categories.

In line with previous findings, we found that children with comorbid ASD and ADHD had the most severe attention problems (Hoffmann, Weber, König, Becker, & Kamp-Becker, 2016). Children with comorbid ASD and ADHD have been reported to have more problems in cognitive and adaptive functioning (Rao & Landa, 2014). Furthermore, children with ASD had more internalizing problems, regardless of ADHD comorbidity (Bauminger, Solomon, & Rogers, 2010; Craig et al., 2015). There were no differences in externalizing behaviors between the three diagnostic groups, whereas previous work has shown elevated externalizing behaviors in children with comorbid

ASD and ADHD (Goldin, Matson, Tureck, Cervantes, & Jang, 2013; Yerys et al., 2009). In general, the presence and severity of comorbid symptomatology has been associated with increased symptom severity, and with elevated peer problems, lower functional outcome and lower quality of life (Armstrong, Lycett, Hiscock, Care, & Sciberras, 2015; Mansour, Dovi, Lane, Loveland, & Pearson, 2017).

Consistent with previous work, we found that children with co-morbid ASD/ADHD had the most severe symptoms (Sprenger et al., 2013), and that children with ADHD showed more restricted and repetitive behavior than typically developing children (Grzadzinski et al., 2011, 2016; Jang et al., 2013; Martin et al., 2014). Elevated autistic traits in individuals with ADHD have been associated with more severe (comorbid) psychopathology and impairments in daily life (Cooper, Martin, Langley, Hamshere, & Thapar, 2014; Kotte et al., 2013). Notably, phenotypic correlations between restricted and repetitive behavior and ADHD symptoms, and genetic correlations between ASD and ADHD symptoms have been observed, even in the general population (Polderman et al., 2014; Reiersen, Constantino, Grimmer, Martin, & Todd, 2008; Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 2008).

The severity of ADHD symptoms and restricted and repetitive behavior decreased over development for children with ASD and ADHD, yet symptoms were persistent in the comorbid group. This converges with previous work showing subgroups with different developmental trajectories of symptom severity in ASD (Chowdhury, Benson, & Hillier, 2010; Esbensen, Seltzer, Lam, & Bodfish, 2009; Kim et al., 2018; Richler, Huerta, Bishop, & Lord, 2010) and ADHD (Agnew-Blais et al., 2016; Biederman, Mick, & Faraone, 2000; Biederman, Petty, Evans, Small, & Faraone, 2010; Karam et al., 2015). It has been suggested that different trajectories of behavioral development may represent distinct phenotypes of developmental disorders, and as such may have

distinct neurobiological etiologies (Lombardo, 2018; Lord, Bishop, & Anderson, 2015; Shaw et al., 2013).

Our latent-profile analysis yielded four patterns of comorbidity between symptoms of ASD and ADHD. While there were two classes showing symptoms of ADHD alone, there was no latent class of children that showed symptoms of ASD alone (Van Der Meer et al., 2012). Furthermore, the profiles showing co-occurrence of ASD and ADHD symptoms are in line with high estimates of comorbid ADHD in ASD (Gadow et al., 2009; Grzadzinski et al., 2016; Mayes et al., 2012; Simonoff et al., 2008). Interestingly, two classes of children showed elevated symptoms of ADHD and repetitive sensorimotor behaviors, converging with earlier work showing stereotypic behaviors in ADHD (Clark et al., 1999; Sokolova et al., 2017), and associations between restricted and repetitive behavior and hyperactivity/impulsivity and general motor problems in ADHD (Cooper et al., 2014). Future work should investigate whether restricted and repetitive behaviors in ADHD are qualitatively similar to those seen in ASD. Understanding how symptoms cluster irrespective of DSM-V categories is important given the current challenges in diagnosing and treating children with comorbid psychiatric symptoms (e.g. Joshi et al., 2017; Kentrou et al., 2018).

Our findings should be interpreted in light of some limitations. First, our results are based on parent-ratings only. Parents may interpret the meaning of questions differently. However, repeating the analyses using teacher- and self-reports yielded similar findings (see Supplemental Materials). Future work using clinical observations and neuropsychological testing, for example, should be used to confirm our findings. Furthermore, there was a small, but significant, difference in mean age across diagnostic groups. We added age as a covariate in all relevant analyses, and a supplemental analysis on age-matched subgroups did not meaningfully alter the results (see Supplemental Materials).

In sum, this study investigated the relation between restricted and repetitive behavior and attention problems in children with ASD and/or ADHD. Our findings show severe and persistent symptoms across all domains for children with co-morbid ASD and ADHD, and more moderate symptoms that improved with age in children with a diagnosis of ASD or ADHD only. Furthermore, parents reported increased levels of restricted and repetitive behavior, specifically of repetitive sensorimotor behaviors, in children with ADHD, which may warrant further investigation using clinical and neuropsychological measures.

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Conflicts of Interest

None of the authors report (financial) conflicts of interest.

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Table 1. Demographics of the sample

		TDC	ADHD	ASD	ASD/ADHD	*p*	*Pairwise comparisons*
	N	188	155	95	46		
	Gender (M/F)	124/64	127/28	86/9	44/2	<.001	
	Age	12.2 (2.8)	11.5 (2.9)	12.7 (2.8)	11.0 (2.5)	<.001	ADHD < TD, p = .026; ASD/ADHD < TD, p = .013; ADHD < ASD, p < .001; ASD/ADHD < ASD, p < .001
	Parental educational level	14.3 (2.1)	13.4 (2.8)	13.6 (2.5)	14.0 (1.8)	.008	ADHD < TD, p = .001
	Tanner status	2.4 (1.5)	2.0 (1.5)	2.4 (1.7)	1.7 (1.3)	.001	ADHD < TD, p = .021; ASD/ADHD < TD, p = .008; ASD/ADHD < ASD, p = .028
Cognitive abilities & symptom severity							
	TIQ	112.9 (14.5)	103.4 (15.9)	107.5 (19.7)	108.9 (16.8)	<.001	ADHD < TD, p < .001; ASD < TD, p = .008
	VIQ	112.2 (14.5)	103.0 (16.8)	107.6 (19.0)	110.6 (18.4)	<.001	ADHD < TD, p < .001; ASD < TD, p = .033, ADHD < ASD, p = .045; ADHD < ASD/ADHD, p = .010
	PIQ	110.3 (18.6)	103.2 (17.5)	104.4 (19.0)	102.9 (18.3)	<.001	ADHD < TD, p < .001; ASD < TD, p = .033, ASD/ADHD < TD, p = .025
	ADI Communication	-	-	14.8 (4.1)	13.5 (3.6)	.249*	
	ADI Social Interaction	-	-	19.3 (5.1)	15.8 (6.0)	.035*	
	ADI Repetitive Behavior	-	-	5.4 (2.7)	4.1 (2.4)	.133*	
No. measurements						.502	
	1	131	111	69	40		
	2	36	36	27	8		
	>3	22	10	9	1		

Supplemental material to "Overlapping symptoms in Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorders: more similarities than differences"

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Supplemental methods

In order to follow up on the findings in the main paper, and to account for the fact that under DSM IV many children with ASD and ADHD symptoms were formally only diagnosed with ASD, we ran a second analysis where we grouped participants with ASD according to whether they fell above or below the clinical cut-off on the ADHD-subscale of the CBCL (T-score > 69) instead of by clinical diagnosis. This resulted in four diagnostic groups: 1) TDC, 2) ADHD, 3) ASD^{CBCL}, and 4) ASD and ADHD ($ASD/ADHD^{CBCL}$). Subsequently, the same LME-models as in the main paper were fit on all RBS-R subscales, but now using the grouping based on CBCL-scores.

In another follow-up analysis and in order to investigate whether differences in rater affected the results, we repeated the LME-models in a subgroup of participants grouped according to teacher- and self-report ratings on ADHD-subscale of the TRF and YSR.

We again investigated the longitudinal development of symptoms by follow-up analyses on raw CBCL scores. If interaction effects between diagnostic status and age were present, we further investigated these using Pearson's correlations. Pearson's correlations were also run between CBCL and RBS-R scores.

Supplemental results

Follow-up analyses using CBCL ADHD subscale scores to determine presence of ADHD comorbidity in ASD yielded similar effects for all subscales of interest: Stereotyped Behaviors (dx: $F(3,613) = 9.0$, $p < .001$, age: $F(1,606) = 5.0$, $p = .026$, gender: n.s., dx*age interaction: n.s.), Compulsive Behaviors (dx: $F(3,678) = 7.9$, $p < .001$, age: n.s., gender: n.s., dx*age interaction: n.s.), Ritualistic Behaviors (dx: $F(3,640) = 14.3$, $p < .001$, age: $F(1,635) = 19.1$, $p < .001$, gender: n.s., dx*age interaction: $F(1,647) = 2.7$, $p = .043$), Insistence on Sameness (dx: $F(3,562) = 9.1$, $p < .001$, age: n.s., gender: $F(1,530) = 4.1$, $p = .042$, dx*age interaction: n.s.) and Restricted Behaviors (dx: $F(3,683) = 11.4$, $p < .001$, age: n.s., gender: n.s., dx*age interaction: $F(1,683) = 6.6$, $p < .001$). Pairwise comparisons between diagnostic groups are given in Supplemental Table S3. Using parent-rated ADHD symptom severity yielded slightly different results compared to the main analyses using clinical diagnostic groups. Again, children with ASD and/or ADHD showed increased stereotyped behaviors compared to typically developing children (all p's < .001), yet this analysis also showed increased stereotyped behaviors in children with ASD/ADHD compared to children with ASD or ADHD only (p's < .008). For Ritualistic behaviors, the comparison between typically developing children and children with ADHD also reached significance ($p = .021$) in addition to the other comparisons (p's < .001). For Compulsive Behaviors, Insistence on Sameness and Restricted Behaviors all pairwise comparisons remained significant (all p's < .002).

When defining ADHD-comorbidity based on TRF or YSR ADHD subscale scores yielded highly similar results.

Table S1. Pairwise comparisons between diagnostic groups on the CBCL subscales rather than clinical diagnosis.

Attention Problems (T-scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-12.5	0.7	18.0	**< .001**
TD – ASD	-10.7	0.8	13.7	**< .001**
TD – ASD/ADHD	-18.0	1.0	17.4	**< .001**
ADHD – ASD	1.8	0.8	2.2	0.128
ADHD – ASD/ADHD	-5.5	1.0	5.3	**< .001**
ASD – ASD/ADHD	-7.3	1.1	6.7	**< .001**
Rule breaking behavior (T-scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-6.2	0.6	10.6	**< .001**
TD – ASD	-5.9	0.7	8.9	**< .001**
TD – ASD/ADHD	-6.5	0.8	7.3	**< .001**
ADHD – ASD	0.4	0.7	0.5	0.948
ADHD – ASD/ADHD	-0.3	0.9	0.3	0.990
ASD – ASD/ADHD	-0.6	0.9	0.7	0.900

Aggressive behavior (T-scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-10.2	0.8	12.8	**< .001**
TD – ASD	-9.5	0.9	10.6	**< .001**
TD – ASD/ADHD	-11.1	1.2	9.4	**< .001**
ADHD – ASD	0.7	0.9	0.7	0.891
ADHD – ASD/ADHD	-0.9	1.1	0.7	0.882
ASD – ASD/ADHD	-1,5	1.2	1.2	0.603
Internalizing Problems (T-scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-10.4	0.9	11.4	**< .001**
TD – ASD	18.5	1.0	17.9	**< .001**
TD – ASD/ADHD	-18.4	1.4	13.2	**< .001**
ADHD – ASD	-8.0	1.1	7.5	**< .001**
ADHD – ASD/ADHD	-8.0	1.4	5.6	**< .001**
ASD – ASD/ADHD	0.1	1.5	0.0	0.999

Externalizing Problems (T-scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-16.8	1.0	17.5	**< .001**
TD – ASD	-15.3	1.1	14.1	**< .001**
TD – ASD/ADHD	-17.8	1.4	12.5	**< .001**
ADHD – ASD	1.5	1.1	1.3	0.534
ADHD – ASD/ADHD	-1.0	1.4	0.7	0.890
ASD – ASD/ADHD	-2.5	1.5	1.7	0.337

Abbreviations: ADHD = Attention Deficit/Hyperactivity Disorder, ASD = Autism Spectrum Disorder, ASD/ADHD = Autism Spectrum Disorder with comorbid ADHD, CBCL = Child Behavior Checklist, S.E. = standard error

Table S2. Pairwise comparisons between diagnostic groups on the RBS-R subscales (using diagnostic groups defined based on clinical diagnosis).

Stereotyped behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-1.7	0.2	8.4	**< .001**
TD – ASD	-2.2	0.2	10.0	**< .001**
TD – ASD/ADHD	-2.2	0.3	7.3	**< .001**
ADHD – ASD	-0.5	0.2	2.3	0.091
ADHD – ASD/ADHD	-0.5	0.3	1.8	0.288
ASD – ASD/ADHD	0.0	0.3	0.0	> .999
Compulsive behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-0.7	0.2	3.9	**< .001**
TD – ASD	-2.9	0.2	13.8	**< .001**
TD – ASD/ADHD	-1.8	0.3	6.4	**< .001**
ADHD – ASD	-2.2	0.2	10.2	**< .001**
ADHD – ASD/ADHD	-1.1	0.3	3.9	**< .001**
ASD – ASD/ADHD	1.1	0.3	3.5	**0.003**

Ritualistic behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-0.6	0.2	2.6	**0.048**
TD – ASD	-4.3	0.3	15.9	**< .001**
TD – ASD/ADHD	-2.7	0.4	7.5	**< .001**
ADHD – ASD	-3.7	0.3	13.4	**< .001**
ADHD – ASD/ADHD	-2.1	0.4	5.8	**< .001**
ASD – ASD/ADHD	1.6	0.4	4.2	**< .001**
Insistence on sameness (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-1.4	0.4	3.9	**< .001**
TD – ASD	-7.0	0.4	16.8	**< .001**
TD – ASD/ADHD	-4.6	0.5	8.5	**< .001**
ADHD – ASD	-5.6	0.4	13.2	**< .001**
ADHD – ASD/ADHD	-3.2	0.5	6.0	**< .001**
ASD – ASD/ADHD	2.3	0.6	4.2	**< .001**

Restricted behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-0.5	0.1	3.9	**< .001**
TD – ASD	-2.5	0.2	15.4	**< .001**
TD – ASD/ADHD	-1.7	0.2	7.8	**< .001**
ADHD – ASD	-2.0	0.2	11.9	**< .001**
ADHD – ASD/ADHD	-1.2	0.2	5.1	**< .001**
ASD – ASD/ADHD	0.8	0.2	3.5	**0.003**

Abbreviations: ADHD = Attention Deficit/Hyperactivity Disorder, ASD = Autism Spectrum Disorder, ASD/ADHD = Autism Spectrum Disorder with comorbid ADHD, RBS-R = Repetitive Behavior Scale - Revised version, S.E. = standard error

Table S3. Pairwise comparisons between diagnostic groups on the RBS-R subscales, based on parent-rated severity of ADHD symptoms (CBCL).

Stereotyped behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-1.7	0.2	8.6	**< .001**
TD – ASD	-2.0	0.2	9.2	**< .001**
TD – ASD/ADHD	-3.0	0.3	9.1	**< .001**
ADHD – ASD	-0.3	0.2	1.3	0.524
ADHD – ASD/ADHD	-1.3	0.3	4.0	**< .001**
ASD – ASD/ADHD	-1.0	0.3	3.2	**0.008**
Compulsive behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-0.8	0.2	4.1	**< .001**
TD – ASD	-2.2	0.2	10.7	**< .001**
TD – ASD/ADHD	-3.5	0.3	10.8	**< .001**
ADHD – ASD	-1.4	0.2	6.8	**< .001**
ADHD – ASD/ADHD	-2.8	0.3	8.5	**< .001**
ASD – ASD/ADHD	-1.4	0.3	4.2	**< .001**

Ritualistic behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-0.7	0.2	2.9	**0.021**
TD – ASD	-3.2	0.3	12.3	**< .001**
TD – ASD/ADHD	-4.4	0.4	10.7	**< .001**
ADHD – ASD	-2.5	0.3	9.5	**< .001**
ADHD – ASD/ADHD	-3.7	0.4	9.1	**< .001**
ASD – ASD/ADHD	-1.2	0.4	2.9	**0.018**
Insistence on sameness (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-1.5	0.4	4.0	**< .001**
TD – ASD	-5.7	0.4	14.4	**< .001**
TD – ASD/ADHD	-7.8	0.6	13.1	**< .001**
ADHD – ASD	-4.3	0.4	10.6	**< .001**
ADHD – ASD/ADHD	-6.3	0.6	10.8	**< .001**
ASD – ASD/ADHD	-2.0	0.6	3.7	**0.002**

Restricted behavior (raw scores)	*Estimate*	*S.E.*	*t*	*P*
TD – ADHD	-0.6	0.1	3.9	**< .001**
TD – ASD	-1.9	0.2	12.4	**< .001**
TD – ASD/ADHD	-3.4	0.3	13.2	**< .001**
ADHD – ASD	-1.4	0.2	8.6	**< .001**
ADHD – ASD/ADHD	-2.8	0.3	11.0	**< .001**
ASD – ASD/ADHD	-1.4	0.3	5.6	**< .001**

Abbreviations: ADHD = Attention Deficit/Hyperactivity Disorder, ASD = Autism Spectrum Disorder, ASD/ADHD = Autism Spectrum Disorder with comorbid ADHD, RBS-R = Repetitive Behavior Scale - Revised version, S.E. = standard error

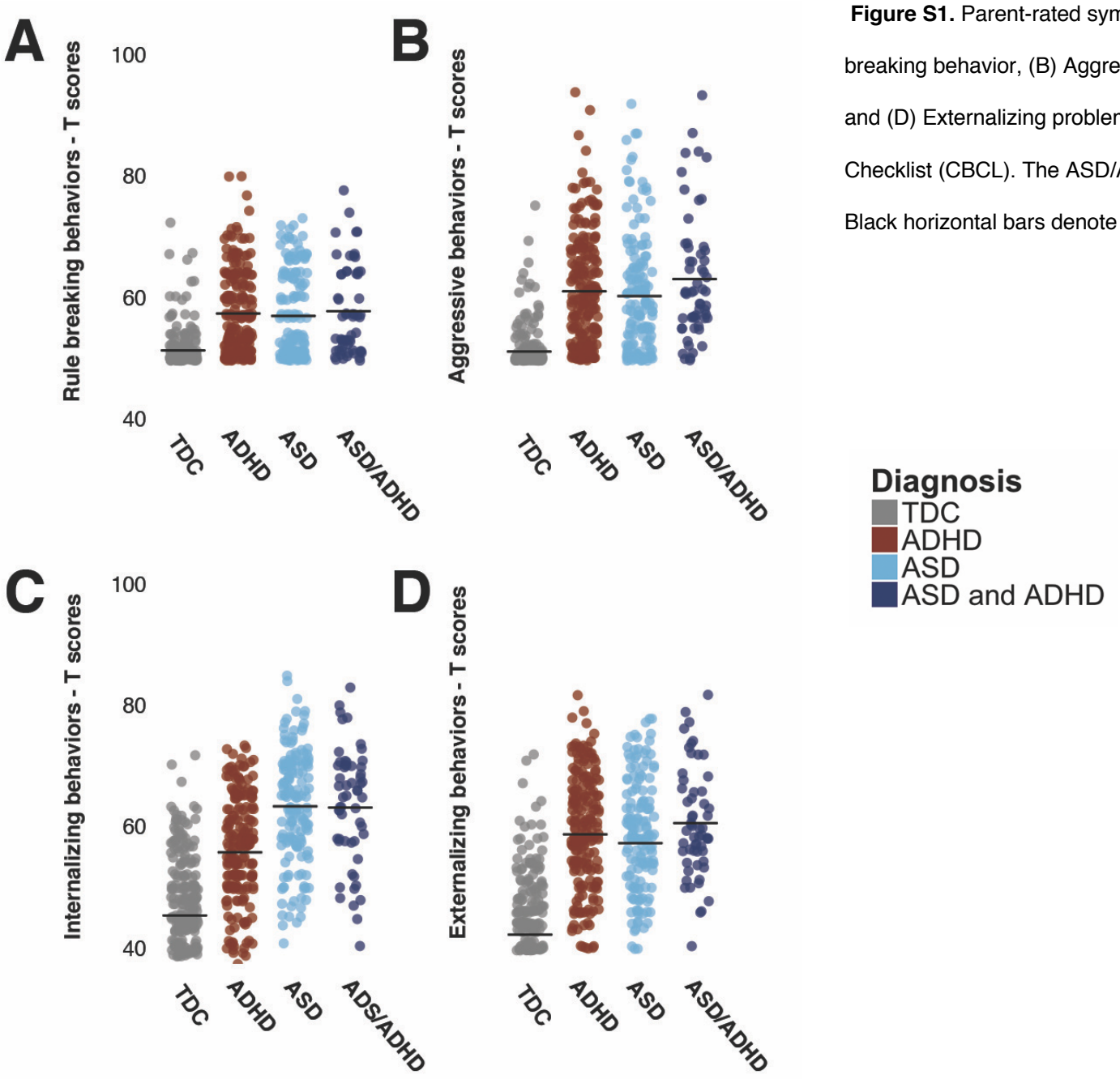

Figure S1. Parent-rated symptom severity (T-scores) on the (A) Rule breaking behavior, (B) Aggressive behavior, (C) Internalizing problems and (D) Externalizing problems subscales of the Child Behavior Checklist (CBCL). The ASD/ADHD group is defined by clinical diagnosis. Black horizontal bars denote the group mean.

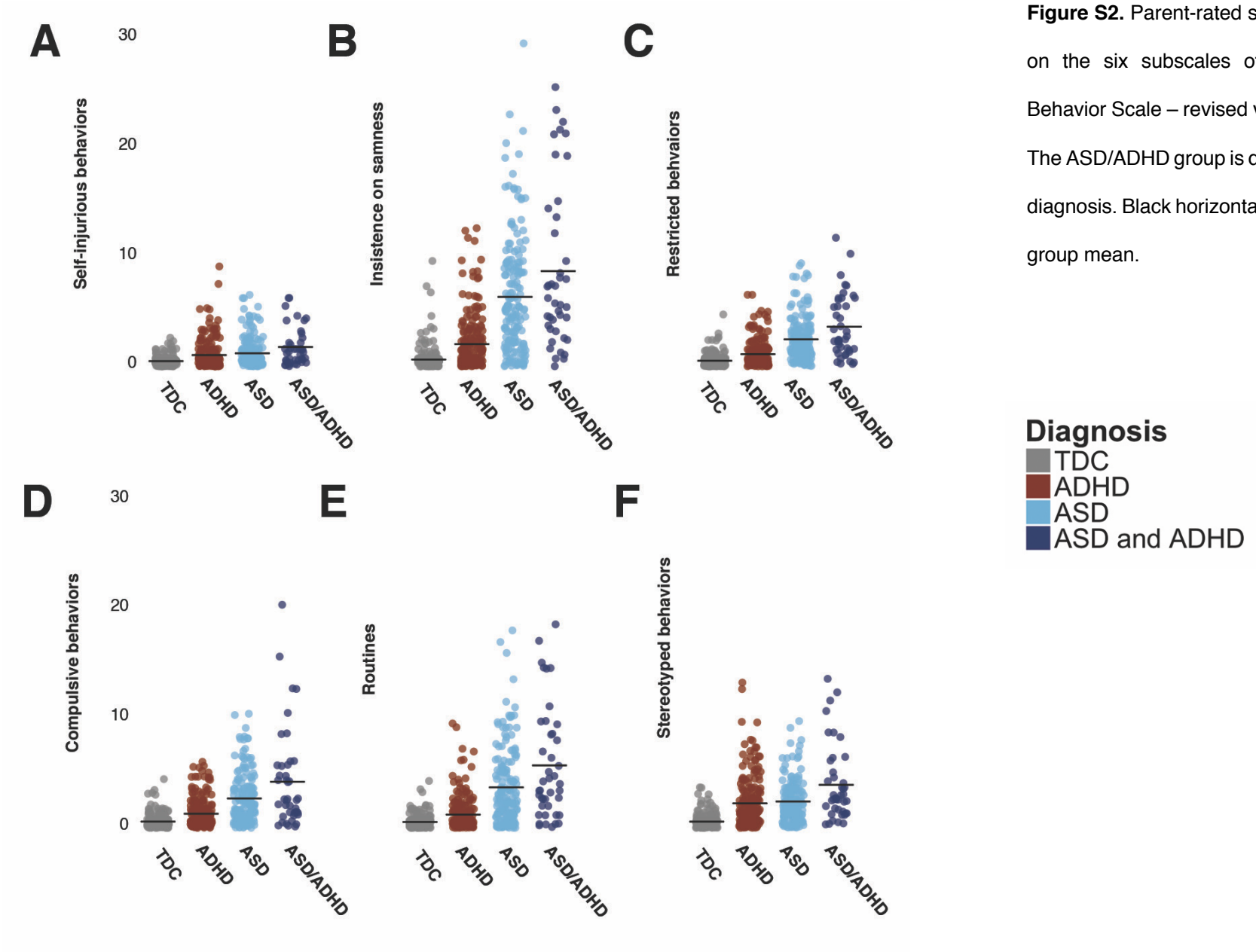

Figure S2. Parent-rated symptom severity on the six subscales of the Repetitive Behavior Scale – revised version (RBS-R). The ASD/ADHD group is defined by clinical diagnosis. Black horizontal bars denote the group mean.

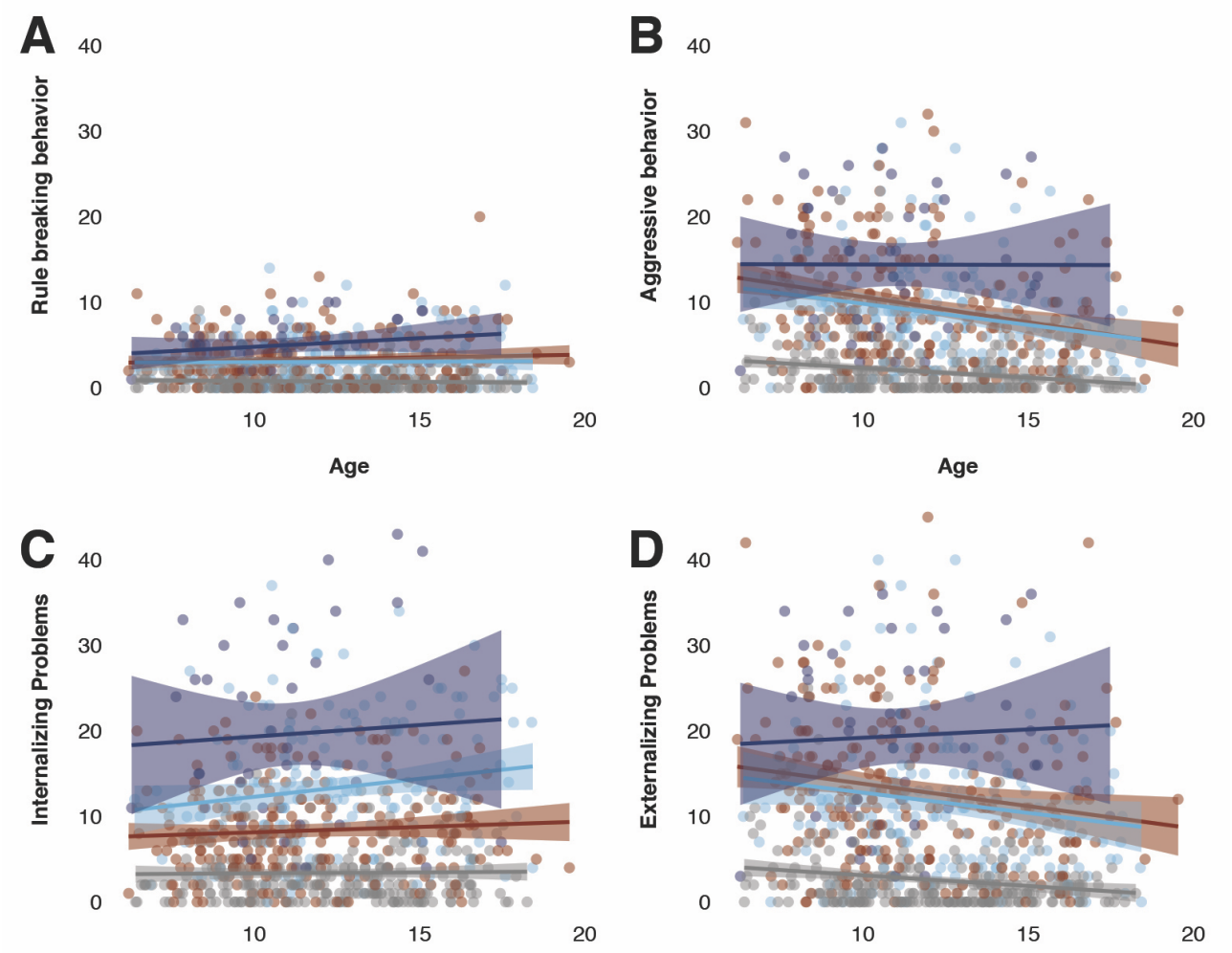

Figure S3. Panel A-D show parent-rated symptom severity (T-scores) on subscales of the Child Behavior Checklist (CBCL) plotted against age.

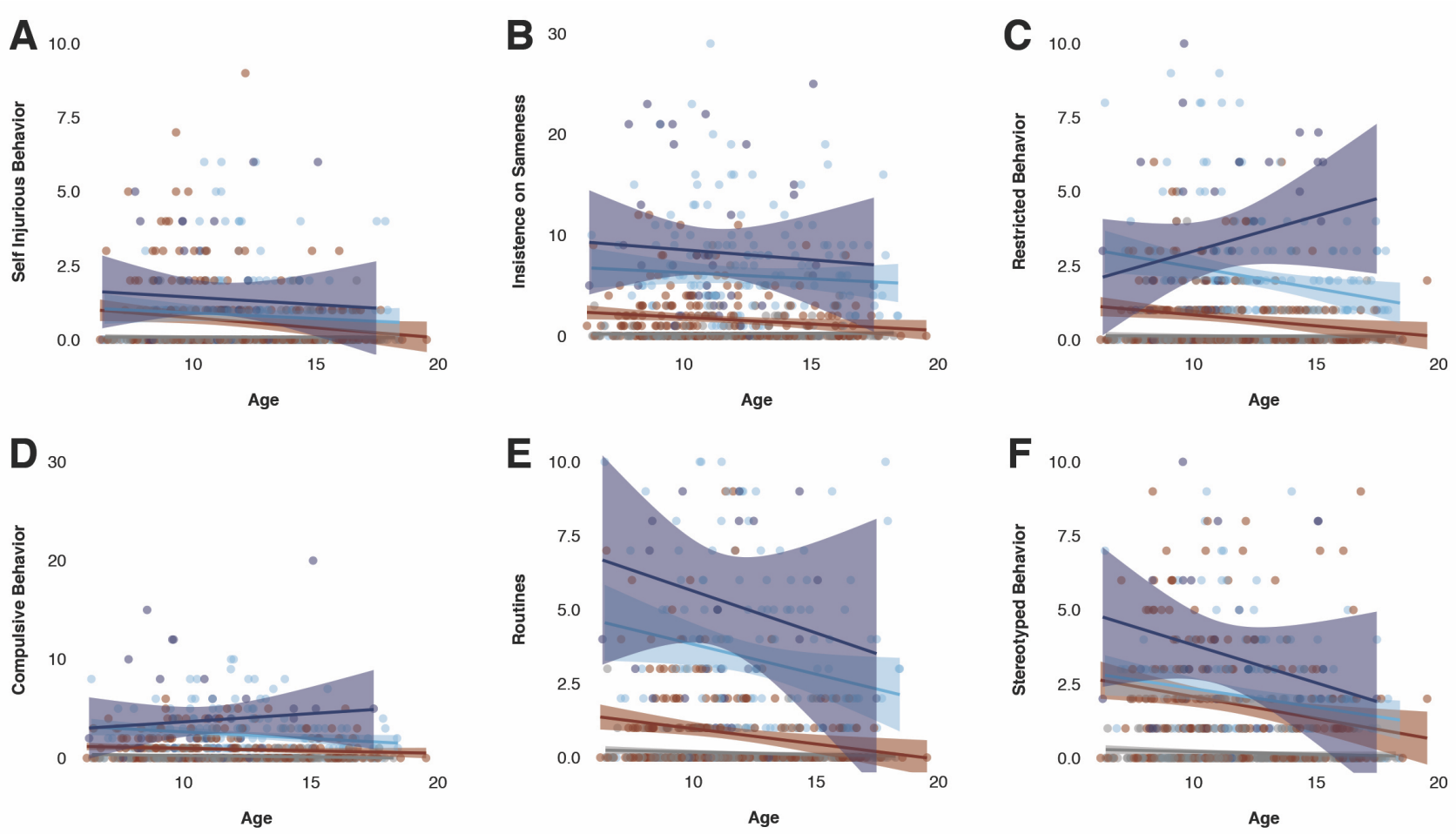

Figure S4. Panel A-F show parent-rated symptom severity on subscales of the Repetitive Behavior Scale – revised version (RBS-R) plotted against age.