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Comparison of Attention Deficit Hyperactivity Disorder in typically developing children and children with Down syndrome

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Abstract

Objective: This study aimed to evaluate ADHD symptom patterns among children with Down syndrome with or without ADHD as well as typically developing children with ADHD.

Method: Parents and teachers rated symptoms of inattention, hyperactivity, and general behavioral concerns for 22 children with Down syndrome and comorbid diagnoses of ADHD (DS+ADHD), 66 gender- and age-matched children with Down syndrome with no diagnosis of ADHD (DS-ADHD), and 66 gender- and age-matched typically developing children with ADHD (TD+ADHD). Children with Down syndrome were recruited from the community. Typically developing children with ADHD were recruited from a speciality clinic evaluating for ADHD.

Results: Parents tended to report higher scores of inattention and hyperactivity for typically developing children with ADHD compared to children with Down syndrome and no ADHD. Although mean ADHD symptom summary scores were not significantly different in DS+ADHD and DS-ADHD, specific parent report items (e.g., distractibility and being “on the go”) did tend to differentiate these groups. In contrast, teachers tended to report higher inattention and hyperactivity scores for DS+ADHD compared to both DS-ADHD and TD+ADHD. Specific

teacher-reported items tending to differentiate DS+ADHD and DS-ADHD included difficulties following through on tasks, avoiding tasks, leaving one's seat, and excessive talking.

Conclusion: Variability in response patterns between parent- and teacher-reports for children with and without Down syndrome highlight the need to evaluate ADHD symptoms across environments. Our findings also suggest specific items that may particularly helpful in distinguishing children with Down syndrome who do and do not have ADHD, although replication is needed.

Keywords

Down syndrome; ADHD; children

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurobehavioral disability, with a prevalence rate estimated to be 6–8% in the general population¹. Prevalence rates of ADHD in atypically developing populations have been found to differ from the general population. Comorbid ADHD in individuals with intellectual disabilities has been *estimated* to be between 13–16%² and, more specifically, in individuals with Down syndrome (DS), may be as high as 20–44%^{3–6}.

Diagnostic criteria for ADHD according to the DSM-5 includes a persistent pattern of inattention and/or hyperactivity that 1) is inconsistent with developmental level, 2) interferes with functioning or development, 3) manifests prior to age 12, 4) is present in two or more settings, and 5) is not better explained by another mental health disorder⁷. Additionally, the ADHD diagnosis requires six or more symptoms of inattention and/or hyperactivity to have persisted for at least 6 months⁷. Although these criteria may seem straightforward on the surface, their application to children with DS can be complex, as it may be difficult to determine whether some ADHD features (e.g., behavioral inattention, task avoidance, forgetting daily activities) are a result of the individual's intellectual disability or whether comorbid ADHD is present^{8,9}. It is possible that specific DSM ADHD symptoms may have no clinical utility for identifying ADHD in children with DS (e.g., “difficulty sustaining attention”) as these symptoms are part of the behavioral phenotype typically seen in children with DS, while other symptoms may possess better specificity for the differentiation of individuals with DS who also meet criteria for ADHD.

Unfortunately, there is minimal research and no evidence-based guideline for diagnosing ADHD in children with DS. The most authoritative set of consensus-based recommendations from the Diagnostic Manual – Intellectual Disability¹⁰ suggest using the same criteria and thresholds for children with DS as for typically developing (TD) children because the DSM already specifies that the level of symptomatology and impairment must be inconsistent with an individual's developmental level to meet criteria for ADHD¹¹. No guidance is provided as to whether specific ADHD symptoms or symptom domains, or associated challenges with maladaptive behaviors, might have better diagnostic utility among children with DS, as previous research has not compared the symptoms and characteristics of individuals with DS and comorbid ADHD to their TD peers with ADHD or to individuals with DS without ADHD. Comparing these populations will allow for better understanding of what characteristics and symptoms are present as a result of DS and what

characteristics and symptoms are specific to ADHD in children with DS, thereby informing diagnostic practices.

Hence, the present study was designed to evaluate the differences between children with DS with or without ADHD in comparison to TD children with ADHD. First, we evaluated group differences on the *summary scores* generated from parent- and teacher-rated behavioral measures of ADHD symptomatology. We hypothesized that children with ADHD, whether they have coexisting DS or are TD, would have higher scores on parent and teacher measures of ADHD-related symptoms, such as hyperactivity/impulsivity, than children with DS and no diagnosis of ADHD, and that all groups would demonstrate comparable levels of difficulty with symptoms of inattention. We further hypothesized children with ADHD (TD or DS) would have higher scores on parent and teacher measures of associated behavioral concerns of rule-breaking behavior, aggression, and externalizing problems than children with DS and no diagnosis of ADHD. Second, we evaluated group differences at the *item level* on parent- and teacher-report measures of specific ADHD symptoms. We again hypothesized that both TD children and children with DS who have comorbid ADHD would have higher item-level scores for most hyperactivity/impulsivity symptoms than children with DS and no comorbid diagnosis of ADHD and comparable item-level scores for most inattention symptoms.

Method

Participants

Participants were children with DS recruited as part of several larger community-based single- and multi-site studies of behavior and cognition, aged between 6–17 years. Based on parent-reports of comorbid clinical diagnoses that were corroborated through medical chart review, 22 children with DS had a diagnosis of ADHD (DS+ADHD). From the pool of other children participating in these studies, age- and gender-matched controls, using a 3:1 ratio, were used to generate a group of 66 children with DS who did not have a comorbid diagnosis of ADHD (DS-ADHD). Age- and gender-matched children with ADHD seen clinically were selected using a 3:1 ratio to generate a group of 66 TD children with diagnoses of ADHD (TD+ADHD).

Procedures

Parents of children with DS were recruited through a pediatric medical center, a DS specialty clinic, or through newsletters distributed by local DS associations for several single-site (8/2015–5/2018) or multi-site longitudinal community-based studies (6/2018–3/2020) focused on measurement of cognition and behavior. Eligibility criteria for study participation included having a child with DS between the ages of 6–17 years, and English as the primary language spoken at home. Parents reported on whether their child had been previously diagnosed with ADHD.

Parents of TD children with ADHD were recruited through an ADHD specialty care clinic at a pediatric medical center. These children were all being seen clinically for diagnosis of ADHD. All participants were diagnosed with ADHD based on an unstructured clinical

interview and parent- and teacher ADHD rating scales. Moreover, all families consented to allowing their child's clinical data to be used for research purposes.

Parents of children with DS and of typically developing children completed demographic information forms as well as the ADHD and general behavior measure forms listed below. Parents were provided with paper copies or electronic links to provide to their child's teacher who knew them best to obtain teacher-report forms. Raters were asked to rate the child's current behaviors, regardless of medication or other comorbid conditions. Because study participation occasionally occurred during school summer and winter breaks, some teacher reports were missing. All study activities were approved and overseen by the Institutional Review Board at the medical center.

Measures

ADHD Rating Scales.—The Vanderbilt ADHD Rating Scales – Parent and Teacher Forms (VADPRS and VADTRS) are DSM-based scales that provide clinical information regarding the frequency and severity of symptoms related to ADHD across the home and school domains^{12,13}. Internal consistency and reliability are excellent across the nine-item inattention and hyperactivity/impulsivity subscales among typically developing children¹⁴. Items are rated on a 4-point scale ranging from 0 (never) to 3 (very often). Subscales for the VADPRS and VADTRS include Inattention, Hyperactivity, and Total Symptom Score, with the raw scores being summed across the nine items for inattention, nine items for hyperactivity, and the combined 18 items respectively. The Vanderbilt ADHD Rating Scales have been recommended for use in individuals with intellectual and developmental disabilities by the National Institutes of Health Down Syndrome Outcome Measures working group meeting convened in 2015^{15,16}.

General Behavior Rating Scales.—The Achenbach System of Empirically Based Assessment (ASEBA) checklists were used to assess general child behaviors. The ASEBA checklists include the Child Behavior Checklist (CBCL) and the Teacher Report Form (TRF). The CBCL obtains parent ratings of 112 problem behaviors for children ages 6–18 years, in addition to descriptions of their child's strengths and challenges¹⁷. The TRF obtains similar ratings on problem behaviors from teachers. Items are rated on a 3-point scale from (0) not true to (2) very true, and t-scores are created based on an age and gender normative sample. The CBCL and TRF assesses symptoms on the following subscales: Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behavior and Aggressive Behavior. An Externalizing Problems score is derived from symptoms of Rule-Breaking Behavior and Aggressive Behavior. Internal consistency and one-week test-retest reliability ranges from good to excellent for each of the subscales for TD children¹⁷. The present analyses are focused on selected subscales of Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Problems from the CBCL and TRF, as these subscales are related to specific concerns for ADHD and common comorbid behavioral challenges in children with ADHD. Although not initially designed for use with children who have intellectual disabilities, these scales are considered promising for use with individuals with

DS as internal consistency is moderate to high for all subscales when used in samples of children who have intellectual disabilities or DS^{15,18,19}.

Data Analysis

Demographic and clinical characteristics were compared across the three groups of children (DS+ADHD, DS-ADHD, and TD+ADHD) using ANOVAs and chi-square tests to identify any potential covariates/confounders.

Multivariate analyses of covariance (MANCOVA) were used to compare differences between the three groups on subscale *summary scores* generated from the parent and teacher Vanderbilt rating scales (VADPRS and VADTRS respectively), as well as for the selected subscales t-scores for the CBCL and TRF, controlling for multiple comparisons and significant covariates. Multivariate analyses of covariance (MANCOVA) were also used to compare differences between the three groups on *items* of the parent and teacher Vanderbilt rating scales (VADPRS and VADTRS respectively), controlling for multiple comparisons and significant covariates. Statistically significant MANCOVAs (Pillai's Trace) were followed up with the ANCOVA analyses and estimated marginal means. Statistically significant group differences were followed up with post-hoc tests using a Bonferroni correction.

Results

Group comparison on demographic and clinical characteristics

Percentages, mean scores, and standard deviations for demographic and clinical characteristics by participant group are presented in Table 1. There were no group differences on child demographic variables of gender or age. The TD+ADHD group included more African-American and fewer Caucasian participants than the DS+ADHD or DS-ADHD groups [$\chi^2(6) = 13.7, p = .033$]. As race is not related to symptoms of ADHD in the general population when assessed using standardized diagnostic assessments, race was not included as a covariate in subsequent analyses¹. Children with DS+ADHD had higher rates of being prescribed medication for ADHD compared to children with DS-ADHD and TD+ADHD [$\chi^2(2) = 79.1, p < .001$]. Hence, receipt of medication for ADHD was included as a covariate in subsequent analyses.

Group comparison on parent- and teacher-report measures

Estimated marginal means and standard errors for measures of parent- and teacher-reports by group are presented in Table 2, which adjust for covariates. On MANCOVAs investigating *parent-rated* Vanderbilt ADHD Rating Scale (VADPRS) scores and adjusted for ADHD medication use, we found significant group differences [$F(4,262) = 14.4, p < .001$]. Specifically, significant group differences were found using follow-up ANCOVAs on the VADPRS subscales for Inattention [$F(2,131) = 33.51, p < .001$], Hyperactivity [$F(2,131) = 10.53, p < .001$], and Combined [$F(2,131) = 28.30, p < .001$] total symptom scores. Follow-up post-hoc analyses demonstrated higher parent-rated Vanderbilt scores in the TD+ADHD group compared to the DS+ADHD for Inattention, and significantly higher scores in the TD+ADHD group than the DS-ADHD group for the Inattention, Hyperactivity,

and Combined scores (see Table 2). In contrast, MANCOVAs evaluating *teacher-rated* Vanderbilt ADHD Rating Scale (VADTRS) scores did not find group differences between DS+ADHD, DS-ADHD or TD+ADHD. Furthermore, ADHD medication was not related to VADPRS or VADTRS scores in these analyses.

On the ASEBA checklists, MANCOVAs were significant at the group level for the subscales of interest from the CBCL [$F(8,260) = 6.12, p < .001$] and TRF [$F(8,200) = 2.92, p = .004$]. The ADHD medication variable was not related in the MANCOVAs to either the selected CBCL or TRF subscales.

Significant group differences were found using follow-up ANCOVAs on the parent-rated CBCL subscales for Attention Problems [$F(2,132) = 26.38, p < .001$], Rule-Breaking Behavior [$F(2,132) = 3.80, p = .025$], and Aggressive Behavior [$F(2,132) = 8.87, p < .001$], as well as for Externalizing Problems [$F(2,132) = 6.96, p = .001$]. Follow-up post-hoc analyses demonstrated significantly higher CBCL t-scores in the TD+ADHD group compared to both the DS+ADHD and DS-ADHD groups for the Attention Problems and Aggressive Behavior subscales. In addition, the TD+ADHD group had higher t-scores than the DS-ADHD group on the Externalizing Problems scale.

Significant group differences were found using follow-up ANCOVAs on the TRF subscales for Attention Problems [$F(2,102) = 4.50, p = .013$] and Externalizing Problems [$F(2,102) = 4.36, p = .015$]. Follow-up post-hoc analyses demonstrated significantly higher TRF t-scores in the DS+ADHD group compared to both the DS-ADHD and TD+ADHD groups for Attention Problems.

Group comparisons on parent- and teacher-rated Vanderbilt items

Estimated marginal means and standard errors for items on the VADPRS and VADTRS by group are presented in Table 3, which adjust for covariants. MANOVAs were significant at the group level for the VADPRS items [$F(36,226) = 3.69, p < .001$], but not for VADTRS items [$F(36,148) = 1.38, p = .092$]. The ADHD medication variable was not related in MANCOVAs evaluating to either the VADPRS or the VADTRS items. Item level missing data contributed to different samples sized in subsequent analyses.

Follow-up ANCOVAs found that *parent* Vanderbilt ratings varied by group for all nine VADPRS *Inattention* items, with parents of TD children with ADHD generally rating their children as having more severe symptoms on each item compared to the ratings made by parents of children with DS whether or not comorbid ADHD was present (see Table 3). Follow-up post-hoc analyses demonstrated significantly higher VADPRS item scores for the TD+ADHD group than both the DS+ADHD and DS-ADHD groups for 3 of the 9 Inattention items, as well as higher VADPRS item scores in the TD+ADHD group compared to the DS-ADHD group for the remaining 6 of 9 Inattention items. Follow-up post-hoc analyses demonstrated significantly higher VADPRS items scores among children with DS+ADHD than children with DS-ADHD for only 1 of 9 Inattention items (distracted).

Significant group differences in parent ratings were found using follow-up ANCOVAs on 7 of the 9 VADPRS *Hyperactivity* Items, although this pattern was somewhat different

than that observed for the Inattention items (see Table 3). Follow-up post-hoc analyses demonstrated significantly higher VADPRS items scores among TD+ADHD than DS-ADHD for all 7 of the Hyperactive items that showed group-level differences. Follow-up post-hoc analyses also demonstrated significantly higher VADPRS items scores among DS+ADHD than DS-ADHD for only 1 of the 9 Hyperactivity items (on the go). However, in contrast to the VADPRS Inattention items, no parent-rated Hyperactivity item score differed significantly between the TD+ADHD and DS+ADHD groups.

Significant group differences were found using follow-up ANCOVAs on only 2 of the 9 *teacher-rated Inattention* items (see Table 3). Follow-up post-hoc analyses demonstrated a significantly higher VADTRS item score for the DS+ADHD than the TD+ADHD group for 1 of 9 Inattention items (avoids tasks), and higher VADTRS item scores for the TD+ADHD than the DS-ADHD group for 1 of 9 Inattention items (follow through).

Significant group differences were found using follow-up ANCOVAs on only 2 of the 9 *teacher-rated Hyperactivity* items (see Table 3). Follow-up post-hoc analyses demonstrated a significantly higher VADTRS item score for the DS+ADHD than the DS-ADHD group for 1 of 9 Inattention items (leaves seat), and higher VADTRS item scores for the TD+ADHD than the DS-ADHD group for 1 of 9 Inattention items (talks too much).

Discussion

The current study examined differences among children with DS with and without ADHD, and in comparison to TD children with ADHD, on parent- and teacher-report measures. Overall, the pattern of group differences in this pilot study varied by rater, with parents reporting the highest concern for symptoms of inattention, hyperactivity and behavioral concerns in TD children with ADHD, and teachers reporting the highest concern for such symptoms in children with DS and comorbid ADHD. This pattern of findings was supported both at the subscale level and at the item level. Thus, the present findings highlight the need to consider ADHD symptoms across environments when considering the appropriateness of this diagnosis for children with DS, and to recognize that the profile of symptoms presents somewhat differently across settings compared to TD children.

The hypothesis that children with ADHD, whether with DS or TD, would have worse symptoms of hyperactivity than children with DS and no comorbid ADHD was only supported by the parent-report data. Scores for children with DS and ADHD fell in the middle, but were not statistically higher than children with DS and no comorbid ADHD or statistically lower than TD children with ADHD. On teacher reports, children with DS and ADHD had the highest rated mean scores, followed by TD children with ADHD and then children with DS and no comorbid ADHD, but there were no statistically significant group differences. Thus, hyperactive symptoms appear to clearly differentiate TD children with ADHD from children with DS and no ADHD. In contrast, hyperactive symptoms do not appear to strongly demarcate children with DS and ADHD from children with DS who do not have ADHD, since those with DS and ADHD present with hyperactive symptoms, but not to the same degree as reported by parents of TD children with ADHD.

The hypothesis that children in the three groups would demonstrate comparable concerns for inattention was not supported on parent reports and demonstrated inconsistent findings for teacher reports. On parent-reports of inattention on the VADPRS and CBCL, TD children with ADHD were reported to have significantly higher concerns for inattention than children with DS with or without ADHD. Scores for children with DS and ADHD fell in between the TD children with ADHD and children with DS and no ADHD groups again, and were not statistically higher than children with DS and no comorbid ADHD. In contrast, teacher reports of inattention on the VADTRS supported our hypothesis: children in all groups had reported concerns with inattention, with no statistically significant group differences. However, on teacher reports of inattention on the TRF, children with DS and comorbid ADHD were reported to have the highest rated mean scores, which were significantly worse than both TD children with ADHD and children with DS and no comorbid ADHD. This pattern of findings suggests that teacher are identifying concerns for inattention in the school environment for children with DS and comorbid ADHD, beyond the concerns of their peers of the same age and developmental level. While not statistically significant, a similar pattern was identified on parent reports. Activities completed at school may provide teachers with more opportunity to observe challenges with inattention in children with DS than do activities typical of the home environment. These findings suggest that challenges with inattention are observed at school for children with DS and ADHD, with symptoms seen as worse than their TD peers in that context, whereas challenges with hyperactivity are marginally observed at home and even less evident in the school environment.

A similar pattern of findings across raters was noted for related behavioral concerns, with parents reporting higher concerns for aggression in TD children with ADHD than children with DS with or without ADHD, and higher concerns for externalizing behaviors in TD children with ADHD than children with DS and no comorbid ADHD. However, these group findings were not statistically significant in analyses of teacher reports. These findings suggest that aggression may be more highly associated with ADHD in TD children than in with DS and comorbid ADHD, especially in the home rather than the school setting.

All item-level symptoms of inattention and most item-level symptoms of hyperactivity differentiated TD children with ADHD from children with DS and no comorbid ADHD based on parent-report, consistent with the subscale findings reported above. TD children with ADHD scored higher on only a few parent-report items than children with DS and ADHD, including having challenges with following through on tasks, losing things, and being forgetful. In contrast, teachers reported children with DS and ADHD to have the highest concerns for following through on tasks. On other teacher-reported items, no statistically significant difference was noted, suggesting comparable levels of concern for children with ADHD across TD and DS. Children with DS and ADHD were only noted to have higher symptoms of concern differentiating them from children with DS without comorbid ADHD on parent-reports of being distracted and being “on the go,” and teacher-reports of leaving their seat. Of note, however, five additional parent-rated inattention items and six additional hyperactivity items as well as eight additional teacher-reported items in both the inattention and hyperactivity domains had higher mean scores for children with DS with versus without ADHD, although the differences were not statistically significant. An overall pattern emerges of parents reporting highest item-level concerns for inattention and

hyperactivity for TD children with ADHD, followed by children with DS and ADHD, and then fewest item-level concerns for children with DS and no comorbid ADHD. In contrast, on the few items that differ across groups based on teacher reports, the highest item-level concerns are noted for children with DS and comorbid ADHD. These findings corroborate the pattern described above, with parents of children with DS reporting less concern about symptoms of inattention or hyperactivity than parents of TD children with ADHD, and of teachers reporting comparable concerns for children with DS, with or without ADHD, to TD children with ADHD.

Medication was more commonly prescribed for children with DS and comorbid ADHD than TD children with ADHD or children with DS and no comorbid ADHD. This finding is reassuring that children with DS are being prescribed medication appropriate to their clinical diagnosis. The higher rate of medication in children with DS and ADHD than TD children with ADHD is very likely due to differences in recruitment. Children with DS were recruited from the community, and were presenting with diagnoses previously obtained in clinic. In contrast, TD children were recruited from a specialty ADHD clinic where children were being assessed for ADHD by a psychologist and most would not yet have connected to a prescribing physician for medication. Use of medication was controlled for in all analyses to account for these group differences. It is a potential limitation of the study that not all children were being assessed for ADHD at their initial diagnostic clinic visit, however, recruiting from the community for children with DS allows for greater generalizability by capturing children of older ages that may have already been diagnosed with ADHD. Further, although typically developing children with ADHD cannot be equated to a community-based epidemiological sample, parent- and teacher-reported symptoms in our typically developing sample were comparable to ratings collected from children seen at community practices²⁰.

This study has several additional limitations. Samples with teacher reports were smaller given the challenge of obtaining teacher reports during school summer and winter breaks. In addition, in this inaugural pilot study investigating differences in ADHD symptom ratings for children with DS with and without ADHD group (as we do not know of any prior studies on this topic), the DS with comorbid ADHD group had a relatively small sample size of 15 teacher reports that were returned (due to data collection during school breaks). This is likely why estimated marginal mean scores for parent- and teacher-rated Vanderbilt inattention, hyperactivity and total ADHD symptom scores, as well as estimated marginal mean scores for the vast majority of the individual Vanderbilt items, had higher scores in the DS with ADHD compared to without ADHD group, yet the differences were often not statistically significant. Hence, further studies enrolling a larger group of participants with DS and comorbid ADHD are planned. Furthermore, in the present pilot study, groups were identified from parent-reports of ADHD diagnoses in children with DS. Given the current results supporting parent and teacher reports of inattention and hyperactivity, future studies are warranted to evaluate group differences when groups are established using standardized ADHD criteria. Future studies are encouraged to consider clinical interviews in addition to rating forms to establish clinical diagnoses of ADHD. Future research is also needed to identify any differential patterns in symptoms of ADHD across different comorbid medical conditions common in children with DS, such as obstructive sleep apnea.

Nonetheless, the varying patterns of reporting concerns for inattention and hyperactivity across parents and teachers for TD children and children with DS highlights the critical need for evaluating concerns across environments when diagnosing ADHD. Specifically, parent report items such as distractibility and being “on the go” had particular utility in differentiating ADHD from non-ADHD in children with DS, while teacher reports on a separate set of items—those related to difficulties following through on tasks, avoiding tasks, leaving one’s seat, and excessive talking—appeared to better demarcate these groups. These differences highlight the need for evaluation of symptoms across environments, as is consistent with current recommended clinical practice for diagnosing ADHD in individuals with intellectual disability²¹.

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References

1. Froehlich TE, Lanphear BP, Epstein JN, et al. Prevalence, recognition, and treatment of attention-deficit/hyperactivity disorder in a national sample of US children. *Archives of Pediatrics & Adolescent Medicine*. 2007;161(9):857–864. [PubMed: 17768285]
2. Dekker MC, Koot HM. DSM-IV disorders in children with borderline to moderate intellectual disability. I: Prevalence and impact. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2003;42(8):915–922. [PubMed: 12874493]
3. Edvardson S, Msallam N, Hertz P, et al. Attention Deficit Hyperactivity Disorders Symptomatology Among Individuals With Down Syndrome. *Journal of Policy and Practice in Intellectual Disabilities*. 2014;11(1):58–61.
4. Oxelgren UW, Myrelid Å, Annerén G, et al. Prevalence of autism and attention-deficit-hyperactivity disorder in Down syndrome: a population-based study. *Developmental Medicine and Child Neurology*. 2017;59(3):276–283. [PubMed: 27503703]
5. Ornoy A, Rihtman T, Parush S. Adaptive and behavioral development in children with Down syndrome at school age with special emphasis on attention deficit hyperactivity disorder (ADHD). In: Dey S, ed. *Prenatal Diagnosis and Screening for Down Syndrome*. IntechOpen; 2011:17.
6. Ekstein S, Glick B, Weill M, et al. Down syndrome and Attention-Deficit/Hyperactivity Disorder. *Journal of Child Neurology*. 2011;26:1290–1295. [PubMed: 21628698]
7. Association AP. *Diagnostic and Statistical Manual of Mental Disorders*. In. 5th edition ed. Arlington, VA: American Psychiatric Association; 2013.
8. Jopp DA, Keys CB. Diagnostic overshadowing reviewed and reconsidered. *American Journal on Mental Retardation*. 2001;106(5):416–433. [PubMed: 11531461]
9. Reiss S, Szyszko J. Diagnostic overshadowing and professional experience with mentally retarded persons. *American Journal of Mental Deficiency*. 1983;87:396–402. [PubMed: 6829617]
10. Fletcher R, Barnhill J, Cooper SA. *Diagnostic Manual, Intellectual Disability (DM-ID-2): A textbook of diagnosis of mental disorders in persons with intellectual disability*. Kingston, NY: NADD Press; 2016.
11. Lee P, Friedlander R. Attention Deficit and Disruptive Behavior Disorders. In: Flecher R, Loscher E, Stavrakaki D, First M, eds. *Diagnostic Manual - Intellectual Disability: A textbook of Diagnosis of Mental Disorders in Persons with Intellectual Disability*. New York City, NY: National Association of Developmental Disabilities; 2007.

12. Wolraich ML, Bard DE, Neas B, et al. The psychometric properties of the Vanderbilt attention-deficit hyperactivity disorder diagnostic teacher rating scale in a community population. *Journal of Developmental and Behavioral Pediatrics*. 2013;34(2):83–93. [PubMed: 23363973]
13. Bard DE, Wolraich ML, Neas B, et al. The psychometric properties of the Vanderbilt attention-deficit hyperactivity disorder diagnostic parent rating scale in a community population. *Journal of Developmental and Behavioral Pediatrics*. 2013;34(2):72–82. [PubMed: 23363972]
14. Wolraich ML, Lambert W, Doffing MA, et al. Psychometric properties of the Vanderbilt ADHD diagnostic parent rating scale in a referred population. *Journal of Pediatric Psychology*. 2003;28(8):559–568. [PubMed: 14602846]
15. Esbensen AJ, Hooper SR, Fidler D, et al. Outcome measures for clinical trials in Down syndrome. *American Journal on Intellectual and Developmental Disabilities*. 2017;122(3):247–281. [PubMed: 28452584]
16. NICHD. Outcome measures for clinical trials in individuals with Down syndrome. 2015; https://www.nichd.nih.gov/about/meetings/2015/Documents/DS_outcomes_meeting_summary.pdf
17. Achenbach TM, Rescorla L. ASEBA School-Age Forms & Profiles. Aseba; 2001.
18. Esbensen AJ, Hoffman EK, Shaffer R, et al. Reliability of parent report measures of behaviour in children with Down syndrome. *Journal of Intellectual Disability Research*. 2018;62(9):785–797. [PubMed: 30022564]
19. Jacola LM, Hickey F, Howe SR, et al. Behavior and adaptive functioning in adolescents with Down syndrome: Specifying targets for intervention. *Journal of Mental Health Research in Intellectual Disabilities*. 2014;7(4):287–305. [PubMed: 28539987]
20. Epstein JN, Langberg JM, Lichtenstein PK, et al. Attention-deficit/hyperactivity disorder outcomes for children treated in community-based pediatric settings. *Archives of Pediatrics & Adolescent Medicine*. 2010;164(2):160–165. [PubMed: 20124145]
21. Fletcher R, Loschen E, Stavrakaki C. *Diagnostic Manual-Intellectual Disability (DM-ID): a textbook of diagnosis of mental disorders in persons with intellectual disability.*: N.A.D.D.; 2007.

Table 1.

Demographic and clinical characteristics of children.

	DS+ADHD (n=22)		DS-ADHD (n=66)		TD+ADHD (n=66)	
	Percent	Percent	Percent	Percent	Percent	Percent
Gender (male)	72.7%		72.7%		72.7%	
Race						
White	86.4%		95.3%		72.3%	
Black	9.1%		4.7%		20.0%	
Asian	0.0%		0.0%		1.5%	
Other	4.5%		0.0%		6.2%	
Medication for ADHD	86.4%		0.0%		16.4%	
	M (SD)		M (SD)		M (SD)	
Age	12.1 (3.4)		11.9 (3.2)		12.1 (3.4)	

Table 2. Comparison between children with and without ADHD and typically developing children with ADHD on parent and teacher measures (Estimated Marginal Means (SE)).

	Parent report			Teacher report			<i>p</i>
	DS+ADHD (n=21)	DS-ADHD (n=60)	TD+ADHD (n=54)	DS+ADHD (n=16)	DS-ADHD (n=39)	TD+ADHD (n=43)	
Inattention	14.0 (1.6) ^b	11.3 (0.8) ^c	19.6 (0.7) ^{bc}	18.4 (2.0)	13.2 (1.0)	15.0 (0.9)	.097
Hyperactivity	10.5 (1.9)	5.9 (0.9) ^c	11.4 (0.8) ^c	11.6 (2.6)	6.2 (1.3)	8.5 (1.1)	.185
Combined	24.5 (2.9)	17.2 (1.4) ^c	31.0 (1.3) ^c	29.9 (3.9)	19.3 (1.9)	23.6 (1.7)	.069
CBCL/TRF	DS+ADHD (n=21)	DS-ADHD (n=59)	TD+ADHD (n=56)	DS+ADHD (n=16)	DS-ADHD (n=38)	TD+ADHD (n=52)	<i>p</i>
Attention Problems	63.6 (2.7) ^b	59.6 (1.3) ^c	71.8 (1.2) ^{bc}	68.1 (2.4) ^{ab}	59.1 (1.3) ^a	60.8 (1.0) ^b	.013
Rule Breaking	52.9 (1.9)	55.3 (0.9)	57.5 (0.8)	60.0 (2.2)	56.2 (1.1)	54.9 (0.9)	.076
Aggression	54.8 (2.9) ^b	57.0 (1.4) ^c	63.4 (1.3) ^{bc}	64.8 (2.9)	60.2 (1.5)	57.8 (1.2)	.058
Externalizing	50.8 (3.3)	52.8 (1.6) ^c	59.4 (1.5) ^c	63.0 (3.0)	59.1 (1.6)	55.3 (1.2)	.015

^a Significant group difference between DS+ADHD and DS-ADHD.

^b Significant group difference between DS+ADHD and TD+ADHD.

^c Significant group difference between DS-ADHD and TD+ADHD.

Table 3.

Comparison between children with and without ADHD and typically developing children with ADHD on items of the VADPRS and VADTRS (Estimated Marginal Means (SE)).

	Parent report			Teacher report			<i>p</i>
	DS+ADHD (n=20)	DS-ADHD (n=59)	TD+ADHD (n=54)	DS+ADHD (n=15)	DS-ADHD (n=36)	TD+ADHD (n=43)	
1. Careless mistake	1.9 (0.3)	1.3 (0.1) ^c	2.4 (0.1) ^c	2.3 (0.3)	1.8 (0.1)	1.8 (0.1)	.230
2. Keeping attention	2.0 (0.2)	1.5 (0.1) ^c	2.5 (0.1) ^c	2.4 (0.3)	1.9 (0.1)	2.1 (0.1)	.186
3. Not listening	1.5 (0.2)	1.1 (0.1) ^c	1.9 (0.1) ^c	1.9 (0.3)	1.0 (0.2)	1.3 (0.1)	.100
4. Follow through	1.2 (0.2) ^b	1.2 (0.1) ^c	2.2 (0.1) ^{bc}	1.9 (0.3)	1.1 (0.2) ^c	1.6 (0.1) ^c	.028
5. Organize	1.5 (0.3)	1.5 (0.1) ^c	2.1 (0.1) ^c	2.4 (0.3)	1.7 (0.2)	1.8 (0.1)	.219
6. Avoids tasks	1.7 (0.3)	1.7 (0.1) ^c	2.2 (0.1) ^c	2.4 (0.4) ^b	1.7 (0.2)	1.4 (0.2) ^b	.022
7. Loses things	1.0 (0.3) ^b	0.8 (0.1) ^c	1.8 (0.1) ^{bc}	1.2 (0.3)	1.1 (0.2)	1.3 (0.1)	.710
8. Distracted	2.2 (0.2) ^d	1.3 (0.1) ^{ac}	2.4 (0.1) ^c	2.6 (0.3)	1.8 (0.2)	2.2 (0.1)	.109
9. Forgetful	1.2 (0.3) ^b	0.9 (0.1) ^c	2.0 (0.1) ^{bc}	1.4 (0.4)	1.2 (0.2)	1.6 (0.2)	.161
10. Fidgets	1.5 (0.3)	1.0 (0.1) ^c	1.7 (0.1) ^c	1.8 (0.4)	1.3 (0.2)	1.3 (0.2)	.417
11. Leaves seat	1.4 (0.3)	0.8 (0.1) ^c	1.3 (0.1) ^c	1.8 (0.4) ^a	0.6 (0.2) ^a	1.0 (0.2)	.039
12. Runs/climbs	0.8 (0.3)	0.5 (0.1)	0.7 (0.1)	0.9 (0.3)	0.4 (0.1)	0.4 (0.1)	.266
13. Playing quietly	0.9 (0.3)	0.5 (0.1)	0.8 (0.1)	0.9 (0.4)	0.6 (0.2)	0.6 (0.2)	.805
14. On the go	1.4 (0.3) ^d	0.4 (0.1) ^{ac}	1.0 (0.1) ^c	0.9 (0.4)	0.6 (0.2)	1.0 (0.2)	.357
15. Talks too much	1.3 (0.3)	0.5 (0.1) ^c	1.5 (0.1) ^c	1.2 (0.4)	0.6 (0.2) ^c	1.2 (0.2) ^c	.036
16. Blurts	0.8 (0.3)	0.3 (0.1) ^c	1.4 (0.1) ^c	1.1 (0.4)	0.5 (0.2)	1.0 (0.2)	.098
17. Waiting	1.2 (0.3)	0.8 (0.1) ^c	1.4 (0.1) ^c	1.6 (0.4)	0.6 (0.2)	1.1 (0.2)	.056
18. Interrupts	1.2 (0.3)	1.0 (0.1) ^c	1.7 (0.1) ^c	1.3 (0.4)	0.7 (0.2)	1.0 (0.2)	.387

^aSignificant group difference between DS+ADHD and DS-ADHD.

^bSignificant group difference between DS+ADHD and TD+ADHD.

^cSignificant group difference between DS-ADHD and TD+ADHD.