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Sex Differences in ADHD Symptom Severity

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Abstract

Background—Males show higher rates of attention deficit hyperactivity disorder (ADHD) than do females. Potential explanations include genuine etiological differences or artifact.

Methods—2,332 twin and sibling youth participated in behavioral and cognitive testing. Partially competing models of symptom severity distribution differences, the mean difference and variance difference models, were tested within a randomly selected subsample. The Delta method was used to test for mediation of sex differences in ADHD symptom severity by processing speed, inhibition and working memory.

Results—The combined mean difference and variance difference models fully explained the sex difference in ADHD symptom severity. Cognitive endophenotypes mediated 14% of the sex difference effect.

Conclusions—The sex difference in ADHD symptom severity is valid and may be due to differing genetic and cognitive liabilities between the sexes.

Sex differences in the rate of Attention Deficit Hyperactivity Disorder (ADHD) diagnoses are well documented in the literature. ADHD affects approximately 5–7 percent of the school age population, with a male to female ratio of about 3:1 in community-based samples of youth (Willcutt, 2012). There is disagreement on whether males likewise show more severe inattentive and comorbid neuropsychological symptoms among diagnosed individuals (Elkins, Malone, Keyes, Iacono, & McGue, 2011; Gaub & Carlson, 1997; Gershon, 2002; Kan et al., 2012). For example, in a population based, longitudinal study, affected females had larger effect sizes for behavioral and cognitive functioning deficits, but this could be explained by the better performance of unaffected females compared to unaffected males (Arnett, MacDonald, & Pennington, 2013). Thus, at this point it is unclear whether the behavioral and etiological features of ADHD are the same in both sexes.

The sex discrepancy in ADHD is of interest because it could provide clues to the etiology of the disorder. Additionally, there is little research on females with ADHD (Gaub & Carlson, 1997), which limits our understanding of how they develop and cope with associated symptoms. The present study tests competing explanations for the sex difference in ADHD symptom severity, using a community-based twin sample that is enriched for ADHD symptoms.

Theories on the ADHD Sex Difference

Hypotheses explaining the ADHD sex difference are presented as ovals in the flow chart in Figure 1. The initial question, Is the difference valid (i.e. due to genuine etiologic differences)?, distinguishes two broad categories of hypotheses. If invalid, the three potential explanations include selection bias, lack of measurement invariance across sexes, and missing symptoms. Selection bias has been observed in clinically referred samples (Gershon, 2002). However, our own sample, although overselected for participants with ADHD symptoms, was recruited from community rather than clinical settings. “Case” families were identified based on parent and/or teacher symptom ratings, rather than previous clinical diagnoses, minimizing bias that could result from overparticipation by families with higher rates of ADHD. Further, the results of many other community samples (Graetz, Sawyer, Hazell, Arney, & Baghurst, 2001; Willcutt, 2012; Willcutt, Pennington, Chhabildas, Friedman, & Alexander, 1999) indicate that the gender difference is not due to bias. Thus, selection bias is not considered as a possible explanation in the current study.

Lack of measurement invariance would mean that ADHD rating scales are not psychometrically equivalent for females and males, such that the measure differs in internal or external validity by sex. Over-referral of males for clinical services in the past could have biased the selection of symptoms that define the diagnostic construct, a possibility that has been supported for conduct disorder, in which relational aggression is more common in females (Zahn-Waxler, Crick, Shirtcliff, & Woods, 2006). In other words, the same underlying liability can be expressed differently as a function of sex. Studies of familial patterns have shown conflicting results regarding rates of psychiatric disorder in relatives of male versus ADHD probands (e.g. Faraone, Biederman, Keenan & Tsuang, 1991; Stawicki & Nigg, 2003). However, measurement invariance for ADHD symptoms across sexes has been established in several community and clinical samples (Collett, Crowley, Gimpel, & Greenson, 2000; Conners, Sitarenios, Parker, & Epstein, 1998; Hudziak et al., 1998; Martel, von Eye, & Nigg, 2010; Reid et al., 2000), suggesting that this is not a valid explanation. We will examine internal and external validities across sex in the current sample to further rule out this hypothesis.

A third possibility is the “missing symptoms” hypothesis. A group of symptoms that was not included in either the DSM-IV or DSM-5 criteria, the Sluggish-Cognitive Tempo (SCT) cluster, presents an alternative, theoretically plausible candidate for ADHD symptoms that are more commonly expressed by females. These symptoms are present more frequently in children with the predominantly inattentive subtype of DSM-IV ADHD, but maintained independence in factor analysis of a community sample (Hartman, Willcutt, Rhee, & Pennington, 2004). While previous research did not find a difference in SCT levels between

ADHD males and females in another community sample (Carlson & Mann, 2002), no study that we know of has examined the severity of these symptoms among females who do not already meet criteria for ADHD. The present study will test whether inclusion of these symptoms in the ADHD profile eliminates the sex difference.

Within the second broad category of hypotheses, which requires the sex difference in ADHD prevalence to be valid (i.e. not an artifact of selection or measurement), two possible explanations are proposed in Figure 1: the Mean Difference Model (MDM), and the Variance Difference Model (VDM). The MDM proposes that the female liability distribution is shifted in the less-affected direction relative to that of males, similar to a multiple threshold model originally described by Carter (1972). Given equivalent variances across sexes and an absolute cutoff for the disorder, fewer females will fall into the affected tail of the overall distribution (Figure 2). Hence, there will be more affected males.

The other valid explanation that we propose is the VDM, which was tested in reading disorder by Hawke, Olson, Willcutt, Wadsworth & DeFries (2009). These authors found that more variance in males' reading performance accounted for the higher number of males who met criteria for the disorder, despite equivalent mean performance between sexes (see Figure 2). Given the strong comorbidity between reading disorder and ADHD (Pennington, 2002), it is logical that the same explanation could apply to the sex difference in ADHD prevalence. Since the VDM predicts a two-tailed variance difference, we would also expect to see a higher male to female ratio at the non-symptomatic end of the distribution when means are centered.

The MDM and VDM are not mutually exclusive. With variance controlled in the MDM analyses and means controlled in the VDM analyses, there is a possibility that both models explain the sex difference in ADHD to some extent.

Mediation by Cognitive Endophenotypes

We propose that the MDM and VDM apply not only to the symptom distributions, but also to intermediate pathogenetic factors that lie between the etiology and behavior, such as endophenotypes. Cognitive endophenotypes for ADHD are heritable, cognitive risk factors that explain some variance in the disorder and are theoretically more closely tied to the underlying genotype than are the behavioral symptoms of ADHD (Bidwell, Willcutt, DeFries, & Pennington, 2007; Gottesman & Gould, 2003). Youth with ADHD are impaired in a variety of cognitive domains, including IQ, executive functions, and processing speed (For reviews, see Frazier, Demaree, & Youngstrom, 2004; Kofler et al., 2013; Oosterlaan, Logan, & Sergeant, 1998; Pennington, 2002). Although they cannot account for all of the variance in ADHD, cognitive endophenotypes are nonetheless good candidates for explaining individual characteristics of the disorder, including the sex difference.

If we find support for the MDM or VDM at the symptom level, then we also hypothesize that valid cognitive endophenotypes will demonstrate a pattern of male to female ratios that corresponds to the MDM or VDM. Cognitive endophenotypes that display this expected pattern of sex differences will be tested as mediators of the association between sex and ADHD severity.

Method

Participants

Participants were drawn from the Colorado Learning Disabilities Research Center (CLDRC) twin project, which studies the etiology of learning disorders, including ADHD (DeFries et al., 1997). The CLDRC recruits from 27 school districts within a 150-mile radius of the Denver/Boulder area. Case families, in which at least one twin was identified as having a positive history of attention and/or reading problems, were recruited at a rate of about 2:1 relative to control families, in which neither twin was symptomatic. Positive history of ADHD symptoms was defined as at least six attention and/or hyperactivity/impulsivity symptoms indicated by the combined ratings of parents and teachers on a DSM-IV ADHD checklist. Exclusion criteria were pervasive developmental disorder, closed-head injury, full scale IQ less than 70, and rare major gene disorders. Participants recruited prior to the year 1996 were not administered the DSM-IV ADHD inventories and thus excluded from the present analyses. An additional 238 participants tested after 1996 were missing both parent and teacher ADHD ratings. Thus, the final sample in this study consisted of 2,332 twins and siblings, of which 1,579 (67.7%) were recruited as part of a case family.

Participant demographics are described in Appendix A, Table A1. The age of participants ranged from 8 to 19 years old. Average full scale IQ was significantly higher than that of the normative sample ($t[2331]=27.452$, $p<.001$), but still within the Average range. As expected, the proportion of participants with behavioral ratings consistent with ADHD (24%) or reading problems (31%) was higher than the current U.S. prevalence (ADHD = 6–7%, RD = 7–10%; Willcutt, 2012; Peterson & Pennington, 2012). Participants meeting research criteria for ADHD did not differ from controls on age (ADHD M=11.46, SD=2.54; Control M=11.68, SD=2.65); however, consistent with previous literature, ADHD participants did have significantly lower IQ scores than controls (M(SD)=103.31(11.90) versus M(SD)=108.68(13.03), respectively). The disorder classifications in this study are likely over-inclusive relative to clinical standards, since we depended solely on symptom criteria and did not consider degree of impairment, consistency across situations, or age of onset.

Procedures

Cognitive testing took place during two six-hour days of testing typically scheduled within one month of each other. Parents and youth who were 18 years or older provided consent prior to testing, and minor youth provided written assent. Procedures were in compliance with the institutional review boards at the University of Denver and University of Colorado, Boulder. Neuropsychological testing was administered by trained examiners with at least a bachelor's degree in psychology and prior experience working with children. Examiners were blind to participants' case or control designation. Behavioral questionnaires were mailed to teachers and received within a year of testing.

Measures

ADHD—Parents and teachers completed the Disruptive Behavior Rating Scale (DBRS), a DSM-IV ADHD checklist. Items were rated on a four-point Likert scale ranging from “0 =

never or rarely" to "3 = very often." Parent- and teacher-ratings were averaged to form inattentive, hyperactive/impulsive, and total ADHD severity scores. When teacher scores were not available, parent ratings were used (9.1%), and vice versa (1.8%). The "and/or" rule was applied to identify participants who met diagnostic criteria for ADHD: symptoms rated as "often" or "very often" by the teacher and/or the parent were considered positive. Participants with at least six positive symptoms in either the inattentive or hyperactive/impulsive subscales, or both, were classified as meeting research criteria for ADHD.

Sluggish Cognitive Tempo—Following previous research (Hartman et al., 2004), five items were selected for inclusion in the SCT symptom cluster: sluggish/slow to respond, seems to be "in a fog," drowsy or sleepy, easily confused and *daydreams/stares into space*. Items were rated on the same scale as the DBRS and administered to parents and teachers as part of the same questionnaire packets.Parent- and teacher-ratings were again averaged, except when only one responder was available.

Cognitive Endophenotypes—Candidate endophenotypes were selected for strong, previously established associations with ADHD. Additionally, given the high comorbidity between ADHD and RD, and the overselection of participants with reading problems in the current sample, phonemic awareness (PA), the primary endophenotype for RD, was also included for consideration. Factor scores were calculated for each of the cognitive endophenotype constructs using theoretically-driven neuropsychological tests. Individual measures comprising each factor have been described in previous research (Bidwell et al., 2007; McGrath et al., 2011; Pennington et al., 2012; Willcutt, Pennington, Olson, Chhabildas, & Hulslander, 2005) and are detailed in Appendix A. Each composite for a given construct comprised several indicators and the model fits were in the acceptable range (see Appendix A, Table A2).

Preliminary Analyses

Cognitive and behavioral measures were winsorized to within three standard deviations of the mean. These corrections affected fewer than 3.5% of participants on each variable. The Gordon Diagnostic System (Gordon, 1983) Vigilance Commission Errors variable was further log transformed to reduce skew and kurtosis to acceptable values (.443 and −.308, respectively). All other variables were within acceptable skew and kurtosis ranges (absolute value < 2). Next, cognitive variables (except for Wechsler tests) were standardized within the sample by regressing raw scores on the participant's age and squared age. Wechsler test scale scores were transformed into z scores using the sample means and standard deviations. Mplus 6.0 was used to compute two-level confirmatory factor analysis, from which factor scores were computed for the cognitive composites. Family was modeled at level two in order to control for non-independence of sibling and twin data. When two subtests of the same test were given (e.g. Trails A and B), these scores were permitted to covary in the model. Additionally, the Wechsler Object Assembly and Block Design subtests were permitted to covary in the nonverbal reasoning factor as this significantly improved the model fit. All model fits were acceptable, with at least two of the following fit statistics: non-significant chi-square, CFI>.90, RMSEA<.08 (see Appendix A, Table A2).

Results

Sex Differences in ADHD

To confirm that ADHD was more prevalent in males in our sample, we selected one random participant from each family ("subsample"; n=1,074) for group comparison analyses. The subsample was comparable to the full sample on all demographic variables (see Appendix A, Table A1). As expected, males had more severe scores than females on the inattention (male M(SD) = 8.44(6.40); female M(SD) = 5.15(5.31); t(1072)=9.21, p<.001), hyperactivity/ impulsivity (male M(SD) = 5.24(5.07); female M(SD) = 3.19(3.92); t(1072)=7.44, p<.001) and total ADHD (male M(SD) = 13.72(10.40); female M(SD) = 8.34(8.49); t(1072)=9.32, p<.001) scores than females. Likewise, more males met research criteria for ADHD (χ^2[1]=64.09, p<.001), with a male to female ratio similar to that in the general population, at 2.43:1. The results were the same when parent- and teacher-ratings were tested separately. The subsequent analyses tested explanations of this sex difference in ADHD symptoms.

Measurement Invariance Hypothesis

We examined internal and external reliabilities across sexes to test the theory that lack of measurement invariance explained the sex difference in ADHD symptoms. Lower-bound internal reliability was compared across sexes by examining monozygotic twin correlations for ADHD severity scores (Byrne et al., 2007). As expected, twin correlations were comparable across both males and females for total ADHD (male r=.73, p<.001; female r=.77, p<.001), inattention (male r=.69, p<.001; female r=.69, p<.001) and hyperactivity/ impulsivity (male r=.72, p<.001, female r=.78, p<.001) subscales. Fisher r to z transformations confirmed that the correlation coefficients were not statistically different for each comparison. Using the subsample, gender invariance in external validity was examined next by correlating total ADHD severity scores with each of the cognitive endophenotypes, within sex. Each of the correlations was comparable across males and females. Z statistics were not statistically significant, with absolute values ranging from .09 to 1.01. These results, in conjunction with previously published literature, support measurement invariance of the 18 DSM-IV ADHD symptom criteria across sexes.

Missing Symptoms Hypothesis

To test the hypothesis that females' lower ADHD symptom severity could be due to a difference in symptom expression, severity of SCT items was compared across sexes within the subsample. Contrary to the missing symptoms hypothesis, males' SCT severity (*M*=1.78) was higher than females' (*M*=1.23; t[765]=4.00, p<.001), although the SCT sex effect was smaller than that of standard ADHD symptoms (male *M*=13.72; female *M*=8.34; t[1004]=9.26, p<.001). Males also showed worse severity when SCT and standard ADHD symptoms were combined (male *M*=15.01; female *M*=9.47; t[783]=7.63, p<.001). Thus, we concluded that the sex difference in ADHD symptoms is valid and proceeded to test the two partially competing models for this valid sex difference.

Mean Difference Model

The MDM specifies that males will show more severe symptoms than will females. To test this initial hypothesis, we transformed the ADHD severity scores so that males and females in the subsample would have equivalent variances (i.e. standard deviation = 1) by dividing scores by their respective group standard deviations. As expected, t-tests revealed that males had significantly higher total ADHD ($t(1072)=5.51$, $p<.001$), inattention ($t[1072]=5.72$, $p<.001$) and hyperactivity/impulsivity ($t[1072]=3.60$, $p<.001$) scores when variances were equivalent across groups. Further, with variances equated, males were more prevalent in the affected 10th percentile ($\chi^2(1)=13.74$, $p<.001$) and females were more prevalent in the favorable (i.e. non-symptomatic) 10th percentile ($\chi^2(1)=22.72$, $p<.001$) of the distribution. The results were consistent when the 25th percentiles were applied as cutoffs. The male to female ratios in the affected 10th and 25th percentiles (1.85:1 and 1.64:1, respectively) were about half the sex ratio of participants meeting research criteria for ADHD.

Variance Difference Model

To test the VDM hypothesis that a sex difference in symptom variance explains males' worse ADHD severity, Levene's test for variance differences was run on the subsample. We first subtracted male and female mean severities from the respective individual scores so that the groups would have equivalent means, i.e. zero. Males had significantly more variance in inattention ($F[1, 1072]=30.29$, $p<.001$), hyperactivity/impulsivity ($F[1, 1072]=45.36$, $p<.001$), and total ADHD ($F[1, 1072]=36.62$, $p<.001$) severities. Consistent with the VDM, more males than females fell into both the affected ($\chi^2(1) = 11.84$, $p=.001$) and favorable 10th percentiles ($\chi^2(1) = 126.14$, $p<.001$) when means for both groups were equated. Results were replicated using the 25th percentiles as cutoffs. Again, the male to female ratios in the affected 10th and 25th percentiles were approximately half that of those who met research criteria, at 1.78:1 and 1.22:1, respectively.

Combined MDM and VDM

Next, we tested both the MDM and VDM simultaneously within the Subsample, with the hypothesis that the combined models would fully explain the full sex discrepancy in ADHD symptom severity. We standardized the total ADHD severity scores within sex, such that male and female groups each had a mean of zero and standard deviation of one. The number of males and females who fell into the affected extreme (i.e. z score > 1) was not significantly different ($\chi^2(1)=1.82$, $p=.177$) with a male:female ratio of 0.91:1. At the favorable end (z score < −1), a significant difference remained ($\chi^2(1)=104.27$, $p<.001$), with 90 males and zero females in that tail.

Cognitive Endophenotype Hypothesis

We next tested whether the results of the MDM and VDM were replicated using cognitive endophenotypes, and whether such endophenotypes mediated the sex difference in symptoms. Within the subsample, candidate endophenotypes were tested for 1) a negative correlation with total ADHD severity, 2) a sex main effect, wherein males performed more poorly than females once variances were equated, and 3) a variance difference once means were equated. Endophenotypes that fit the first two criteria, consistent with the MDM,

included inhibition (INH) and processing speed (PS). Endophenotypes that fit the first and third criteria, consistent with the VDM, were PS and working memory (WM). See Appendix A, Table A3.

Two-level mediation analyses were computed using the entire sample, with family at level two to control for non-independence of sibling data. Mediation models included sex as the independent variable, ADHD severity as the outcome, and PS, INH and WM as mediating variables. MPlus 6.0 was used to run the Delta method of testing for mediation (MacKinnon, 2008). The results supported partial mediation of total ADHD severity, with a standardized total indirect effect (i.e. via PS, INH and WM) of .04 ($p<.001$), which constituted 14% of the total effect (.29, $p<.001$). PS and INH contributed greater indirect effects than did WM, although all endophenotypes were independently significant (Table 1). Results were similar for inattention and hyperactivity/impulsivity subscales.

Discussion

The MDM and VDM were both supported as explanations for the sex differences in ADHD symptom severity. The MDM specifies that, assuming equivalent variances across sex, males have a shifted distribution relative to females, such that the male mean is closer to the diagnostic threshold. In contrast, the VDM specifies that males have a greater variance than females, so that more males fall into the extreme tails, assuming equivalent means. When both the MDM and VDM assumptions were met, the number of extreme affected males and females was comparable, with a ratio of nearly 1. Each model partially explained, and the combined models fully explained, the sex discrepancy at the affected tail.

Our community based sample was overselected for participants with a history of ADHD symptoms, and we used the “and/or” rule to classify participants as case individuals. This resulted in a higher rate of ADHD symptoms in our sample relative to population estimates. Alternative approaches for recruiting and classifying participants might change our results. However, the sex ratio in our study was comparable to population ratios, suggesting that the sex difference is consistent regardless of the diagnostic algorithm. Nonetheless, the current results should be interpreted specifically as explanations for the sex difference in ADHD symptom severity, rather than the rate of clinical diagnosis.

We attempted to get one step closer to the polygenic liability for ADHD by testing a mediation model using cognitive endophenotypes that demonstrated distribution patterns consistent with either the MDM or the VDM. Our mediation model supported PS, INH and WM as partial mediators of the association between ADHD severity and sex in the overall sample. These neurocognitive mediators accounted for 14% of the overall association, which is moderate, given that ADHD symptoms are estimated to be about 70% genetic in origin (Pennington, 2002). INH, which was consistent only with the MDM, had a greater partial mediation effect than did WM, which was consistent only with the VDM. PS had the largest effect and was consistent with both models. These results strengthen the results supporting both models, but also suggest that mean differences in underlying cognitive processes may contribute to the sex difference in ADHD symptoms more than do variance differences.

Because cognitive endophenotypes are genetically correlated with ADHD symptoms, (Willcutt et al., 2010), these results suggest at least a partial genetic etiology for the differential liability of ADHD in males and females that is due to sex differences in neuropsychological processes. This is consistent with the findings from our previous research that reading disability and ADHD share cognitive deficits that are primarily due to genetic influences (Willcutt et al., 2010).

Although we did not have power to test it in this sample, we expect that both the MDM and VDM correspond to patterns of sibling differences. At the affected end of the distribution, we would expect that females' siblings would have more severe symptoms than affected males' siblings, because in both models affected females are more distant from the population mean in terms of standard deviations. Consistent with this, tests of the polygenic multiple threshold model for total ADHD symptoms (Rhee, Waldman, Hay, & Levy, 1999) and individual ADHD symptom dimensions (Rhee & Waldman, 2004) have both found that siblings of females with ADHD had more symptoms than did siblings of ADHD males. In contrast, the MDM and VDM sibling predictions diverge at the favorable end of the distribution. The MDM would predict that siblings of favorable males would be less symptomatic, due to high loading for favorable polygenes, while the VDM would predict the opposite, because favorable females are less common than favorable males in the VDM.

The distinction at the favorable end of the distribution is difficult to test in this study in part because we used the DBRS, which only measures ADHD symptoms at the dysfunctional end of the distribution. Measurement of favorable attention and impulse regulation is curtailed (Arnett et al., 2013). This is a possible explanation for the fact that a sex difference remained in the favorable tail of the distribution even when both the MDM and VDM assumptions were met. Thus, a measure that captures variance at both ends of the ADHD symptom distribution, such as the SWAN (Swanson et al., 2006) rating scale, would be useful for testing sibling predictions and replicating our results.

Conclusion

Higher ADHD symptom severity for males relative to females can be explained by the MDM and VDM. The sex difference in ADHD symptom severity is partially moderated by PS, INH and WM, three commonly identified cognitive endophenotypes for ADHD that themselves exhibit a corresponding sex difference (females outperform males). Since these endophenotypes are genetically correlated with ADHD, the sex difference in ADHD may be genetically mediated, but our study did not directly test that possibility.

Appendix A

Table A1

Demographics

Variable	Subsample n=1,074	Full Sample n=2,332
Mean Age (SD)	11.63 (2.70)	11.63 (2.63)

Variable	Subsample n=1,074	Full Sample n=2,332
% Female	52%	50%
% Monozygous Twins	31%	32%
% Siblings of Twins	9%	8%
% Primary Caregiver Caucasian	87%	88%
Median Years of Mother's Education[a]	14	14
Median Years of Father's Education[b]	12	12
Mean Full Scale IQ (SD)	107.84 (12.72)	107.37 (12.97)
% History of Reading Problems in School	29%	31%
% Meeting Symptom Criteria for ADHD	23%	24%

[a] 14 years=Associate's Degree or Equivalent

[b] 12 years=High School Graduate or Equivalent

Table A2

Individual Measures of Composites and Model Fits of Confirmatory Factor Analyses

Composite	Measures	X^2(df, n)	*P*	CFI	RMSEA
Processing Speed (PS)	Wechsler Symbol Search & Coding B; Colorado Perceptual Speed (DeFries et al., 1997), Identical Pictures (French, Ekstrom, & Price, 1963), Trails A & B (Reitan, 1971)	41.97(8, 2332)	<.001	.990	.043
Working Memory (WM)	Wechsler Digit Span & Arithmetic; Sentence Span (Siegel & Ryan, 1989), & Counting Span (Case, Kurland, & Goldberg, 1982)	7.26(2, 2332)	.027	.997	.034
Phoneme Awareness (PA)	Phoneme Deletion 1 and 2 (Olson, Forsberg, Wise, & Rack, 1994), Weighted Pig Latin (Olson, Wise, Conners, Rack, & Fulker, 1989), Lindamood Auditory Conceptualization Test (Lindamood & Lindamood, 1971)	1.30(1, 2145)	.254	1.000	.012
Verbal Reasoning (VR)	Wechsler Information, Similarities, Vocabulary, & Comprehension	28.38(2, 2332)	<.001	.993	.075
Nonverbal Reasoning (NVR)	Wechsler Block Design, Object Assembly, Picture Completion, & Picture Arrangement	.28(1, 2332)	.594	1.000	.000
Inhibition (INH)	GDS Vigilance Commission Errors (Gordon, 1983); Stop Signal Task (Logan, 1994); Stroop Color Word Interference (Golden, 1978)	0.00(0, 2146)	<.001	1.000	.000
Standard Deviation of Reaction Time (SDRT)	Stop Signal Task (Logan, 1994)	n/a	n/a	n/a	n/a
Risk	Cambridge Gambling Task (CGT; Rogers et al., 1999) Overall Proportion Net & Risk Taking	0.00(0, 244)	<.001	1.000	.000
Monitor	CGT Delay Aversion, Quality of Decision Making, & Risk Adjustment	0.00(0, 244)	<.001	1.000	.000

Note: The Wechsler test version varied depending on testing date and participant age. Sixty-one percent of participants completed subtests from the Wechsler Intelligence Scale for Children, Revised (WISC-R; Wechsler, 1974); 36% the Wechsler Intelligence Scale for Children, Third Edition (WISC-III; Wechsler, 1991); 1% the Wechsler Adult Intelligence Scale, Revised (WAIS-R; Wechsler, 1981); and 2% the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III;

Wechsler, 1997). The symbol search subtest always originated from the WISC-III battery and was administered to 70% of participants. The Stop Signal Task (Logan, 1994) standard deviation of reaction time (SDRT) was a single measure and thus not transformed into a factor score.

Table A3

Associations Between Cognitive Endophenotypes, ADHD and Sex

Cognitive Endophenotype	Correlation with Total ADHD	Mean Sex Difference	Variance Difference
PS	***r*=−.32, *p*<.001**	***t*(1072) = 5.50, *p*<.001†, *d*=.27**	***F*(1, 930) = 6.79, *p*=.009**
WM	***r*=−.22, *p*<.001**	t(1050) = −3.03, *p*=.003†, *d*=−.14	***F*(1, 1072) = 5.57, *p*=.018**
PA	***r*=−.22, *p*<.001**	t(976) = −0.51, *p*=.611, *d*=−.03	F(1, 976) = 1.60, *p*=.206
VR	***r*=−.16, *p*<.001**	t(1072) = −3.90, *p*<.001, *d*=−.20	F(1, 1072) = 3.23, *p*=.072
NVR	***r*=−.06, *p*=.063**	t(1072) = −3.97, *p*<.001, *d*=−.16	F(1, 1072) = .06, *p*=.812
INH	***r*=−.34, *p*<.001**	***t*(977) = 3.26, *p*=.001, *d*=−.12**	F(1, 977) = 2.80, *p*=.095
SDRT	***r*=−.28, *p*<.001**	t(930) = −2.36,*p*=.018, *d*=.16	F(1, 930) = 1.60, *p*=.207
Risk	***r*=−.16, *p*=.090**	t(111) = −2.50, *p*=.014, *d*=−.46	F(1, 111) = 1.21, *p*=.275
Monitor	***r*=−.10, *p*=.292**	***t*(111) = 3115, *p*=.002, *d*=39**	F(1, 111) = .72, *p*=.400

Note: P-values are two-tailed.

† T-test statistic reported using unequal variances assumed. Bold italics indicate significant results in the expected direction.

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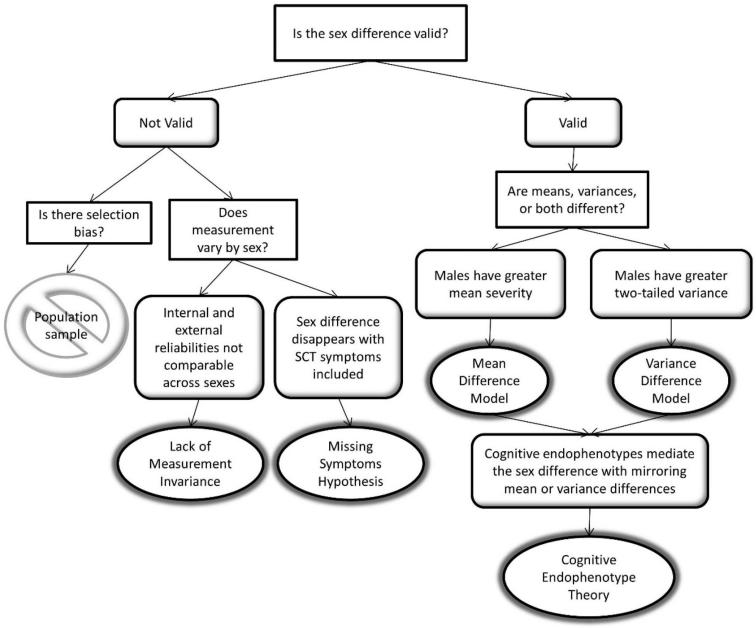

Figure 1.

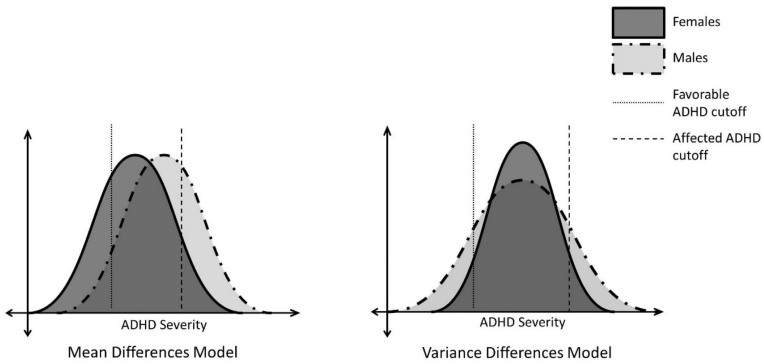

Figure 2.

Table 1

Standardized Effects in Mediation Models

	Total ADHD	Inattention	Hyperactivity/Impulsivity
Processing Speed	.03***	04***	.01**
Inhibition	.02***	.02***	.02***
Working Memory	.01*	.01*	.00
Total Indirect	04***	.05***	.03**
Total Indirect + Direct	.29***	.29***	.23***

* $p<05$,

** $p<.01$,

*** $p<.001$