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The Impact of Attention-Deficit/Hyperactivity Disorder on Preadolescent Adjustment May Be Greater for Girls than for Boys

Irene J. Elkins, Ph.D., Steve Malone, Ph.D., Margaret Keyes, Ph.D., William G. Iacono, Ph.D., and Matt McGue, Ph.D.

Department of Psychology, University of Minnesota, Twin Cities Campus

Abstract

Whether gender differences exist in the impairment associated with ADHD is still largely unknown, because most samples have few affected girls or include only one sex. The current study evaluated whether ADHD affects adjustment differently for girls than boys in a population-based cohort of 11-year-olds (520 females; 478 males). Those with a DSM-IV diagnosis of ADHD (predominantly inattentive, hyperactive-impulsive, or combined) were compared to those without ADHD on teacher, parent, and child reports of academics, peer relationships, self-concept, clinical symptoms, and treatment. Although boys and girls with ADHD experienced difficulties in all areas, girls with ADHD, especially the inattentive subtype, were more negatively affected in academics and peer relationships. Inattentive girls were less popular and more likely to be bullied than girls without ADHD, whereas inattentive boys were not. The social isolation experienced by many girls with ADHD deserves greater attention.

Keywords

ADHD; Attention deficit disorder; Gender; Sex differences

Attention-deficit/hyperactivity disorder (ADHD), one of the most common childhood behavioral disorders worldwide (Faraone, Sergeant, Gillberg, & Biederman, 2006), has male-female ratios ranging from 2:1 to 9:1 (American Psychiatric Association, 2000). While the gender difference in ADHD prevalence may provide clues to its etiology, until recently, many studies included only males (Rutter, Caspi, & Moffitt, 2003). The DSM-IV field trials established that the inclusion of a “predominantly inattentive” (IN) subtype might identify substantially more girls affected by ADHD (Lahey et al., 1994). Consequently, several cohorts of girls followed longitudinally have identified impairments accompanying ADHD in females, advancing our understanding of the challenges girls with ADHD may face (Fontaine et al., 2008; Hinshaw, Owens, Sami, & Fargeon, 2006; Monuteaux, Faraone, Gross, & Biederman, 2007). However, boys were not included in these studies, which precluded direct comparisons of boys and girls.

Furthermore, most of what we know about ADHD and gender comes from clinically-ascertained samples. In adolescent follow-ups of two primarily clinically-based samples of girls, persistent impairments were found in multiple domains (e.g., peer rejection, academic achievement; Hinshaw et al., 2006) and increased risk for developing other psychopathology

Correspondence: Correspondence concerning this article should be addressed to Irene Elkins, Department of Psychology, University of Minnesota, 75 E. River Rd., Minneapolis, MN 55455; ielkins@umn.edu.

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(e.g., conduct disorder, depression) was evident (Monuteaux et al., 2007). In a rare longitudinal study including both genders, while a minority of boys and girls with ADHD were well-adjusted across multiple domains in adolescence (Lee, Lahey, Owens, & Hinshaw, 2008), an earlier report on the same sample (Lahey et al., 2007) noted the lack of significant gender differences observed could be due to the small number of girls. Finally, while outcome measures are characteristically comprehensive and carefully chosen in these studies, which provide critically important insights into those likely to appear in treatment settings, clinically-ascertained samples are likely to over-represent severely impaired and comorbid cases (Goodman et al., 1997).

Emerging data from community-based samples including both sexes has replicated important findings from clinical studies (e.g., hyperactivity-inattention in childhood predicts negative academic outcomes; Galera et al., 2009), yet due to insufficient numbers of females with clinically significant levels of symptoms, these studies have yet to shed light on whether gender differences may exist. Recently, a diverse, community-based sample with an oversampling of girls found that even subthreshold ADHD might lead to adverse educational and juvenile justice outcomes in adolescence, but the authors expressed concern that insufficient sample sizes may have contributed to the lack of significant interactions detected with gender, race, and poverty (Bussing, Mason, Bell, Porter, & Garvan, 2010).

The current study began as an extension of our previous work, which found a prospective relationship of ADHD (particularly HI) and conduct disorder (CD) with the initiation of substance use by age 14 and the development of substance use disorders by age 18 (Elkins, McGue, & Iacono, 2007). Although no significant gender differences were found, we noted that a larger sample of females with ADHD was needed. Thus, we are now following a new 11-year-old cohort of twins prospectively, selected from a community sample for presence of ADHD and CD, with an over-representation of affected females and a focus on indices of academic, interpersonal, and behavioral adjustment relevant during preadolescence (similar to Lee et al., 2008). For example, peer adjustment, which has received less attention than academic and behavioral problems in the ADHD literature, may be of heightened significance at this age, when adaptive peer relationships are central to competency (Masten & Curtis, 2000) and other psychopathology has yet to develop. It has been suggested that girls with ADHD may have more difficulty in peer relationships than do boys with ADHD (Mikami & Hinshaw, 2003); yet as noted by Mikami (2010), this has yet to be empirically tested. Identifying which areas are more or less problematic for girls might add to the evidence for assertions that more multimodal treatment approaches are needed for girls (Waite, 2010; Young and Amarasinghe, 2010).

The primary question we wished to address was whether different realms of adjustment are impacted by ADHD comparably for preadolescent girls and boys. An early meta-analysis by Gaub and Carlson (1997) noted that with the possible exception of intellectual functioning, girls with ADHD appeared less severely affected than boys, with fewer comorbid externalizing and internalizing behaviors. However, they also stressed the need for large-scale epidemiological studies of gender differences in ADHD to address the confounding effects of referral biases, which may result in more disruptive boys being referred for treatment. Subsequently, a study of non-referred siblings of ADHD probands (Biederman et al., 2005) found no gender differences in comorbidity or other areas of functioning but included only 25 girls with ADHD. By contrast, a “gender paradox” has been described (Eme, 1992), which predicts greater impairment in the sex for which a disorder is less common, as is true for ADHD in girls. Evidence for a gender paradox has been demonstrated for CD, with risk for comorbid conditions (e.g., depression) being higher for girls than for boys with CD (Keenan, Loeber, & Green, 1999). Reconciling these

inconsistent findings and determining whether or not a gender paradox exists for ADHD remains to be done.

Furthermore, we also wished to examine the relative importance of each ADHD subtype (IN, HI, or Combined) for each gender. For example, if there is a gradient of severity for ADHD, the Combined subtype, with the most symptoms, should be relatively the most impaired for both sexes when compared to unaffected individuals. However, because the Combined subtype of ADHD tends to dominate clinical samples, it has been difficult to evaluate outcomes across subtypes, and outcomes for the relatively rare hyperactive-impulsive (HI) subtype remain largely unknown. Community-based samples utilizing multiple reporters of impairment are needed to evaluate whether there are gender differences in the difficulties encountered by girls and boys with ADHD and whether they are subtype-specific (Gershon, 2002; Graetz, Sawyer, & Baghurst, 2005). Recently, a community-based sample of adults with ADHD (Kessler et al, 2010) relied on oversampling those positive on earlier screens to enrich their sample, ensuring a sufficient number of affected individuals with the diagnosis (often problematic in community samples), while circumventing the referral biases inherent in clinical samples. A similar strategy was utilized here.

Method

PARTICIPANTS

The Enrichment Study (**ES**) extends the Minnesota Twin Family Study (**MTFS**), a longitudinal investigation of the adolescent origins of substance abuse. This cohort was recruited to yield a genetically-informative sample of preadolescent children at high risk for substance abuse due to having a childhood disruptive disorder. The sample was ascertained from Minnesota birth records of 2717 like-sex twin pairs born between 1988 and 1994; 82% were successfully located and were recruited to participate when the twins were age 11. Prior to recruitment, families were randomly assigned to either a screened or an unscreened subsample. This allowed us to achieve our dual goals of 1) maximizing the number of cases included in the full sample, while 2) preserving a representative subsample to facilitate comparison with previously unselected MTFS twins (see Keyes, et al., 2009, for a detailed overview of the ES study approach and sample characteristics).

Seventy-six percent of the families were allocated to the screened subsample and were interviewed by phone for parent-reported DSM-IV (and III-R) symptoms of ADHD and CD, as well as indications of academic disengagement. Screened families were invited to participate further by visiting our labs if at least one twin exceeded a pre-determined threshold, set to ensure that the sample would be enriched for having a childhood disruptive disorder. If neither twin exceeded the threshold, the family was deemed ineligible and not recruited for a visit. The screening effort was successful, as 52% of screened males and 41% of screened females met criteria for a diagnosis of ADHD, CD, or oppositional defiant disorder (ODD) at the visit (Keyes et al., 2009). Furthermore, by screening out unaffected cases (which are predominantly female), a greater proportion of affected females was obtained (see Appendix A for items used in the screening interview and information on the threshold). The remaining families were recruited from the 24% of the sample that was unscreened, other than for a disability that precluded completing the assessment.

A total of 663 twin pairs were eligible and were invited to participate in the ES study (336 in the unscreened sample and 327 in the screened sample). Seventy-five percent of the eligible families completed an intake visit, and participation rates did not vary by screening status. Eligible non-participating families included refusals (18%) as well as those unable to schedule before the children became too old for their birth cohort (7%). Marital status, income, father's education, and mother's occupational status did not differ significantly

between participating and non-participating families. Years of education were higher among participating mothers ($M=14.3$, $SD=1.9$) than nonparticipating mothers ($M=13.8$, $SD=2.0$; $p<.01$), and occupational status indicators (codes ranged from 1 to 7, with 7 reflecting the highest status) were higher among participating fathers ($M=4.7$, $SD=1.7$) than nonparticipating fathers ($M=4.2$, $SD=1.8$; $p<.01$). While this indicates some positive selection, the effect appears slight. Standardized effect-size estimates equal .26 and .29 for mother's education and father's occupational status, respectively. Thus, the sample is generally representative of the population from which it was drawn.

The final sample consisted of 998 individuals (520 females; 478 males, from 499 pairs), with 48% from the screened sample. The mean age at assessment was 11.9 for both boys ($SD=0.41$) and girls ($SD=0.44$). Ninety-one percent were white, which is representative of children born in Minnesota in the birth years sampled. Although the twin design was not utilized for this report, twins do not differ in rates of psychopathology from single offspring (Kendler, Martin, Heath, & Eaves, 1995), and the prevalence of ADHD in our sample was consistent with expectations based on non-twin samples (see "Diagnostic Procedure" below). The research protocol was approved by the University of Minnesota's IRB. At the visit, after a thorough description of the study, written informed consent was obtained from the parents and written assents from the twins.

DIAGNOSTIC PROCEDURE

Each parent and child was interviewed separately at the visit by a different interviewer, each of whom had a B.A. or M.A. in psychology and went through extensive training. Maternal (or primary caregiver) reports of lifetime symptoms of DSM-IV ADHD, CD, ODD, major depressive disorder, and separation anxiety disorder in each child were obtained with a modified version of the Diagnostic Interview for Children and Adolescents – Revised (DICA-R; Reich, 2000). Child reports of the same disorders were obtained using a parallel child version. A "best-estimate" strategy in which a symptom is considered present if reported by either parent or child was adopted, a procedure that results in greater validity than either report alone at this age (Burt, Krueger, McGue, & Iacono, 2001). Symptom presence was determined by consensus of two individuals with advanced clinical training (supervised by a Ph.D. clinical psychologist), who reviewed examples of each symptom, including severity, frequency, and associated impairment. A set of guidelines and examples was provided for each symptom, to maintain consistency. For example, if a teacher complained about an ADHD behavior or it resulted in lower grades, such information about impairment, along with frequency, was considered in determining whether the behavior was severe enough to be considered a symptom. Similar to Kessler et al. (2010), however, impairment was only required at the level of the diagnosis, rather than for each symptom. Reliability of the consensus diagnoses (kappa) exceeded .73 for all disorders.

Four groups were formed; three corresponding to the DSM-IV ADHD subtypes and a fourth with no diagnosis of ADHD. In DSM-IV, 6 symptoms of a specific subtype (IN or HI) are required for a diagnosis, along with impairment at school and home, and onset prior to age 7. To maximize sensitivity in this population-based sample, ADHD diagnoses were made at two levels: definite = all diagnostic criteria satisfied, and probable = one symptom short of definite. This method, which avoids underreporting of lifetime symptoms in population-based samples, did not inflate our rates of ADHD (i.e., the DSM-IV lifetime prevalence among our unscreened sample was lower than other community-based samples which have also included probable cases, e.g., Smalley et al., 2007). Thus, Combined cases represented those with 5 or more symptoms in both the IN and HI categories, whereas predominantly IN or HI cases had only 2 symptoms of the other subtype, on average. Although the No Diagnosis group was defined based on absence of any ADHD diagnosis, they were not symptom-free (IN symptoms: $M=1.2$, $SD=1.4$; HI symptoms: $M=1.0$, $SD=1.2$).

Consistent with expectations given our screening procedure, 25.4% of the sample (144 boys; 109 girls) were diagnosed with ADHD. Comparable to a nationally representative sample (Froehlich et al., 2007), the IN subtype was most common: 13.2% of boys and 11.3% of girls were predominately IN, 7.3% of boys and 4.8% of girls were predominantly HI, and 10.3% of boys and 5.0% of girls were Combined. A composite measure of socioeconomic status, consisting of the sum of the standardized scores for highest parental occupational status, education in years for mom and dad, and household income, did not differ significantly between those with and without an ADHD diagnosis.

MEASURES OF ADJUSTMENT

Parent and child reports of adjustment were obtained at the family's visit; teacher ratings were obtained by mail. Composite teacher ratings were calculated based on the number of teacher reports available, ranging from one to three. All measures were available for well over 90% of the sample except for teacher ratings, which were available for 85%.

Academics—Teacher reports on behavior in the academic setting were utilized whenever possible. Academic achievement was evaluated through grade-point average (GPA), calculated as the mean of grades in language arts, math, social studies, and science, provided by each teacher, on a standard 0.0 (Fs) to 4.0 (As) scale. In a separate sample, Johnson, McGue, and Iacono (2006) reported that teacher-reported GPA in these core subjects, using our teacher rating form, correlated .89 with overall GPA from school transcripts. Academic motivation (interested in schoolwork, enjoys attending school, turns in assignments on time, is liked by teachers, has a good attitude about school, motivated to earn good grades), was also rated by teachers, with each behavior on a 4-point scale ranging from “never true” to “always true” (internal consistency and interteacher reliabilities of .91 and .77, respectively). In two independent samples, this measure of academic motivation, though moderately correlated with achievement as reflected by school grades (approximately .50), correlated only weakly with IQ (approximately .15; Johnson, McGue, & Iacono, 2007).

Several academic measures were available only from children or parents. Academic aptitude was assessed in each child with an abbreviated Wechsler Intelligence Scale for Children – Revised (WISC-R), consisting of two verbal (Vocabulary and Information) and two performance (Block Design and Picture Arrangement) subscales selected for their high correlation (.90) with (and used to pro-rate) full-scale IQ (Sattler, 1974). An earlier version of the WISC was used to maintain comparability with previously assessed MTFS cohorts. Parent reports of academic problem behaviors (e.g., the degree to which the child did or did not study at home, learn quickly, concentrate in class, turn in homework on time, etc.) were assessed with 6 items rated on a 4-point scale from definitely true to definitely false. Academic expectations were assessed by asking mothers: “How far do you expect (CHILD) to go in school?”, from 1 (not completing high school) to 6 (college plus professional degree).

Relationships—The child's perspective on his/her popularity with peers was assessed with the Popularity scale from the Piers-Harris Self-Concept Scale, a reliable (5-month test-retest $r = .70$ for overall score), 80-item measure of self-confidence, further developed through factor analysis (Hur, McGue, & Iacono, 1998). The Piers-Harris is one of the most widely used self-report measures of self-concept in children, with considerable evidence supporting its validity (Alexopoulos & Foudoulaki, 2002). Because we did not wish to rely solely on self-reported popularity, teachers also rated a single item regarding how popular or well-liked the child is relative to other students. Teachers characterized each child's peers on two 5-item scales: Positive Peers (popular, athletic, smart/good student, entertaining/funny, involved in school activities; $\alpha = .88$) and Deviant Peers (good fighter, dangerous to be with,

rebellious, drug/alcohol using, bad influence; $\alpha = .82$). Teacher ratings of the child's popularity and peers were provided relative to other students (1=lowest 5%; 2= lower 30%; 3=middle 30%; 4=higher 30%; 5=highest 5%), averaged across teachers. Additional psychometric evidence supporting the reliability and validity of the teacher ratings of peer group characteristics is provided by Walden et al. (2004). Finally, victimization by peers was assessed by asking each child: "Have you ever been bullied or picked on a lot by other kids?"

Mental Health, Treatment, and Medication—Our clinical interviews at the visit included parent- and child-reported symptoms of a range of childhood psychiatric disorders, including DSM-IV ADHD, CD, ODD, major depressive disorder, and separation anxiety disorder. Presence of symptoms during the child's lifetime was assessed using DSM-IV criteria though DSM-III-R criteria were included in the pre-visit screening procedure, because the previous cohort used for developing the threshold was initially assessed on DSM-III-R. In addition, as part of our clinical interviews, parents endorsing any ADHD symptom were asked: "Did you ever take (CHILD) to a doctor or counselor because he/she was showing these behaviors?" and whether medication was prescribed.

STATISTICAL ANALYSES

The association between ADHD and adjustment was investigated using two-way analyses of variance (ANOVAs) for quantitative outcomes and logistic regressions for categorical outcomes. The two factors were ADHD group (IN, HI, Combined, or no ADHD diagnosis) and sex. Quantitative outcomes with strong positive skew (e.g., deviant peers; symptom counts) were log-transformed before analysis; those with negative skew (e.g., academic expectations; self-concept) were squared. ANOVAs were performed via PROC SURVEYREG in SAS, and significant main effects of ADHD were followed by sets of three contrasts in which the No Diagnosis group was compared with each ADHD subtype group. These main effects contrasts were chosen because compared to contrasting only those affected by ADHD with each other (e.g., IN vs. HI), comparisons of each subtype against those without ADHD best documents the degree of impairment experienced by each subtype. In addition, this analytic approach allowed us to capitalize on the power afforded by the inclusion of the large No Diagnosis group. Similarly, significant Group $\times$ Sex interactions were followed by three 2×2 contrasts determining whether the difference between each of the three subtypes and the No Diagnosis group varied by sex. Logistic regression models (with the same contrasts) were implemented using PROC SURVEYLOGISTIC.

To account for twin similarity with respect to outcome measures, both SURVEYREG and SURVEYLOGISTIC used a sandwich (robust) estimator, computed at the cluster level to adjust for the correlated nature of twin data and produce appropriate standard errors (also lessening the likelihood of Type 1 errors; see Williams, 2000, for a demonstration with non-survey data). Both procedures use as the denominator degrees of freedom the number of independent clusters (i.e., twin pairs).

Results

SEX SIMILARITIES AND DIFFERENCES IN ADHD SYMPTOMS

Among the 253 boys and girls with an ADHD diagnosis, there were no significant sex differences in total ADHD symptoms (for boys, $M = 10.1$; $SD = 3.0$; for girls, $M = 9.5$, $SD = 3.1$), nor in the number of IN symptoms (for boys, $M = 5.6$; $SD = 2.0$; for girls, $M = 5.6$, $SD = 2.4$). Although ADHD boys had significantly ($p < .05$) more HI symptoms ($M = 4.6$; $SD =$

2.4) than girls ($M=3.9$, $SD = 2.5$), our findings are consistent with overall ADHD severity being similar among affected individuals of both sexes.

SEX AND SUBTYPE DIFFERENCES IN ADJUSTMENT

Means (SDs) for quantitative outcomes are presented separately for girls and boys with each ADHD subtype in Table 1, along with the ANOVA results. To facilitate comparisons in the table, some scores are presented as T-scores relative to the No Diagnosis group of girls, who were scaled to a mean of 50 and SD of 10. Because significant interactions with sex were present, the significance of the individual main effects contrasts comparing each ADHD subtype to the No Diagnosis group are reported separately for girls and boys in Figure 1. Figure 1 also displays the magnitude of the standardized effect sizes (d = the difference in the means divided by pooled SD), which provide a useful indicator of the degree of impairment associated with each subtype, by illustrating how much those with each subtype differed relative to unaffected individuals of the same sex. Furthermore, to examine which subtypes contributed to the eight significant ADHD Group $\times$ Sex Interactions in Table 1, each significant overall 4 (Group) $\times$ 2 (Sex) interaction was broken down further into three 2 $\times$ 2 contrasts, comparing each ADHD subtype to the No Diagnosis group across sexes. These are presented later in Table 3, following results for the categorical outcomes in Table 2, since one categorical outcome showed a significant interaction effect as well. Numerator degrees of freedom (df) associated with each group contrast is 1. Denominator df, based on the number of clustered pairs rather than individuals, varied between 222–259 for girls and 200–237 for boys (for Figure 1 contrasts conducted within each sex) and doubled for those conducted across sexes (to follow up significant Group $\times$ Sex interactions).

For academics, the main effect of ADHD was significant for all five measures (Table 1), indicating poorer academic functioning in those with ADHD. Significant main effects of sex were evident only for academic motivation (girls were higher) and full-scale IQ (boys were higher). However, there were significant ADHD group $\times$ Sex interactions on GPA, academic motivation, academic expectations, and academic problems; no significant interaction was found for IQ. For all four interactions, follow-up analyses revealed that the difference between the IN and No Diagnosis groups was significantly greater in girls than boys (see first column in Table 3), indicating that when boys and girls are compared to those without ADHD, IN girls in particular did worse on academic measures. No other significant sex-by-subtype effects were observed, except for academic problems, for which the difference between the Combined and No Diagnosis group was also significantly greater for girls than for boys (see last column in Table 3). The differential magnitude of subtype effects in girls and boys can be seen in Figure 1; academics effect sizes were consistently larger among IN girls than boys, whereas effect sizes for HI or Combined types were relatively similar across the sexes.

For relationships, there were significant main effects of ADHD on all outcomes. Those with ADHD experienced lower popularity and self-concept, fewer positive peers, and increased deviant peers. A main effect of sex was observed for deviant peers (boys were higher). Significant ADHD $\times$ Sex interactions were found for self- and teacher-rated popularity, positive peers, and nearly for self-concept ($p = .06$). As with the academic outcomes, the difference between the IN and No Diagnosis groups on both popularity measures and for positive peers was significantly greater for girls than boys (Table 3), with IN girls being relatively lower (compared to unaffected girls) than IN boys in popularity and positive peers. No other sex-by-subtype interactions were significant except for positive peers, for which the difference between the Combined and No Diagnosis groups was significantly greater for boys than girls. Effect sizes and contrasts comparing the IN and No Diagnosis groups within each sex (Figure 1) were also consistently larger and more likely to be significant for girls than boys (overall self-concept was also significantly lower for HI girls,

but not boys), whereas those comparing the Combined and No Diagnosis groups were more likely to be significant for boys than girls. This pattern is also illustrated in Figure 2, which shows the least popular group (according to self and teacher reports) was the IN group for girls but the Combined group for boys.

In the mental health domain, children with ADHD showed significantly more oppositional and CD symptoms than children without ADHD (Table 1); boys had more CD symptoms than girls. There were no significant interactions with sex on these externalizing symptoms, with the largest effect sizes for both sexes most evident for the HI and Combined groups (Figure 1). For internalizing symptoms, those with ADHD showed significantly more depression and anxiety overall. There was a significant main effect of sex on separation anxiety (girls higher) and a significant interaction, with ADHD girls (but not boys) having more separation anxiety. Finally, Table 2 provides results for the three categorical outcomes, along with significance of the contrasts and odds ratios (ORs) from logistic regression. Not surprisingly, those with ADHD were much more likely to have seen a physician/counselor or received medication than those without; there was no significant interaction with sex. Furthermore, those with ADHD were far more likely to report having been bullied or picked on than those with No Diagnosis, and girls with ADHD were more likely to be picked on than boys, compared to their unaffected peers ($p=.04$ interaction). Within each sex, whereas IN girls were significantly more likely to be bullied than girls with No Diagnosis ($OR = 4.8$), IN boys were not ($OR=1.40$). Follow-up sex-by-subtype contrasts in Table 3 demonstrated that only the comparison between the IN and No Diagnosis group in likelihood of being bullied was significantly different for girls than for boys with ADHD ($p<.01$).

Discussion

In a unique, community-based study representing all three ADHD subtypes, we found that preadolescent boys and girls with ADHD were similar in the severity of their ADHD and experienced adjustment problems in all areas. Despite these similarities, the magnitude of problems varied significantly depending upon gender and subtype. Compared to those without ADHD, girls with ADHD were more negatively affected than boys in the academic and social realms, supportive of a gender paradox in at least these two areas of adjustment. Previous clinic-based studies have been dominated by the Combined subtype; indeed, we found that regardless of gender, Combined cases had the highest prevalence of treatment contact (68.8% of boys and 65.4% of girls; Table 2) or medication. However, the primary contributor to the significant overall interactions of gender and ADHD was that unexpectedly, girls with the predominantly IN subtype consistently fared worse than boys with the IN subtype.

The IN subtype was associated with a particularly problematic profile of academic outcomes among girls. When compared to those with no ADHD diagnosis, girls with the IN subtype had significantly greater deficits in GPA, academic motivation, academic expectations, and significantly more academic problems than did boys with this subtype (Table 3). Given the number of significant overall gender differences obtained, we did not directly contrast subtypes of ADHD with each other (e.g., IN vs. HI) but chose instead to do more parsimonious follow-up analyses comparing each subtype to those without ADHD. In terms of magnitude of these effects (Figure 1), girls with the IN subtype appeared not only particularly low on IQ and achievement when compared to unaffected girls, but in motivation, an important component of achieving in school.

Similarly, significantly greater effects of the IN subtype on peer relationships and self-concept were seen in girls as compared to boys. This pattern is strikingly evident in Figure

2, which shows the negative effect of the IN subtype on popularity was more pronounced for girls. Compared to their respective No Diagnosis reference groups, girls with ADHD were also significantly more likely to report being bullied or picked on than ADHD boys; in addition, 50% of IN girls reported being bullied compared to 29% of IN boys. Why girls, but not boys, with the IN subtype would be bullied more, and lacking in popularity and positive peers, is not clear. Perhaps since girls are more academically motivated than boys overall (see main effect of sex in Table 1), IN girls are in violation of a common gender role expectation and are thereby subjected to greater social stigma. Alternatively, inattention may impair the ability to be attuned to subtle social cues and norms, and girls may be expected to be aware of and responsive to these cues to a greater degree than boys. Because being bullied is a risk factor for internalizing and externalizing symptoms (Arseneault et al. 2008; Barker et al., 2008), the disadvantage for girls with ADHD, especially the IN type, may be a portent of greater adjustment problems during adolescence.

By contrast, the effect of the Combined subtype tended to be greater for boys than girls. For example, boys with Combined subtype had relatively lower exposure to positive peer models than did girls with this subtype (Table 3). Furthermore, contrasts comparing the Combined and no diagnosis groups within each sex were more often significant for boys than girls (see Figure 1). The HI subtype had the lowest prevalence of treatment contact and medications for both sexes, which perhaps explains why this group is infrequently seen in clinical research. While HI cases may not appear much impaired compared to their unaffected peers during preadolescence (e.g., HI boys even had elevated IQs; Figure 1 note), they did have significantly elevated externalizing symptoms and more deviant peers compared to those with no diagnosis. This bears watching in our ongoing follow-ups at ages 14 and 17, when growth in externalizing behaviors (including CD, ODD, and relational aggression) may increase the relative impairment associated with HI symptoms. Whereas CD symptoms were not very common among this sample of preadolescents (e.g., in Table 1, most subtypes had only a single symptom, on average), ADHD children continue to be at risk for later-developing CD (Mannuzza, Klein, Abikoff, & Moulton, 2004). Our previous ADHD research using a different community sample (Elkins, McGue, & Iacono, 2007) suggests those with HI symptoms (i.e., both HI and Combined subtypes) might later be at elevated risk for substance abuse. Furthermore, aggression in hyperactive girls has been associated with poor adjustment in adulthood (Fontaine et al., 2008).

Unlike in the academic and social realms, we found few gender differences in clinical symptoms and treatment utilization. The lack of gender differences in comorbid symptoms and likelihood of treatment is consistent with Biederman et al (2005), even though our findings of gender differences on academic and social measures are not. Consistent with a questionnaire-based study (Levy, Hay, Bennett, & McStephen, 2005), we found no significant gender differences in the relationship of ADHD to externalizing symptoms; the only gender difference was for separation anxiety. As the preponderance of depression in females during adolescence may be related to earlier differences in anxiety (Zahn-Waxler, Shirtcliff, & Marceau, 2008), sex differences in depression may emerge among ADHD adolescents. A recent follow-up of Lahey et al (2007) found that ADHD predicted depression and suicide attempts in adolescence more for girls than for boys, though only 18 girls had ADHD (Chronis-Tuscano et al., 2010).

Limitations and Implications for Research, Policy, and Practice

Although the current study is limited by cross-sectional data, a diagnosis of ADHD requires onset before age 7; thus, adjustment difficulties at age 11 should partially reflect the impact of earlier symptoms. However, given emerging evidence that requiring onset by age 7 lacks empirical support (Kieling et al., 2010) and that subtype classification may change across development as HI symptoms decline (Lahey, Pelham, Loney, Lee, & Willcutt, 2005),

incorporating late-onset cases and having more predominantly IN cases at our adolescent follow-ups may affect future results. For example, boys classified as the Combined subtype at age 11 may shift to the IN subtype as HI symptoms become less frequent, which could affect the pattern of gender differences observed. Furthermore, we do not wish to suggest that symptoms of inattention do not exacerbate adjustment problems for boys, as boys with the Combined subtype exhibited considerable impairment and were required to have the same number of IN symptoms as those with the IN subtype. Finally, although twins were considered as separate cases here, it is possible that the experiences of twins concordant for ADHD might have differed from the experiences of those discordant for ADHD.

Our finding in a community-based sample that likelihood of treatment did not differ by sex could be due to our reliance on parents for diagnosis, as teachers identify more problem behavior in boys, which may contribute to higher numbers of boys presenting for treatment in clinical settings (Derks et al., 2007). However, although we did not find girls with ADHD were less likely to receive treatment compared to boys, evidence for long-term benefits of standard treatment with stimulant medication on academic, behavioral, and social outcomes in those with ADHD is lacking (Molina et al, 2009). Based on our findings, it is in these areas that girls with ADHD may be relatively more impaired, suggesting multimodal treatments for girls which focus more on social factors may be warranted (Young and Amarasinghe, 2010).

In conclusion, while the overall adjustment of those with ADHD during preadolescence is of significant concern, we found that ADHD, particularly the IN subtype, may have worse implications for girls than boys in academics and peer relationships. By contrast, the Combined subtype was associated with relatively more adjustment problems for boys. Fewer sex differences were seen in symptoms of other disorders and treatment utilization. The greater social isolation experienced by many girls with ADHD suggests that this area merits greater attention. Future research regarding gender differences in ADHD needs to include sufficient numbers of girls affected by ADHD, as this may explain why gender differences have not been consistently detected in previous research.

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Figure 1.

Effect sizes (d) associated with each attention-deficit/hyperactivity disorder (ADHD) subtype, presented separately for girls (on left) and boys (on right). Abbreviations for reporters: (T) Teacher; (M) Mother; (C) Child; (MC) best-estimate mother/child. Effect sizes (ES) are based on the unadjusted means and SDs (i.e., each ADHD subtype mean - the No Diagnosis group mean/the pooled SD for all boys or all girls). Because those with ADHD generally scored in a less desirable direction than those without ADHD, only the absolute values of ESs are presented. Arrows indicate exceptions: hyperactive-impulsive boys were .31 SD above the mean in IQ; hyperactive-impulsive girls had fewer depression symptoms ($ES = -.14$). Significance levels (i.e., * $p < .05$, ** $p < .01$, *** $p < .001$, **** $p < .0001$).

*** $p < .001$, **** $p < .0001$), are associated with the within-sex contrasts and reflect the adjustment due to clustered data.

Popularity By ADHD Subtype & Sex

Figure 2.

Self- and teacher-reported popularity of 11-year-olds, according to attention-deficit/hyperactivity disorder subtype (inattentive, hyperactive-impulsive, or combined) and sex. Note: Scores are presented as T-scores relative to the No Diagnosis group of girls, who were scaled to a mean of 50 and SD of 10.

TABLE 1

Mean Scores on Adjustment Measures and Results of ANOVAs for 11-Year-Old Females and Males (N=998^a), by ADHD Group and Sex

	ADHD Subtype Group										PROC SURVEYREG (ANOVA) ^b Results					
	Girls (N=515)					Boys (N=468)					ADHD Group		Sex		Group × Sex	
	No Diagnosis	IN ^c	HI	CO	No Diagnosis	IN	HI	CO			F	p	F	p	F	p
	N=406 ^a	N=58	N=25	N=26	N=324 ^a	N=62	N=34	N=48								
Measure (reporter)																
Academic Adjustment																
WISC-R Full-Scale IQ (C)	102.3	96.1	101.4	98.8	104.6	101.8	108.7	102.8			5.45	.001	10.01	.002	1.07	.36
SD	(13.1)	(13.1)	(13.4)	(11.0)	(13.0)	(11.9)	(13.1)	(15.0)								
Grade-point average (T)	3.1	2.2	3.0	2.6	2.9	2.5	2.8	2.4			22.28	<.0001	0.66	.42	4.00	<.01
SD	(0.8)	(0.8)	(0.8)	(0.6)	(0.9)	(0.7)	(0.9)	(1.0)								
Academic Motivation (Ty) ^d	50.0	37.0	44.5	39.0	44.3	38.1	40.3	34.6			33.71	<.0001	4.88	.03	2.82	.04
SD	(10.0)	(10.4)	(13.4)	(8.8)	(12.5)	(10.8)	(11.4)	(10.9)								
Academic Expectations (M) ^d	50.0	44.1	44.7	45.6	47.2	47.6	45.9	36.3			9.32	<.0001	1.31	.25	3.28	.02
SD	(10.0)	(15.1)	(13.7)	(10.9)	(13.6)	(10.0)	(13.3)	(14.1)								
Academic Problems (M) ^d	50.0	69.2	58.3	71.2	54.4	65.7	63.4	69.1			108.4	<.0001	0.65	.42	6.04	<.001
SD	(10.0)	(8.8)	(11.2)	(10.3)	(10.5)	(10.2)	(9.7)	(10.8)								
Peer Relationships & Self-Concept																
Self-reported Popularity (C) ^d	50.0	42.9	46.2	47.4	49.7	48.5	50.5	44.3			5.37	.001	1.27	.26	3.13	.02
SD	(10.0)	(12.4)	(11.8)	(14.4)	(10.3)	(10.9)	(10.5)	(12.1)								
Overall Self-Concept (C) ^d	50.0	41.0	43.3	43.9	49.4	44.1	50.1	42.0			18.31	<.0001	1.86	.17	2.50	.06
SD	(10.0)	(12.9)	(12.8)	(12.6)	(9.1)	(11.3)	(10.5)	(11.6)								
Popularity (Ty) ^d	50.0	40.2	46.2	49.0	49.3	46.6	46.4	43.1			9.93	<.0001	0.00	.99	4.10	<.01
SD	(10.0)	(10.2)	(14.7)	(8.8)	(11.6)	(11.8)	(13.4)	(12.1)								
Positive Peers (Ty) ^d	50.0	41.0	48.7	48.7	49.4	46.5	47.1	39.9			8.83	<.0001	0.51	.48	3.79	.01
SD	(10.0)	(11.1)	(15.9)	(11.1)	(11.7)	(11.1)	(14.0)	(12.7)								
Deviant Peers (Ty) ^d	50.0	51.9	53.6	55.9	53.9	54.2	61.1	58.4			3.23	.02	4.51	.03	0.43	.73

	ADHD Subtype Group										PROC SURVEYREG (ANOVA) ^b Results					
	Girls (N=515)					Boys (N=468)					ADHD Group			Sex		
	No Diagnosis N=406 ^a	IN ^c N=58	HI N=25	CO N=26	No Diagnosis N=324 ^d	IN N=62	HI N=34	CO N=48			F	p	F	p	F	p
SD	(10.0)	(13.2)	(14.9)	(16.5)	(15.5)	(14.8)	(14.2)	(17.1)								
DSM-IV symptoms (best estimate)																
Conduct disorder	0.3 (0.7)	0.8 (1.0)	1.0 (1.0)	1.0 (1.0)	0.7 (1.1)	1.2 (1.6)	1.3 (1.3)	2.3 (1.6)			27.96	<.0001	14.59	.0002	1.85	.14
SD																
Oppositional defiant	0.9 (1.4)	1.6 (1.6)	2.5 (1.9)	2.6 (2.2)	1.1 (1.6)	1.7 (1.7)	1.9 (1.6)	3.2 (1.8)			40.90	<.0001	0.45	.50	1.01	.39
SD																
Major Depression	0.3 (1.2)	0.6 (1.4)	0.2 (0.8)	0.6 (1.6)	0.4 (1.3)	0.6 (1.8)	0.3 (1.0)	0.9 (2.2)			2.72	.04	0.33	.57	0.23	.88
SD																
Separation Anxiety	0.5 (0.9)	0.8 (1.2)	1.1 (1.3)	1.2 (1.4)	0.4 (0.8)	0.5 (1.0)	0.4 (0.8)	0.4 (0.9)			4.33	.005	20.55	.0001	3.09	.03
SD																

Abbreviations: IN, Predominately Inattentive; HI, Predominately Hyperactive/Impulsive; CO, Combined (i.e., qualifies for both IN and HD); T, Teacher; M, Mother; C, Child

^a 15 late-onset cases were excluded.

^b For ANOVAs, numerator degrees of freedom were 3 for the main effect of group, 1 for the main effect of sex, and 3 for the ADHD Group $\times$ Sex interaction.

^c Because 90 females were not assessed on three of the nine DSM-IV IN symptoms, their IN symptom count and diagnosis were prorated by multiplying the number of symptoms by 1.5; those with a score of 6 or greater were given the diagnosis. The prorated diagnosis was compared with that obtained using all nine DSM-IV IN symptoms in twins from the later birth years. The cutoff score maximized both positive and negative predictive power (91.5% of actual cases and 92.5% of non-cases correctly identified).

^d To facilitate direct comparisons on variables without a well-established scale, scores are presented as T-scores relative to the No Diagnosis group of girls, who were scaled to a mean of 50 and SD of 10.

TABLE 2
Categorical Social and Clinical Outcomes, Regression Results, Main Effects Contrasts^a and Effect Sizes Associated with ADHD Subtypes By Sex

Outcome	Lifetime prevalence, %									
	Girls (N=515)					Boys (N=468)				
	No Diagnosis N=406 ^a	IN N=58	HI N=25	CO N=26	No Diagnosis N=324 ^a	IN N=62	HI N=34	CO N=48	ADHD Group χ^2 (3)	Sex χ^2 (1)
Bullied or picked on a lot by other kids	17.2	50.0	52.0	34.6	22.6	29.0	47.1	43.8	40.4 <.0001	.68
Seen counselor or Dr. because of ADHD	6.2	50.0	16.0	65.4	9.0	43.5	38.2	68.8	148.5 <.0001	.15
Received medication	3.7	29.3	8.0	53.8	6.2	37.1	20.6	54.2	113.1 <.0001	.09
OR ^a (95% CI)										
Outcome	IN only vs. No Diagnosis					HI only vs. No Diagnosis				
	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys
	4.80 ^{****} (2.63, 8.73)	1.40 (0.72, 2.70)	5.20 ^{****} (2.28, 11.88)	3.04 ^{**} (1.38, 6.71)	2.90 (0.94, 9.01)	6.30 ^{****} (2.94, 13.47)	28.79 ^{****} (11.19, 74.07)	2.54 [*] (1.11, 5.81)	2.66 ^{**} (1.28, 5.53)	22.38 ^{****} (10.59, 47.28)
Bullied or picked on a lot										
Seen counselor or Dr. because of ADHD behaviors	15.24 ^{****} (7.16, 32.43)	7.85 ^{****} (3.97, 15.53)	2.27 (0.45, 11.32)	3.94 ^{**} (1.54, 10.05)	2.27 (0.45, 11.32)	3.94 ^{**} (1.54, 10.05)	30.39 ^{****} (11.43, 80.83)	17.96 ^{****} (8.02, 40.21)		
Received medication	10.81 ^{****} (4.49, 26.01)	8.96 ^{****} (4.41, 18.20)								

Abbreviations: OR, odds ratio; CI, confidence interval.

^a ORs reflect increase in odds of a given outcome associated with the presence of each ADHD subtype.

Contrasts were conducted separately for girls and boys; significance levels (i.e., *p<.05, **p<.01, ***p<.001, ****p<.0001) reflect the adjustment due to clustered data.

TABLE 3

Follow-up Contrasts Comparing Each ADHD Subtype to the No Diagnosis Group Across Sexes for Outcomes with a Significant Overall Group $\times$ Sex Interaction

	IN Subtype $\times$ Sex		HI Subtype $\times$ Sex		Combined Subtype $\times$ Sex	
	F	p	F	p	F	p
Quantitative Outcome (from Table 1)						
Academic Adjustment						
Grade-point average (T)	11.77	<.001	0.00	.99	0.02	.90
Academic Motivation (T)	8.45	<.01	0.11	.74	0.17	.68
Academic Expectations (M)	3.85	.05	0.87	.35	3.37	.07
Academic Problems (M)	14.88	.0001	0.05	.83	4.73	.03
Peer Relationships & Self-Concept						
Self-reported Popularity (C)	6.03	.01	2.13	.14	0.92	.34
Teacher-reported Popularity (T)	8.50	<.01	0.04	.85	2.63	.11
Positive Peers (T)	5.20	.02	0.04	.85	4.97	.03
DSM-IV symptoms						
Separation Anxiety (best estimate)	0.06	.81	3.58	.06	6.08	.01
	IN Subtype $\times$ Sex		HI Subtype $\times$ Sex		Combined Subtype $\times$ Sex	
	χ^2 (1)	p	χ^2 (1)	p	χ^2 (1)	p
Categorical Outcome (from Table 2)						
Bullied or picked on a lot	7.37	<.01	0.84	.36	0.01	.93

Abbreviations: IN, Predominately Inattentive; HI, Predominately Hyperactive/Impulsive; T, Teacher; M, Mother; C, Child. Contrasts were conducted for each subtype in PROC SURVEYREG for quantitative outcomes (or in PROC SURVEYLOGISTIC for categorical outcomes) for which the overall interaction of ADHD Group $\times$ Sex was significant. Significance levels reported reflect the adjustment based on clustered data. Numerator degrees of freedom associated w/each of the 3 contrasts is 1; Denominator df, based on the number of clustered pairs rather than individuals, varied between 422–496.

Appendix A

DSM-IV and DSM-III-R Symptoms of ADHD, Conduct Disorder, and Academic Items Assessed in Enrichment Screening Interview^{ab}

ADHD symptoms (Give 1 point for each symptom coded full, based on examples of frequency and severity)

- Often easily distracted by extraneous stimuli (III-R and IV)
- Often fidgets with hands or feet or squirms in seat; in adolescents, may be limited to subjective feelings of restlessness (III-R and IV)
- Often leaves seat in classroom or in other situations in which remaining seated is expected (III-R and IV)
- Often has difficulty sustaining attention in tasks or play activities (III-R and IV)
- Often interrupts or intrudes on others (III-R and IV)
- Often loses things necessary for tasks or activities at school or at home (III-R and IV)
- Difficulty playing (or engaging in leisure activities-IV) quietly (III-R and IV)
- Often does not seem to listen (when spoken to directly-IV) what is being said to him/her (III-R and IV)
- Often talks excessively (III-R and IV)
- Difficulty following through on instructions from others; not due to oppositional behavior or failure of comprehension (III-R and IV)
- Often shifts from one uncompleted activity to another (III-R)
- Often engages in physically dangerous activities without considering possible consequences; not for the purpose of thrill-seeking (III-R)
- Often has difficulty organizing tasks and activities (IV)
- Often forgetful in daily activities (IV)
- Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as school work or homework; IV)
- Often runs about or climbs excessively in situations in which it is inappropriate (IV)
- Often fails to give close attention to detail or makes careless mistakes in school work, work, or other activities (IV)
- Often "on the go" or often acts as if "driven by a motor" (IV)
- Difficulty awaiting turn in games or group situations (III-R and IV)
- Often blurts out answers to questions before they have been completed (III-R and IV)

Conduct disorder symptoms^c (CD; Give 3 points for each symptom coded full, based on examples of frequency and severity)

- Often lies (III-R) to obtain goods or favors or to avoid obligation (IV)
- Used a weapon in more than one fight (III-R) with the potential for causing serious harm (IV)
- Often initiates physical fights (III-R and IV)
- Deliberately engaged in fire-setting (III-R) with the intent of causing serious damage (IV)
- Stolen without confrontation of a victim on more than one occasion (III-R); items stolen are of nontrivial value (IV)
- Physically cruel to animals (III-R and IV)
- Deliberately destroyed others' property (other than by fire-setting; III-R and IV)
- Often bullies, threatens, or intimidates others (IV)
- Physically cruel to people (III-R and IV)
- Often stays out at night despite parental prohibitions, beginning before age 13 (IV)
- Often truant (III-R); truancy must begin before age 13 (IV)
- Broken into someone's house, building, or car (III-R and IV)

Academic Items (Give 1 point for each item answered in indicated direction)

- Lacks interest in schoolwork (true)
- Is well liked by his/her teachers (false)
- Enjoys attending school (false)
- Turns in homework on time (false)

Studies or completes homework at night without being told to do so (false)

Likes his/her teachers (false)

Is motivated to earn “good” grades (false)

Has a good attitude about school (false)

^a Adapted from Keyes, et al., 2009.

^b Only twin pairs in which at least one member met or exceeded a threshold of five points were invited to participate. The items and threshold chosen maximized sensitivity and specificity for predicting ADHD diagnosis by age 11 (or CD by age 14), based on analyses conducted in our previous 11-year-old cohort. Because the previous cohort used for developing the threshold was initially assessed on DSM-III-R, these items were included as part of the screening. We chose not to include oppositional defiant disorder (ODD) symptoms due to concerns that an overly long initial phone screening might discourage participation among families subsequently invited to visit. However, given that 25.7% of screened males and 15.4% of screened females met criteria for a diagnosis of ODD when assessed at the visit (Keyes, et al., 2009), the sample was enriched for ODD as well, an important consideration given that ADHD with comorbid ODD has also been associated with an elevated risk of adolescent drug use (August et al., 2006).

^c Due to their extremely low endorsement frequency, some CD symptoms were omitted from the screening interview but were assessed at the visit.