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The influence of sex on the course and psychiatric correlates of ADHD from childhood to adolescence: A longitudinal study

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Abstract

Background—Little is known about the influence of sex on the course of ADHD and its comorbid psychiatric conditions. The purpose of this study was to examine the effect of sex on the course and psychiatric correlates of ADHD from childhood into adolescence.

Methods—Two identically designed, longitudinal, case-control family studies of male and female probands with and without ADHD and their siblings were combined. All subjects were blindly assessed with structured diagnostic interviews. Among subjects with a lifetime history of ADHD (n=471, mean age 11.5±4.3 years at baseline), we used linear growth curve models to estimate the effect of time on the change in ADHD symptoms, and whether this effect differed by sex. We also we examined the effect of sex on the association between ADHD and the longitudinal progression of comorbid psychopathology using structural equation models.

Results—We found no evidence that sex moderated the effect of age on ADHD symptoms; in both genders, age exhibited a similar effect on the decline of ADHD symptoms. However, the female sample demonstrated greater stability in comorbid psychopathology from childhood into adolescence. Furthermore, we found that the stability of comorbid psychopathology in females remained significant after accounting for the correlation between adolescent psychopathology and adolescent ADHD. In males, childhood and adolescent comorbid psychopathology were no longer correlated when adolescent ADHD was taken into account.

Conclusions—Our findings indicate that while the course of ADHD across childhood and adolescence did not differ between males and females, patterns of psychiatric comorbidity were conditional on sex. Future studies should explicitly test how sex modifies the associations between ADHD and risk factors and ADHD and associated functional outcomes.

Keywords

ADHD; growth curve; sex; longitudinal; structural equation model

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Conflict of Interest

Dr. Monuteaux participated in a symposium in 2007 sponsored by Shire, Inc.

INTRODUCTION

Several studies have examined the longitudinal course of attention-deficit/hyperactivity disorder (ADHD) in samples of male subjects (Biederman et al., 1996, Gittelman et al., 1985, Mannuzza et al., 1991, Barkley et al., 1990, Hart et al., 1995). Although recent studies have begun to examine ADHD in females (Mikami and Hinshaw, 2003, Neuman et al., 2001, Biederman et al., 2006a, Hinshaw et al., 2006, Hinshaw et al., 2007), few studies have examined its longitudinal course in these samples (Hinshaw et al., 2006). Also, the influence of sex on the course of ADHD has yet to be specifically tested. If significant differences between males and females in the longitudinal course of ADHD were found, clinicians would be better able to forecast prognosis for individual patients.

Also, despite ample evidence that ADHD is a strong predictor of psychiatric comorbidity in both males (Biederman et al., 2006b, Gittelman et al., 1985) and females (Biederman et al., 2006a, Hinshaw et al., 2006), little is known about the influence of sex on the pattern and course of these comorbid psychopathological conditions. Using cross-sectional data, we found that girls with ADHD were less likely to have comorbid psychiatric disorders (Biederman et al., 2002b), and that sex significantly modified the association between environmental adversity and both learning disabilities and a global functioning measure, with males being more vulnerable than females (Biederman et al., 2002a). Also, studies have demonstrated subtle but meaningful sex differences in cognition (Rilea et al., 2004, Gallagher et al., 2000, Maitland et al., 2004), brain structure (Goldstein et al., 2001, Luders et al., 2006) and function (Goldstein et al., 2005, Gur et al., 2000, Baxter et al., 2003) that could reflect sex-specific neural organization relating to the expression of ADHD. However, a two-year longitudinal study of 1,478 children with ADHD across 10 European countries did not find evidence of important sex differences in ADHD symptoms or psychiatric comorbidity (Novik et al., 2006). Given this evidence, it is important for additional studies using longitudinal designs to develop our understanding of sex effects on the course of ADHD and its comorbid psychiatric conditions.

The purpose of this study was to examine the effect of sex on the course and psychiatric correlates of ADHD from childhood into adolescence using a large longitudinal sample of males and females with and without ADHD, and their male and female siblings. We tested the following hypotheses: 1) sex will have a moderating effect on the level of ADHD symptoms across time; and 2) sex will have a moderating effect on the correlations between symptoms of comorbid psychopathology and ADHD symptoms over time.

METHODS

Subjects

Subjects were derived from two identically designed, longitudinal case-control family studies conducted at the Clinical and Research Programs in Pediatric Psychiatry and Adult ADHD at Massachusetts General Hospital. The first study began in the late 1980's and ascertained families on the basis of a male case (ADHD) or control (non-ADHD) proband child aged 6–17 years at time of ascertainment. This study was comprised of 140 ADHD probands (with 206 siblings and 280 parents) and 120 non-ADHD control probands (with 167 siblings and 239 parents). Subjects were assessed at baseline and at four and ten-year follow-ups. The second study began in 1993 and ascertained families on the basis of a female case or control proband child also aged 6–17 years at time of ascertainment. This study was comprised of 140 ADHD probands (with 183 siblings and 274 parents) and 122 non-ADHD control probands (with 152 siblings and 238 parents). Subjects were assessed at baseline and at a five-year follow-up. For this investigation, we utilized proband and sibling

data from the ADHD and Control groups of both studies, for a total of 1230 subjects available for analysis.

For both studies, potential probands were excluded if they had been adopted, if their nuclear family was not available, if they had major sensorimotor handicaps (paralysis, deafness, blindness), if they had psychosis or autism, or if they were unable to participate in the assessments due to language barriers or an estimated IQ < 80. After a complete description of the study, parents provided written informed consent for their children, and children and adolescents provided written assent. The Institutional Review Board at Massachusetts General Hospital approved this study.

We used a three-stage ascertainment procedure to select probands (Faraone et al., 1999). For ADHD subjects, the first stage was their referral, which resulted in a clinical diagnosis of ADHD. The second stage confirmed the diagnosis of ADHD through a telephone questionnaire administered to the mother. The third stage was a diagnostic assessment with a structured interview. Only patients who received a positive diagnosis at all three stages were included. Controls were similarly selected though a three-stage procedure. First, we ascertained them from consecutive referrals to medical clinics for routine physical examinations at both the psychiatric and pediatric sources. In stage two, the control mothers responded to the DSM-III-R ADHD telephone questionnaire. Eligible controls meeting study entry criteria were recruited for the study and received the third stage, a diagnostic assessment with a structured interview. Only subjects classified as not having ADHD at all three stages were included in the control group.

Assessment Procedures

Psychiatric Assessment—Psychiatric assessments relied on the K-SADS-E (Epidemiologic Version) (Orvaschel, 1994) for subjects less than 18 years of age and the Structured Clinical Interview for DSM-III-R (SCID) (Spitzer et al., 1992) (supplemented with modules from the K-SADS-E to assess childhood diagnoses) for subjects aged 18 and older. Diagnoses were based on direct interviews with the mothers and the offspring, except for children <12 years that were not interviewed directly. Both lifetime and current (i.e., in the past month) diagnoses were collected. All subjects with ADHD were asked to characterize the impairment to their daily functioning associated with ADHD as mild, moderate, or severe, both at its most impaired lifetime as well as currently, coded as 1, 2, and 3, respectively. Subjects without ADHD were coded as zero on this variable.

We combined data from direct and indirect interviews by considering a diagnosis positive if it was endorsed in either interview. All interviews conducted were blind to the subject's referral source. Diagnoses were considered positive if DSM-III-R criteria were unequivocally met. A committee of board-certified child and adult psychiatrists, who were blind to the subject's ascertainment status and all other data, resolved diagnostic uncertainties. Diagnoses presented for review were considered positive only if a consensus was achieved that criteria were met to a degree that would be considered clinically meaningful.

All interviewers had undergraduate degrees in psychology and were trained to high levels of inter-rater reliability. First, they underwent several weeks of classroom style training, learning interview mechanics, diagnostic criteria, and coding algorithms. Then, they observed interviews by experienced raters and clinicians. They subsequently conducted at least six practice (non-study) interviews and at least two study interviews while being observed by senior interviewers. The principal investigator (JB) supervised the interviewers throughout the study. We computed kappa coefficients of agreement by having child and adult psychiatrists and clinical psychologists diagnose subjects from audio taped interviews.

Based on 500 assessments from interviews of children and adults, kappa coefficients for ADHD and conduct disorder were 0.88 and 1.0, respectively.

Demographic Assessment—Socio-economic status (SES) was assessed with the 5-point Hollingshead scale (Hollingshead, 1975), using the occupational and educational status of the parents.

Statistical Analysis—To test our first hypothesis, we used linear growth curve models to estimate the effect of time on the change in ADHD symptoms, and whether this effect differed by sex. This analysis was restricted to subjects (probands or siblings) with a positive lifetime history of ADHD. These linear mixed effect models are appropriate for analyzing unbalanced longitudinal data (i.e., different numbers of assessments between subjects and different interval lengths between assessments) (Fitzmaurice et al., 2004), as is the case in the present study. For this analysis, we utilized symptom scores provided by our structured interview. Because the early waves of the Boys study used DSM-III-R ADHD symptoms while subsequent assessments used DSM-IV, we standardized the symptom scores within diagnostic version, to place all symptom scores on a common metric (mean of zero, standard deviation of one). We estimated current (i.e., past month) standardized ADHD symptoms as a function of age, sex, and the age-by-sex interaction as fixed effects, with random intercept (allowing a given subjects' intercept to deviate from the mean intercept) and random slopes for age (to allow subjects to differ in their overall rate of symptom change). The interaction term tested whether the trajectory of ADHD symptoms across the range of ages in our data differs by sex. Because we did not consider assumptions about the covariance pattern to be justified in these data, we used an unstructured covariance matrix. These models were estimated using maximum restricted likelihood.

For our second hypothesis, we examined the effect of sex on the association between ADHD and the longitudinal progression of comorbid psychopathology. We choose to assess psychiatric comorbidity because: a) of its clinical relevance; b) it is a well-established correlate of ADHD in both sexes; and c) we have sufficient longitudinal data on these measures. To assess this hypothesis, we estimated a structural equation model (SEM), as implemented in LISREL 8.8. From the entire pool of subjects (i.e., probands and siblings, with or without a lifetime history of ADHD), we selected subjects who: 1) had complete data on all of the variables used in the models; and 2) provided at least one assessment between the ages of 6 and 12 inclusive, as well as at least one assessment between the ages of 13 to 18, inclusive (n=295; 156 males and 139 females). Thus, each subject included in this analysis was assessed twice, once in childhood and once in adolescence. Using data from the childhood assessments, we estimated the following latent factors:

1. a latent childhood comorbid psychopathology factor, estimated as a function of mood disorders (major depression, bipolar disorder, dysthymia), disruptive behavior disorders (conduct disorder, oppositional-defiant disorder), and anxiety disorders (separation anxiety, social phobia, simple phobia, panic disorder, agoraphobia, obsessive-compulsive disorder, generalized anxiety disorder, overanxious disorder). We multiplied a variable indicating absence (0) or presence (1) of the disorder in the year prior to the follow-up assessment by its past impairment score (1, 2, or 3), then summed the products within each of the three categories described above. For example, for a given subject, the disruptive behavior disorders score = [(presence of conduct disorder)*(conduct disorder impairment score)] + [(presence of ODD)*(ODD impairment score)].
2. a latent ADHD factor, estimated as a function of current (i.e., past month at the time of assessment) inattentive symptoms, current hyperactivity/impulsivity

symptoms, and the ADHD impairment measure. The structured interview we administered to each subject provided these data.

Using data from the adolescent assessments, we estimated the following latent factors:

1. a latent adolescent comorbid psychopathology factor, estimated as a function of the same three summary scores (mood disorders, disruptive behavior disorders, and anxiety disorder), with the addition of a substance use disorder score, calculated as described above using the diagnoses of alcohol abuse or dependence, substance abuse or dependence, and smoking dependence that had been evident in the year prior to the follow-up assessment.
2. a latent ADHD factor, estimated as described above.

We first estimated the full model in each group (i.e., males and females), constraining all parameters to be equal across groups. Then, to test whether the model differed according to sex, we allowed the factor loadings, error variances, and factor correlations to be different between groups. If the overall model fit improves, there is evidence that the model differs between males and females. If so, we re-estimated the model within strata of sex. Because some variables in our model were ordinal we used the software program PRELIS to estimate polychoric and polyserial correlations and the corresponding correlation matrix, as well as to estimate the asymptotic covariance matrix. These models were estimated using Weighted Least Squares. Model fit was evaluated using conventional metrics (Satorra-Bentler goodness of fit chi square test, root mean error of approximation, and the Akaike information criterion (AIC)).

RESULTS

Demographic characteristics

Of the 1230 subjects available for analysis, 471 reported a lifetime history of ADHD (38%). The demographic characteristics of the ADHD sample stratified by sex (males, n=268; females, n=203) are presented in table 1. As shown, no differences were found between males and females on their age at first assessment or parental social class at baseline. However, females were significantly more likely to be probands, to be younger at the most recent follow-up assessment, and to have been assessed fewer times compared to males with ADHD.

Linear growth curves of ADHD symptoms

Using the ADHD sample, we estimated latent growth curve models of ADHD symptoms. First, we estimated the total current ADHD symptom score as a function of age, sex, and subject status as fixed effects, with random intercepts and random slopes for age. To increase the efficiency of our estimates for age, we categorized the age variable into quintiles, using the median age of each subgroup as the age value for subjects within that group (i.e., 7.5, 11, 14, 17.5, 21). The model indicated a significant effect for both age and sex (Model 1; see table 2). Next, we added a quadratic age term to the model, which resulted in an improvement in model fit, as evidenced by decreases in the log likelihood, AIC and BIC, an increase in the Wald χ^2 (Model 2) and a significant likelihood ratio test of Model 1 nested within Model 2 (LR $\chi^2_{(1)} = 24.8$, $p<0.01$). The quadratic age term was significant, indicating that the group effect of age on the change in ADHD symptoms was not linear. Next, we estimated the model using sex, age, quadratic age, and the quadratic age-by-sex interaction as fixed effects, to test if the slope of ADHD symptom change was conditional on sex (Model 3). The quadratic age-by-sex interaction term was not significant, and resulted in a worsening of model fit and a non-significant likelihood ratio test of Model 2 nested within Model 3. Thus. Model 2 was the final model with a significant quadratic age

effect, indicating that the decline in ADHD symptoms accelerated with increasing age. Also, there was a significant sex effect, indicating that across age, females exhibited significantly more ADHD symptoms than males.

Structural equation model of psychiatric comorbidity

In fitting a model estimating a latent childhood comorbid psychopathology factor and a latent adolescent comorbid psychopathology factor, with all parameters constrained to be equal across the male and female samples, we found a poor overall fit, as indicated by the statistically significant goodness of fit chi square test (Model 1 in table 3). In Model 2, we allowed the factor loadings, error variances, and factor correlations to be different between groups, and the fit of the model improved. Thus, we then estimated the model within stratum of sex. In males, the full model achieved adequate fit (Model 3). However, the anxiety symptom score was not a significant predictor of adolescent comorbid psychopathology (factor loading = 0.18, t=1.49, error variance=0.97, R^2=0.03). Thus, we re-estimated the model without the anxiety symptom score, and this model fit the data well (Model 4). In females, the full model achieved adequate fit (Model 5); however, the error variance for the adolescent disruptive behavior disorder score was negative, with an R^2 estimate greater than one (i.e., a so-called Haywood case) (Hayduk, 1987). To avoid the hazards of interpreting a model with estimates beyond the admissible parameter space, we re-estimated the model with the error variances of the adolescent and childhood disruptive behavior disorder variables constrained to be equal. This model also fit the data well and provided interpretable estimates (Model 6). The parameter estimates from the final models are depicted in figure 1. As shown, the standardized factor loadings for both the childhood and adolescent psychopathology latent variables are larger in the female sample. Anxiety disorders are relevant to the latent comorbid psychopathology construct in females, but not males. Also, the effect of latent childhood comorbid psychopathology on latent adolescent comorbid psychopathology, which can be interpreted as a stability coefficient of comorbid psychopathology across development, is greater in females compared to males.

Structural equation model of psychiatric comorbidity and ADHD

Next, we estimated a SEM including the association between ADHD in childhood and adolescence with the latent childhood and adolescent comorbid psychopathology factors, respectively, within stratum of sex. In males, the structural equations revealed that ADHD was significantly associated with comorbid psychopathology in both childhood (parameter estimate = 0.67, standard error=0.13, t=5.2) and adolescence (factor loading = 0.66, standard error=0.12, t=5.5); these associations were of a similar magnitude. However, the model did not fit the data well (df=51, Satorra-Bentler χ^2=106.2, p<0.01; RMSEA=0.084; AIC=160.2). In females, the structural equations also revealed that ADHD was significantly associated with comorbid psychopathology in both childhood (parameter estimate = 0.76, standard error=0.08, t=9.3) and adolescence (factor loading = 0.68, standard error=0.10, t=7.1). In contrast to the sample of males, the model in the female sample fit the data well (df=63, Satorra-Bentler χ^2=75.9, p=0.13; RMSEA=0.038; AIC=131.9).

Finally, we re-estimated the final comorbid psychopathology model within strata of sex, including an additional path from adolescent ADHD to adolescent comorbid psychopathology. These models estimated the stability of comorbid psychopathology from childhood to adolescence, while accounting for the contemporaneous correlation between adolescent psychopathology and adolescent ADHD. In males, the association between childhood and adolescent comorbid psychopathology was no longer statistically significant (parameter estimate = 0.20, standard error=0.16, t=1.3), although the association between adolescent ADHD and adolescent psychopathology was significant (parameter estimate = 0.56, standard error=0.16, t=3.5). This model provided a marginal fit to the data (df=24,

Satorra-Bentler χ^2=34.6, p=0.08; RMSEA=0.053; AIC=76.6). In females, the associations between childhood and adolescent psychopathology (parameter estimate = 0.53, standard error=0.20, t=2.7), and adolescent ADHD and adolescent psychopathology (parameter estimate = 0.46, standard error=0.18, t=2.6) were both statistically significant. This model provided a good fit to the data (df=25, Satorra-Bentler χ^2=28.6, p=0.28; RMSEA=0.032; AIC=68.6; see figure 2).

DISCUSSION

In a sample of males and females with and without ADHD assessed prospectively from childhood into adolescence and young adulthood, we tested whether sex moderated: a) course of ADHD; and b) the course and pattern of covariance of comorbid psychopathology. First, we found no evidence that sex moderated the effect of age on ADHD symptoms; in both genders, age exhibited a similar effect on the decline of ADHD symptoms. However, we found evidence that the female sample demonstrated greater stability in comorbid psychopathology from childhood into adolescence. Furthermore, we found that patterns of associations between ADHD symptoms and comorbid psychopathology over time differed by sex; in males, childhood and adolescent comorbid psychopathology were not correlated with adolescent ADHD, while in females, the stability of comorbid psychopathology remained significant after accounting for the correlation between adolescent comorbid psychopathology and ADHD.

The results of our latent growth curve analysis were consistent with our previous findings of declining symptoms with age (Biederman et al., 1996). Also, these data are consistent with studies indicating that the prevalence of ADHD decreases as age increases (Faraone et al., 2006, Costello et al., 2003), and is larger is pediatric samples (Faraone et al., 2003) than in adult samples (Kessler et al., 2006). We also found that a significantly higher level of ADHD symptoms, regardless of age, in females compared to males. However, while this difference was statistically significant, it was of minimal clinical significance because of the small effect size (β=−0.14, corresponding to approximately one-tenth of a standard deviation). Thus, this finding should be interpreted cautiously until confirmed by future studies comparing males versus females with ADHD.

The results of our SEM analyses show that in both genders, comorbid psychopathology in childhood is a significant and robust predictor of comorbid psychopathology in adolescence. However, the results also indicate that the factor structure of comorbid psychopathology across development differs in males compared to females (i.e., larger factor loadings in females, and anxiety disorders included in the latent adolescent comorbid psychopathology factor in females, but not males). These results indicate that in males, the observed psychopathology variables may be measuring another factor (other than the latent psychopathology factor) to a greater degree than in females. Furthermore, the stability of comorbid psychopathology across developmental epoch was greater in females compared to males. This finding is consistent with a prospective study of a large representative population sample examining the 3-month prevalence of psychiatric disorders across childhood and adolescence (Costello et al., 2003). This study found that children with a positive history of a psychiatric diagnosis were significantly more likely to have a disorder at a follow-up assessment, but this association was significantly greater in female children compared to males.

Secondly, both the childhood and adolescent comorbid psychopathology factors were significantly correlated with contemporaneous ADHD factors, in both males and females. However, in males, the model was a poor fit to the data, while in females, the data fit the model well. In the male sample, the specified paths were significant and the modification

indices did not suggest the inclusion of additional path or error covariance terms. Thus, this discrepancy in model fit suggests that in males, additional factors and/or variables may need to be incorporated to account for the covariance between ADHD and comorbid psychopathology across childhood and adolescence.

Thirdly, in the male sample, childhood and adolescent comorbid psychopathology were no longer correlated after the inclusion of adolescent ADHD into the model. However, in the female sample, the stability of comorbid psychopathology remained significant after accounting for the correlation between adolescent comorbid psychopathology and ADHD. Given that ADHD, by definition, begins in childhood, the adolescent ADHD factor can be interpreted as a measure of ADHD persistence. Thus, these results suggest that in males, adolescent comorbid psychopathology may be a function of ADHD severity and persistence, more so than the stability of childhood comorbid psychopathology. However, in females, adolescent comorbid psychopathology was a function of both previous psychiatric disorders as well as persistent ADHD symptoms.

Taken together, these results support the hypothesis that sex is a critical modifying factor in developmental models of the correlates of ADHD. These results are consistent with studies from our group that detected the moderating effect of sex on the association between ADHD and functional outcomes (Biederman et al., 2002a). More broadly, these findings are also consistent with important sex differences that have been found in the prevalence of psychiatric disorders, functional neuroimaging studies, fetal brain development, hormonal responses to stress, and cognitive functioning (Holden, 2005).

These results should be considered in the light of methodological limitations. Because our sampling consisted largely of Caucasian subjects, our results may not generalize to other racial or ethnic groups. The probands in our sample were originally ascertained according to DSM-III-R criteria, and our results may not generalize to samples ascertained by DSM-IV criteria. However, considering the very high overlap between the two definitions (93% of DSM-III-R cases received a DSM-IV diagnosis (Biederman et al., 1997)), any effect should be minimal. Also, since we were compelled to standardize the ADHD symptom scores to combine observations measured with both DSM-III-R and DSM-IV criteria, effect estimates from the growth curve models have limited clinical applicability. Additionally, although our sample comprised probands and their siblings, our analyses did not take familial clustering into account. When repeating our linear growth curve models using only probands, the pattern of results remained the same. We could not replicate our SEMs without siblings because of sample size limitations. Finally, we did not have enough subjects to test more comprehensive SEMs. Future studies with adequate numbers of males and females should incorporate other measures pertinent to ADHD, such as cognitive, academic, and social functioning.

Despite these concerns, our findings indicate that while the course of ADHD across childhood and adolescence did not differ between males and females, patterns of psychiatric comorbidity were conditional on sex. Future studies should explicitly test how sex modifies the associations between ADHD and risk factors and ADHD and associated functional outcomes, consistent with the United States' National Institutes of Health report entitled, "Research Priorities for Women's Health" (Office for Research on Women's Health, 2005), which states that: "Basic, translational, behavioral and clinical research in women's health, especially applied to sex/gender differences, are of particular interest".

Key Points

- ADHD persists into adolescence and is a strong predictor of psychiatric comorbidity in both males and females
- We found no evidence that sex moderated the effect of age on ADHD symptoms; in both genders, age exhibited a similar effect on the decline of ADHD symptoms.
- We found greater stability in psychopathology from childhood into adolescence in females relative to males and that the patterns of association between ADHD symptoms and psychopathology over time differed by sex.
- In forecasting prognosis, sex should be considering as a critical modifying factor of the course of ADHD and its comorbid psychiatric conditions.

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Biographies

Dr. Eric Mick receives research support from the following sources and is on an advisory board for the following sources: McNeil Pediatrics, Ortho-McNeil Janssen Scientific Affairs, Pfizer, Shire Pharmaceuticals, and the National Institute of Mental Health (NIMH) and has had an advisory or consulting relationship with Pfizer and Shire Pharmaceutical.

In the past year, Dr. Stephen Faraone has received consulting fees and has been on Advisory Boards for Eli Lilly and Shire and has received research support from Eli Lilly, Pfizer, Shire and the National Institutes of Health. In previous years, Dr. Faraone has received consulting fees or has been on Advisory Boards or has been a speaker for the following sources: Shire, McNeil, Janssen, Novartis, Pfizer and Eli Lilly. In previous years he has received research support from Eli Lilly, Shire, Pfizer and the National Institutes of Health.

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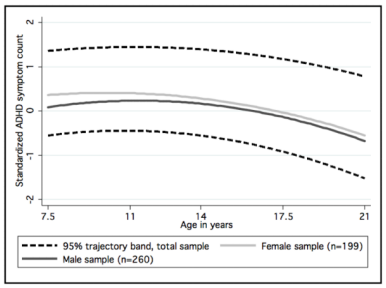

Figure 1.
Predicted change in ADHD symptoms across development in male and female youth

Figure 2.
Standardized parameter estimates of psychiatric comorbidity from final latent models, by sex

Figure 3.
Structural equation models of psychiatric comorbidity and adolescent ADHD, by sex

Table 1

Demographic characteristics of ADHD sample, stratified by sex

Demographic Characteristics	Females	Males	Test Statistic (df), p value
	n=203	n=268	
Number of probands[1]	143 (70)	147 (55)	$\chi^2(1) = 11.9$, $p<0.01$
Age at first assessment	11.7±4.3	11.4±4.3	t (469) = 0.7, p=0.49
Age at most recent follow-up	16.6±5.4	19.2±5.8	t (469) = −4.9, p<0.01
Parental social class at baseline[2]	1.9±0.9	1.9±1.0	t (469) = 0.3, p=0.79
Number of assessments			$\chi^2(2) = 94.4$, $p<0.01$
1	30 (15)	27 (10)	
2	151 (74)	97 (36)	
3	22 (11)	144 (54)	

Values in table represent *mean±standard deviation* or *frequency(percent)*

[1] Number of subjects ascertained as probands. The remaining subjects are siblings of probands

[2] Social class measurement ranges from 1 through 5; 1 indicates most affluent social class, 5 indicates least affluent

Table 2

Linear growth curve models of ADHD symptoms in males and females

Fixed Effects	Model 1	Model 2	Model 3
Sex	β=−0.15, Z=−2.2, p=0.03	β=−0.14, Z=−2.0, p=0.04	β=−0.21, Z=−1.8, p=0.08
Age	β=−0.06, Z=−8.9, p<0.01	β=0.19, Z=4.6, p<0.01	β=0.19, Z=4.7, p<0.01
Age^2	---	β=−0.01, Z=−6.1, p<0.01	β=−0.01, Z=−6.1, p<0.01
Sex * Age^2	---	---	β=0.00, Z=0.7, p=0.46
Goodness of Fit			
Log Likelihood	−1303.0	−1290.6	−1297.1
AIC	2622.0	2599.2	2614.2
BIC	2661.1	2643.1	2663.0
Wald χ^2, p value	χ^2 (3) =125.7, p<0.01	χ^2 (4) = 165.3, p<0.01	χ^2 (5) = 165.6, p<0.01

Table 3

Structural equation models of psychiatric comorbidity in males and females with ADHD

Goodness of Fit Statistics	Males and Females, n=295		Males only, n=156		Females only, n=139	
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Degrees of Freedom	41	26	13	8	13	13
Satorra-Bentler Scaled Chi-Square	χ^2 =58.9, p=0.034	χ^2 =29.2, p=0.30	χ^2 =19.5, p=0.11	χ^2 =1.8, p=0.99	χ^2 =10.9, p=0.62	χ^2 =13.1, p=0.44
RMSEA[1]	0.055	0.029	0.057	<0.01	<0.01	<0.01
AIC[2]	88.92	89.20	49.5	27.76	40.94	43.11

[1] Root Mean Square Error of Approximation

[2] Akaike information criterion