# Absence of Gender Effects on Attention Deficit Hyperactivity Disorder: Findings in Nonreferred Subjects

Joseph Biederman, M.D.

Anne Kwon, M.S.

Megan Aleardi, B.A.

Virginie-Anne Chouinard, B.Sc.

Teresa Marino, B.A.

Heather Cole, B.A.

Eric Mick, Sc.D.

Stephen V. Faraone, Ph.D.

**Objective:** In a previous study, the authors found that, compared with referred boys with attention deficit hyperactivity disorder (ADHD), girls are less likely to manifest comorbid disruptive behavior disorders and learning disabilities—characteristics that could adversely affect identification of ADHD in girls. However, because referral bias can affect outcome, these findings require replication in nonreferred groups of ADHD subjects.

**Method:** The authors evaluated gender effects in a large group of nonreferred siblings (N=577) of probands with ADHD and non-ADHD comparison subjects. Ninetyeight of the nonreferred siblings (N=73 males, N=25 females) met the criteria for diagnosis of ADHD, and 479 (N=244 males, N=235 females) did not meet those criteria. All siblings were systemati-

cally and comprehensively assessed with measures of emotional, school, intellectual, interpersonal, and family functioning. The assessment battery used for the siblings was the same as that used for the probands.

**Results:** The nonreferred males and females with ADHD did not differ in DSM-IV subtypes of ADHD, psychiatric comorbidity, or treatment history. They also showed similar levels of cognitive, psychosocial, school, and family functioning.

**Conclusions:** These findings suggest that the clinical correlates of ADHD are not influenced by gender and that gender differences reported in groups of subjects seen in clinical settings may be caused by referral biases.

(Am J Psychiatry 2005; 162:1083-1089)

roups of subjects with attention deficit hyperactivity disorder (ADHD) seen in clinical settings have been predominantly male. As a result, manifestations of ADHD in female subjects and gender differences in ADHD have been neglected in the extensive ADHD research literature (1). A meta-analysis by Gaub and Carlson (2) documented the scarcity of information in this area and suggested that gender differences in the phenotypic expression of the disorder result in referral of more boys than girls, which would explain why the male predominance in ADHD is greater in clinical groups of ADHD subjects, compared with groups of ADHD subjects in the community.

Consistent with this hypothesis are findings from the large NIMH Collaborative Multisite Multimodal Treatment Study of Children with ADHD (N=498). Several reports from this study showed that girls with ADHD were less impaired than boys on most ratings (3) and that boys with ADHD engaged in more rule-breaking and externalizing behaviors than did girls with ADHD (4). These gender differences in clinically important ADHD features may help explain why boys with ADHD are referred more often than girls.

Also consistent with the Multimodal Treatment Study findings are our group's findings based on data from a large number of boys and girls with and without ADHD ascertained from pediatric and psychiatric referrals (5). Analysis of gender differences showed that, compared with ADHD boys, ADHD girls had a lower prevalence of

disruptive behavior disorders and learning disabilities in reading or mathematics. Taken together, these findings raise concerns that referral bias may account for the gender differences in ADHD that are reported in the literature. These concerns suggest the need to evaluate gender effects in nonreferred groups of ADHD subjects.

Whether gender influences the clinical manifestations of ADHD has important clinical and public health implications. A better understanding of gender effects in ADHD can lead to improved identification of girls with the disorder, helping to reduce the large gender gap in groups of referred ADHD subjects. As ADHD is common (occurring in 8%–10% of schoolchildren) (6) and chronic (lifelong in many cases), an improved identification of ADHD in females can affect the lives of millions of girls and women with ADHD and address a significant public health problem. Because intervention follows identification, an improved understanding of gender differences in ADHD can result in improved therapeutic opportunities for girls with ADHD, which would have an effect on women's health in our society.

This study sought to assess gender effects in a nonreferred community group of subjects with and without ADHD. Based on the large male-to-female ratio in groups of ADHD subjects seen in clinical settings, we hypothesized that no gender differences would be observable in

TABLE 1. Demographic Characteristics of Nonreferred Female and Male Subjects With and Without Attention Deficit Hyperactivity Disorder (ADHD)<sup>a</sup>

		Female	Subjects			Male 9	Subjects					
Characteristic	ADHD (N=25)		No ADHD (N=235)		ADHD (N=73)		No ADHD (N=244)		Interaction of Gender and ADHD Status			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Z	р	beta	95% CI
Age (years) Socioeconomic status <sup>b</sup>	13.6 1.9	4.4 0.9	13.7 1.7	5.5 0.8	12.6 2.0	4.7 1.1	13.4 1.8	5.5 0.9	-0.6 0.4	0.56 0.68	-0.7 0.1	-2.8 to 1.5 -0.3 to 0.5
	N	%	N	%	N	%	N	%	Z	р	Odds Ratio	95% CI
Parents divorced or separated	20	80	195	83	56	77	209	86	-0.7	0.20	0.7	0.4 to 1.2

<sup>&</sup>lt;sup>a</sup> Subjects were nonreferred siblings of probands with ADHD and non-ADHD comparison subjects ages 6–17 years who were recruited from psychiatric and pediatric settings.

nonreferred males and females with ADHD. To our knowledge, this issue has not been previously examined.

#### Method

### Subjects

Subjects were ascertained from two identically designed family studies of boys (ADHD probands: N=140, non-ADHD comparison probands: N=120, siblings: N=303) (7) and girls (ADHD probands: N=140, non-ADHD comparison probands: N=122, siblings: N= 274) (8). Both studies ascertained ADHD probands and non-ADHD comparison probands ages 6-17 years from psychiatric and pediatric sources. Probands were excluded if they had been adopted, their nuclear family was not available for study, or they had major sensorimotor handicaps (paralysis, deafness, blindness), psychosis, autism, inadequate command of the English language, or a full-scale IQ less than 80. The present study reports on the combined group of siblings from both studies (N=577). The siblings were evaluated with the same assessment battery used for the probands. There were no exclusionary criteria for the siblings. This study was reviewed and approved by the Partners Human Research Committee Institutional Review Board at Massachusetts General Hospital. All parents signed written consent for participation, and the children signed age-appropriate assent forms.

Two independent sources provided the index proband children. Psychiatrically referred ADHD probands were selected from consecutive referrals to a pediatric psychopharmacology clinic at a major academic center. Parents, pediatricians, and schools had referred these children for psychiatric evaluations. Pediatrically referred ADHD probands consisted of pediatric patients from a health maintenance organization (HMO). Within each setting, we selected non-ADHD comparison probands from outpatients at pediatric medical clinics.

A three-stage ascertainment procedure was used to select the probands. For ADHD probands, the first stage consisted of the patient's referral to a psychiatric or pediatric clinic resulting in a clinical diagnosis of ADHD by a child psychiatrist or pediatrician, which was recorded in the clinic record. The second stage confirmed the diagnosis of ADHD by screening all children who had a positive ADHD diagnosis at the first stage with a telephone questionnaire asking the primary caregiver about the 14 DSM-III-R symptoms of ADHD. The third stage confirmed the diagnosis made by means of the telephone questionnaire with face-to-face structured interviews with the primary caregiver. Only patients who received a positive diagnosis at all three stages were included as ADHD probands in the final analysis. Non-ADHD comparison probands were ascertained from referrals to medical

clinics for routine physical examinations at both the major academic center and HMO sites and were included only if they did not meet the ADHD criteria at each of the three stages of the ascertainment procedure. There were no selection criteria of any kind to ascertain the siblings.

#### Measures

Psychiatric assessments of all siblings younger than age 18 years (N=453) were made with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version (K-SADS-E) (9). Diagnoses were based on indirect interviews with the primary caregivers and direct interviews with children older than age 12 years. Diagnostic assessments of adult siblings (age 18 years or older, N=124) were based on direct interviews with the Structured Clinical Interview for DSM-III-R (10). To assess childhood diagnoses in adult siblings, we administered modules from the K-SADS-E that covered childhood diagnoses. All assessments were made by raters who were blind to the proband's diagnostic group (ADHD or non-ADHD) and ascertainment site. Different interviewers met with the primary caregivers and the children in order to maintain blindness to ADHD status and to prevent information provided by one informant from influencing the assessment of the other.

A committee of psychiatrists with board certification in both child and adult psychiatry resolved all diagnostic uncertainties. The committee members were blind to the subjects' ascertainment group, ascertainment site, all data collected from family members, and all nondiagnostic data (e.g., neuropsychological test data). Kappa coefficients of agreement were computed between raters and three board-certified psychiatrists who listened to the audiotaped interviews conducted by the raters. On the basis of 173 interviews, the median kappa was 0.86; kappa was 0.99 for ADHD, 0.93 for conduct disorder, 0.80 for multiple anxiety disorders, 0.83 for major depression, and 0.94 for bipolar disorder. Although the cases in the reliability analysis were not included in the study reported here, the interviews for both groups were conducted in the same research laboratory by identically trained staff under consistent supervision from the first author. Thus, these reliability estimates are applicable to the data collection procedures of the present study. These statistics for raters rating the same interview showed excellent agreement of ratings but did not address the degree of agreement that would be attained between two separate interviews of the same subject.

In addition to evaluating psychiatric status, we used indirect structured diagnostic interviews to obtain data on the following variables: social functioning measured with the Social Adjustment Inventory for Children and Adolescents (11), socioeconomic status (12), divorce or separation of parents in family of origin, family environment measured with the Family Environment

<sup>&</sup>lt;sup>b</sup> Measured with the Hollingshead Four-Factor Index of Social Status (12).

TABLE 2. Clinical Characteristics of Nonreferred Female and Male Subjects With Attention Deficit Hyperactivity Disorder (ADHD)

Characteristic	Female ADI (N=	HD Subjects 25)	Male ADHI (N=	,	Analysis		
	Mean	SD	Mean	SD	Z	р	
ADHD characteristics							
Age at onset (years)	2.9	2.4	3.2	2.3	0.6	0.58	
Impairment <sup>a</sup>	2.0	0.7	2.2	0.7	1.2	0.22	
Duration (years)	10.0	5.1	8.7	5.1	-1.1	0.29	
Duration from illness onset to treatment onset (years)	6.3	6.0	6.0	4.6	-0.4	0.69	
	N	%	N	%	Z	р	
Treatment history							
Counseling	2	8	5	7	-0.7	0.50	
Hospitalization	0	0	1	1		1.00 <sup>b</sup>	
Medication	5	20	20	27	-0.2	0.86	
Combined therapy	4	16	21	29	0.5	0.62	

a Measured with the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Epidemiologic Version (9) or the Structured Clinical Interview for DSM-III-R (10).

Scale (13), full-scale IQ measured with the vocabulary and block design subtests of the Wechsler intelligence tests (14), adaptive functioning measured with the Global Assessment of Functioning Scale (GAF) of DSM-III-R, and school difficulties (special class placement, repeated grades, use of tutoring). The definition of learning disabilities under Public Law 94–142 requires a significant discrepancy between a child's potential and achievement (15). We operationalized this discrepancy with the procedure recommended by Reynolds (16), which we have used elsewhere (17).

#### Statistical Analysis

Our main hypothesis was that nonreferred ADHD males and females would not differ with respect to the effect that ADHD exerted on functioning in multiple domains. Data from non-ADHD comparison subjects are presented so that interactions could be tested to determine if ADHD is a similar risk factor in males and females with respect to sex-matched non-ADHD subjects. To determine if ADHD has a different presentation in nonreferred females with the disorder, compared with nonreferred males with the disorder, we also conducted within-ADHD, between-gender pairwise comparisons. Generalized estimating equations were used to estimate logistic and linear regression models for binary and continuous data, respectively. The effect of gender within the ADHD group (pairwise comparison of ADHD females versus ADHD males) was likewise tested by using generalized estimating equations for logistic and linear regression models.

All analyses were adjusted to account for the ascertainment status (ADHD or non-ADHD) of the index proband. Statistical significance was determined at p<0.05. Although several statistical tests were conducted, we chose not to employ a correction for multiple testing (e.g., Bonferroni), because this procedure alters the statistical inference of a study from the testing of a number of specific hypotheses to a test of the universal null hypothesis (i.e., that the null hypotheses across all the variables are simultaneously true) (18-20). Testing the universal null hypothesis is not of interest in the present report, because differences in specific variables could have important interpretive consequences. Other drawbacks to this method include an unacceptable increase in the type II error rate (18, 19) and the issue of how many tests are to be included in the adjustment (18). Throughout the analyses, missing data accounted for, on average, a 12% decrease in study group size and thus had a minimal effect, if any, on our results. Thus, we chose not to implement an imputation procedure, as the information it would add would be outweighed by its interpretative costs.

For all analyses we additionally restricted the study group to only high-risk siblings of referred male and female subjects with

ADHD, and we found no differences in our results. Thus, we present findings for the entire sibling study group.

#### Results

From the combined pool of 577 siblings, stratification by gender and ADHD versus non-ADHD status yielded four groups of nonreferred subjects: 1) ADHD females (N=25), 2) non-ADHD females (N=235), 3) ADHD males (N=73), and 4) non-ADHD males (N=244). Demographic characteristics are presented in Table 1. There were no significant interaction effects among the groups for age, socioeconomic status, or intactness of family. Pairwise comparisons of demographic variables between ADHD males and ADHD females were also nonsignificant (Table 1).

Although the presence or absence of a diagnosis of ADHD was based on DSM-III-R criteria, we constructed proxies for the DSM-IV subtypes from the available information using a method we have previously validated. There were no significant differences (all p values >0.05) in the frequency of subtypes of ADHD between males and females with ADHD, with the combined type emerging as the most prevalent type for both groups (58% of females and 61% of males). Inattentive type was the next most common, found in 25% and 27% of the female and male ADHD groups, respectively. The hyperactive/impulsive type was the least common for both genders, found in 13% of the female ADHD group and 9% of the male ADHD group.

ADHD characteristics such as age at onset, impairment, and duration did not significantly differ between male and female ADHD groups. The number of years from onset of ADHD to the first treatment for the disorder also did not differ by gender. ADHD treatment histories were similarly distributed between ADHD males and females; the most prevalent treatments in both groups were medication only and combined medication and psychotherapy (Table 2).

There were no significant differences between male and female ADHD subjects in the rate of any of the 14 DSM-III-R ADHD symptoms (all p values >0.05). The least prevalent

<sup>&</sup>lt;sup>b</sup> Fisher's exact test.

TABLE 3. Psychiatric Comorbidity in Nonreferred Female and Male Subjects With and Without Attention Deficit Hyperactivity Disorder (ADHD)

	Female Subjects					Male S	ubjects					
	–	HD =25)		DHD 235)		HD =73)		DHD 244)	Interac	tion of 0	Gender and A	DHD Status
Disorder	N	%	N	%	N	%	N	%	Z	р	Odds Ratio	95% CI
Behavior disorders												
Any behavior disorder	13	52	13	6	35	48	31	13	-1.9	0.06	0.3	0.1 - 1.0
Conduct disorder	5	20	2	1	14	19	11	5	-1.8	0.07	0.2	<0.1-1.1
Oppositional defiant disorder	13	52	13	6	29	40	24	10	-1.9	0.053	0.3	0.1 - 1.0
Mood disorders												
Any mood disorder	8	32	17	7	15	21	15	6	-0.7	0.49	0.7	0.2 - 2.2
Major depression (severe)	8	36	15	7	12	20	11	5	-0.7	0.49	0.6	0.2 - 2.3
Bipolar disorder	3	12	3	1	11	15	4	2	< 0.1	0.99	1.3	0.1 - 7.3
Dysthymia	0	0	7	3	5	7	4	2			a	
Anxiety disorders												
Multiple anxiety disorders	7	28	32	14	16	22	20	8	0.4	0.67	1.3	0.4-4.2
Simple phobia	3	12	31	13	13	18	21	9	1.3	0.21	2.6	0.6-11.1
Social phobia	6	24	20	9	12	16	16	7	-0.3	0.78	0.8	0.2 - 3.0
Agoraphobia	3	12	16	7	6	8	11	5	<-0.1	0.97	1.0	0.2 - 4.7
Panic disorder	2	8	6	3	3	4	2	1	0.3	0.72	1.6	0.1-18.6
Separation anxiety	7	28	22	9	14	19	17	7	-0.3	0.81	0.8	0.2 - 3.1
Overanxious disorder	7	28	30	13	12	16	19	8	-0.2	0.83	0.9	0.3 - 2.9
Other disorders												
Any substance use disorder	4	16	14	6	10	14	29	12	-1.3	0.21	0.4	0.1 - 1.7
Psychosis	0	0	0	0	3	4	2	1			<u></u> a	
Obsessive-compulsive disorder	2	8	3	1	5	7	2	1	0.3	0.79	1.3	0.2-11.4
Tic disorder	2	8	4	2	10	14	12	5	-0.5	0.62	0.6	0.1-4.2
Enuresis	3	12	24	10	16	22	51	21	-0.2	0.87	0.9	0.2 - 3.6
Encopresis	0	0	1	1	7	10	6	2			a	
Anorexia	1	4	4	2	0	0	0	0			a	
Bulimia	1	4	4	2	1	1	0	0			a	

a Not defined.

symptom for both genders was "difficulty playing quietly," endorsed for 44% of females and 47% of males. The most common symptom for females was "difficulty sustaining attention" (96%), and the most common symptom for males was "easily distracted" (93%).

The prevalence of psychiatric comorbidity in ADHD versus non-ADHD comparison subjects was similar for males and females. We found no significant interactions between gender and ADHD status. This result shows that the higher risk for psychiatric comorbidity in ADHD children does not differ by gender. Regardless of gender, the prevalence of psychiatric comorbidity was universally higher in ADHD subjects, compared to non-ADHD subjects. Furthermore, there were no significant pairwise differences in rates of comorbid disorders between male and female subjects with ADHD (Table 3).

We found no significant interactions between ADHD status and gender for the measures of functioning. There were no differences in full-scale IQ, rates of learning disabilities, and school performance indices. GAF scores uniformly showed more impairment in ADHD subjects than in non-ADHD subjects in both males and females. Rates of school dysfunction and learning disabilities were generally higher among ADHD subjects, compared to non-ADHD subjects, irrespective of gender. However, there were no significant differences in educational functioning or GAF scores between ADHD males and females (Table 4). Scores on the Social Adjustment Inventory for Children

and Adolescents showed more impaired interpersonal functioning in ADHD subjects, compared to non-ADHD subjects, in both genders, with no significant interaction effects. Likewise, no significant ADHD status-by-gender interactions were found for ratings on the Family Environment Scale; a more negative family environment was seen for subjects with ADHD, compared to non-ADHD subjects, in both genders. Measures of both social adjustment and family environment were not found to be significantly different between ADHD males and ADHD females.

## Discussion

This study systematically evaluated gender effects in a nonreferred group of 577 subjects with and without ADHD. We found no significant differences between genders in subtypes of ADHD, with the combined type emerging as the most common type in both genders. There were no differences between the genders in age at onset, impairment related to ADHD, duration of ADHD, or individual ADHD symptoms. Regardless of gender, comorbid psychiatric disorders were more prevalent in ADHD subjects than in non-ADHD subjects. Likewise, no significant interaction effects were found for cognitive, school, psychosocial, family, or treatment variables. Subjects with ADHD showed greater impairment on these variables irrespective of gender. These results, which show that ADHD is expressed similarly in males and females, both confirm

TABLE 4. Measures of Functioning in Nonreferred Female and Male Subjects With and Without Attention Deficit Hyperactivity Disorder (ADHD)

		Female	Subjects			Male S	ubjects						
Measure	ADHD (N=25)		No ADHD (N=235)			ADHD (N=73)		No ADHD (N=244)		Interaction of Gender and ADHD Status			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Z	р	beta	95% CI	
Global Assessment of									_	P		22/12	
Functioning Scale score													
Past	52.1	8.5	65.5	9.9	52.4	7.9	64.5	10.0	0.7	0.51	1.3	-2.6 to 5.3	
Current	58.7	11.0	70.7	7.2	57.9	8.1	69.3	8.6	0.3	0.80	0.6	-4.0 to 5.2	
Estimated full-scale IQ	107.5	12.1	111.3	11.3	110.0	12.7	111.6	12.5	0.7	0.46	2.2	-3.5 to 7.9	
Social Adjustment													
Inventory for Children													
and Adolescents score													
School behavior	2.6	0.9	1.6	0.6	2.5	8.0	1.8	0.7	-1.6	0.11	-0.4	-0.8 to 0.1	
Spare-time activities	2.2	0.6	1.8	0.6	2.1	0.7	1.9	0.6	-1.0	0.31	-0.2	-0.5 to 0.2	
Spare-time problems	2.3	0.9	1.4	0.6	2.1	0.7	1.5	0.5	-1.5	0.13	-0.3	-0.7 to 0.1	
Activity with peers	2.7	0.6	1.6	0.6	2.1	0.8	1.8	0.7	-1.0	0.33	-0.2	-0.5 to 0.2	
Problems with peers	2.1	0.9	1.4	0.6	2.1	0.9	1.6	0.7	-1.0	0.32	-0.2	-0.6 to 0.2	
Activity with siblings	1.8	0.6	1.7	0.7	1.9	0.7	1.7	0.7	0.6	0.56	0.1	-0.2 to 0.4	
Problems with siblings	2.2	0.9	1.6	0.7	2.1	0.8	1.7	0.7	-1.3	0.19	-0.3	-0.7 to 0.1	
Relationship with													
mother	1.7	0.7	1.4	0.6	1.6	0.7	1.5	0.6	-0.7	0.46	-0.1	-0.5 to 0.2	
Relationship with father	2.0	0.9	1.7	8.0	1.9	0.8	1.6	0.8	-0.5	0.63	-0.1	-0.6 to 0.3	
Problems with parents	1.8	0.9	1.3	0.5	1.9	0.8	1.4	0.6	-0.1	0.90	-0.1	-0.4 to 0.4	
Family Environment Scale													
score													
Cohesion	45.6	18.8	48.1	19.4	42.5	19.5	49.1	19.5	-1.0	0.31	-4.3	-13.0 to 4.2	
Expressiveness	47.8	11.8	48.2	15.8	46.5	13.9	50.4	14.1	-1.1	0.26	-3.5	-9.4 to 2.6	
Conflict	61.8	12.7	53.9	12.7	59.0	13.3	54.6	12.9	-1.1	0.26	-3.2	-8.8 to 2.3	
	N	%	N	%	N	%	N	%	Z	р	Odds Ratio	95% CI	
Learning disability													
Arithmetic	1	4	15	7	13	20	13	6	1.7	0.10	6.6	0.7 to 62.0	
Reading	4	17	7	3	10	15	14	7	-1.1	0.30	0.4	0.1 to 2.1	
School functioning													
Repeated grade	5	20	13	6	17	23	35	14	-1.2	0.21	0.4	0.1 to 1.6	
Tutoring	15	60	66	28	44	60	76	31	-0.3	0.79	0.9	0.3 to 2.3	
Special class placement	1	4	7	3	18	25	20	8	0.9	0.39	2.8	0.3 to 27.0	

our study hypothesis and demonstrate that ADHD-associated impairments are correlates of ADHD in both genders.

The absence of gender effects in this nonreferred group contrasts with previous results reported by us and others in studies of referred subjects. This literature consistently reported that males with ADHD are more disruptive than females with the disorder (2, 5, 21).

The current findings confirm the clinical suspicion that disruptive behavior disorders drive referrals in pediatric ADHD. This phenomenon may help explain the much larger male-to-female ratio of up to 10:1 in pediatric ADHD, compared with the more modest 1.5:1 ratio in adult ADHD. Parents and teachers refer pediatric ADHD subjects, largely because of the comorbidity with disruptive behavior disorders, but adults are self-referred, largely due to the morbidity associated with ADHD itself (22, 23). Although the reasons for this state of affairs are not entirely clear, these findings suggest that gender-specific variations influence clinical pediatric practice in a manner that may adversely affect the identification of ADHD in girls. Considering that many girls are likely to have ADHD, this issue has large public health implications and is worthy of further research.

ADHD in both genders was associated with high levels of psychoeducational impairments. Both male and female ADHD subjects manifested similar impairments in emotional, school, family, and interpersonal functioning, relative to age- and gender-matched comparison subjects. These results extend to nonreferred subjects an extensive body of literature documenting the morbidity and disability associated with ADHD in referred subjects (5, 24, 25) and show that such findings are not caused by referral bias.

We failed to confirm previously described statistically significant findings in referred subjects. We found no gender-by-ADHD interaction between ADHD and substance use disorders (alcohol or drug abuse or dependence), which had been previously identified in referred subjects (24, 26, 27). However, because the current study group was relatively young, more work will be needed to further investigate this issue. Also, no meaningful differences between the genders were identified in the rates of learning disabilities (in reading and math) or major depression, comorbidities that were primarily found to be significantly underrepresented in referred girls, compared with referred boys (28, 29). Taken together, these results suggest that the gender differences previously identified in referred ADHD subjects could represent an artifact of refer-

ral bias rather than true gender effects. More work will be needed to confirm these findings.

No meaningful differences were observed in the treatment variables that we examined. These results are not consistent with the view that girls with ADHD receive inadequate treatment. Rather, these findings could be interpreted as suggesting that once identified, ADHD is treated similarly in both genders.

Our results must be viewed in light of some methodological limitations. Most of the subjects were Caucasian, and thus our results do not generalize to children of other racial or ethnic backgrounds. Because these results are cross-sectional, we cannot test the longitudinal effect of gender on ADHD or the relative effect of treatment in girls and boys. Our assessments relied on indirect parental reports and direct interviews with children older than age 12 years (50% of the study group) but did not include information collected from teachers or younger children. This limitation is not likely to affect the findings presented here because 1) both boys and girls were assessed with the same methods, 2) we found previously that parents' reports were very reliable and stable over time (30), and 3) others have raised questions regarding the validity of reports taken from very young children (31). Also, the number of female ADHD subjects in our study was small, relative to the size of other groups included in these analyses, and this difference may have limited our ability to detect small-size effects. Thus, our conclusions about the lack of gender effects in nonreferred ADHD children await confirmation in larger groups of subjects.

In this study, data from subjects who met the criteria for DSM-III-R ADHD but not for DSM-IV ADHD were included in the analysis. We did not use the DSM-IV ADHD criteria to define the study groups in this study because the probands were ascertained by using the DSM-III-R ADHD criteria. Based on previous work showing that DSM-III-R ADHD is highly convergent (positive predictive value of 93%) with DSM-IV ADHD in both boys and girls (32), we believe that these results will generalize to subjects with DSM-IV ADHD.

Despite these considerations, our results in a nonreferred group of ADHD subjects showed that gender did not influence ADHD-associated morbidity and dysfunction. In both genders ADHD was associated with high levels of psychiatric comorbidity and psychoeducational dysfunction. These results extend to nonreferred boys and girls with ADHD the extensively documented findings from groups of referred ADHD subjects that largely consist of boys, indicating that the reported findings are not due to referral bias. Our findings highlight that both genders are similarly affected by the severe morbidity and disability associated with ADHD. Furthermore, our findings call for more work to reduce the large gender gap in ADHD in pediatric practice and further elucidate the factors that could result in gender-based referral bias unfavorable to females.

Received Jan. 13, 2004; revision received April 21, 2004; accepted May 14, 2004. From the Clinical and Research Program in Pediatric Psychopharmacology, Child Psychiatry Service, Massachusetts General Hospital; Harvard Medical School, Boston; and the Harvard School of Public Health, Boston. Address correspondence and reprint requests to Dr. Biederman, Pediatric Psychopharmacology Unit (WACC 725), Massachusetts General Hospital, 15 Parkman St., Boston, MA 02114; jbiederman@partners.org (e-mail).

Supported in part by NIH grants R01 HD-36317-01 and R01 MH-50657-07 to Dr. Biederman.

#### References

- Arnold L: Sex differences in ADHD: conference summary. J Abnorm Child Psychol 1996; 24:555–569
- Gaub M, Carlson CL: Gender differences in ADHD: a meta-analysis and critical review. J Am Acad Child Adolesc Psychiatry 1997; 36:1036–1045
- Newcorn JH, Halperin JM, Jensen PS, Abikoff HB, Arnold LE, Cantwell DP, Conners CK, Elliott GR, Epstein JN, Greenhill LL, Hechtman L, Hinshaw SP, Hoza B, Kraemer HC, Pelham WE, Severe JB, Swanson JM, Wells KC, Wigal T, Vitiello B: Symptom profiles in children with ADHD: effects of comorbidity and gender. J Am Acad Child Adolesc Psychiatry 2001; 40:137–146
- Abikoff H, Jensen P, Arnold LE, Hoza B, Hechtman L, Pollack S, Martin D, Alvir J, March JS, Hinshaw SP, Vitiello B, Newcorn J, Greiner A, Cantwell DP, Conners CK, Elliott G, Greenhill LL, Kraemer H, Pelham W, Severe JB, Swanson JM, Wells K, Wigal T: Observed classroom behavior of children with ADHD: relationship to gender and comorbidity. J Abnorm Child Psychol 2002; 30: 349–359
- Biederman J, Mick E, Faraone SV, Braaten E, Doyle A, Spencer T, Wilens TE, Frazier E, Johnson MA: Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. Am J Psychiatry 2002; 159:36–42
- Faraone SV, Sergeant J, Gillberg C, Biederman J: The worldwide prevalence of ADHD: is it an American condition? World Psychiatry 2003; 2:104–113
- 7. Biederman J, Faraone SV, Keenan K, Benjamin J, Krifcher B, Moore C, Sprich-Buckminster S, Ugaglia K, Jellinek MS, Steingard R, Spencer T, Norman D, Kolodny R, Kraus I, Perrin J, Keller MB, Tsuang MT: Further evidence for family-genetic risk factors in attention deficit hyperactivity disorder: patterns of comorbidity in probands and relatives in psychiatrically and pediatrically referred samples. Arch Gen Psychiatry 1992; 49: 728–738
- Biederman J, Faraone SV, Mick E, Williamson S, Wilens TE, Spencer TJ, Weber W, Jetton J, Kraus I, Pert J, Zallen B: Clinical correlates of ADHD in females: findings from a large group of girls ascertained from pediatric and psychiatric referral sources. J Am Acad Child Adolesc Psychiatry 1999; 38:966–975
- Orvaschel H, Puig-Antich J: Schedule for Affective Disorders and Schizophrenia for School-Age Children—Epidemiologic Version (K-SADS-E), 4th revision. Fort Lauderdale, Fla, Nova University, Center for Psychological Studies, 1987
- Spitzer RL, Williams JBW, Gibbon M, First MB: Structured Clinical Interview for DSM-III-R—Non-Patient Edition (SCID-NP, Version 1.0). Washington, DC, American Psychiatric Press, 1990
- John K, Gammon GD, Prusoff BA, Warner V: The Social Adjustment Inventory for Children and Adolescents (SAICA): testing of a new semistructured interview. J Am Acad Child Adolesc Psychiatry 1987; 26:898–911
- 12. Hollingshead AB: Four-Factor Index of Social Status. New Haven, Conn, Yale University, Department of Sociology, 1975
- Moos R: Family Environment Scale, in The Ninth Mental Health Measurements Yearbook, vol 1. Edited by Mitchell JV. Lincoln,

- University of Nebraska, Buros Institute of Mental Measurements, 1985, pp 573–575
- 14. Sattler J: Psychological Assessment. New York, McGraw-Hill, 1988
- United States Office of Education: Assistance to states for education for handicapped children: procedures for evaluating specific learning disabilities. Federal Register 1977; 42:G1082– G1085
- Reynolds CR: Critical measurement issues in learning disabilities. J Spec Educ 1984; 18:451–476
- 17. Faraone SV, Biederman J, Lehman BK, Keenan K, Norman D, Seidman LJ, Kolodny R, Kraus I, Perrin J, Chen WJ: Evidence for the independent familial transmission of attention deficit hyperactivity disorder and learning disabilities: results from a family genetic study. Am J Psychiatry 1993; 150:891–895
- 18. Perneger TV: What's wrong with Bonferroni adjustments. BMJ 1998; 316:1236–1238
- Rothman K: No adjustments are needed for multiple comparisons. Epidemiology 1990; 1:43–46
- Savitz DA, Olshan AF: Multiple comparisons and related issues in the interpretation of epidemiologic data. Am J Epidemiol 1995; 142:904–908
- Carlson C, Tamm L, Gaub M: Gender differences in children with ADHD, ODD, and co-occurring ADHD/ODD identified in a school population. J Am Acad Child Adolesc Psychiatry 1997; 36:1706–1714
- Faraone SV, Biederman J, Spencer T, Wilens T, Seidman LJ, Mick E, Doyle A: Attention deficit hyperactivity disorder in adults: an overview. Biol Psychiatry 2000; 48:9–20
- 23. Spencer T, Biederman J, Wilens TE, Faraone SV: Adults with attention-deficit/hyperactivity disorder: a controversial diagnosis. J Clin Psychiatry 1998; 59:59–68
- 24. Wilens T, Biederman J, Brown S, Tanguay S, Monuteaux M, Blake C, Spencer T: Psychiatric comorbidity and functioning in clinically referred preschoolers and school aged youth with ADHD. J Am Acad Child Adolesc Psychiatry 2002; 41:262–268

- Shelton TL, Barkley RA, Crosswait C, Moorehouse M, Fletcher K, Barrett S, Jenkins L, Metevia L: Psychiatric and psychological morbidity as a function of adaptive disability in preschool children with aggressive and hyperactive-impulsive-inattentive behavior. J Abnorm Child Psychol 1998; 26:475–494
- Wilens TE, Spencer T, Biederman J: Attention deficit disorder with substance abuse, in Subtypes of Attention Deficit Disorders in Children, Adolescents, and Adults. Edited by Brown TE. Washington, DC, American Psychiatric Press, 1996, pp 319–339
- 27. Whitmore EA, Mikulich SK, Thompson LL, Riggs PD, Aarons GA, Crowley TJ: Influences on adolescent substance dependence: conduct disorder, depression, attention deficit hyperactivity disorder, and gender. Drug Alcohol Depend 1997; 47:87–97
- Doyle AE, Faraone SV, DuPre EP, Biederman J: Separating attention deficit hyperactivity disorder and learning disabilities in girls: a familial risk analysis. Am J Psychiatry 2001; 158:1666–1672
- Spencer T, Faraone SV, Wozniak J, Mick E, Galdo M, Biederman J: Does the comorbidity with ADHD moderate the gender representation in pediatric major depression? in Scientific Proceedings of the 49th Annual Meeting of the American Academy of Child and Adolescent Psychiatry. Washington, DC, AACAP, 2002, p 114
- Faraone S, Biederman J, Milberger S: How reliable are maternal reports of their children's psychopathology? one-year recall of psychiatric diagnoses of ADHD children. J Am Acad Child Adolesc Psychiatry 1995; 34:1001–1008
- Achenbach TM, McConaughy SH, Howell CT: Child/adolescent behavioral and emotional problems: implications of cross-informant correlations for situational specificity. Psychol Bull 1987; 101:213–232
- 32. Biederman J, Faraone SV, Weber W, Russell RL, Rater M, Park K: Correspondence between DSM-III-R and DSM-IV attention deficit hyperactivity disorder (ADHD). J Am Acad Child Adolesc Psychiatry 1997; 36:1682–1687

Am | Psychiatry 162:6, June 2005 http://ajp.psychiatryonline.org **1089**