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Relationship between ADHD and Anxiety in Boys: Results from a Family Study

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ABSTRACT

Objective: Recent studies have found an increased risk for both anxiety disorder and attention-deficit hyperactivity disorder (ADHD) in the adult relatives of children with ADHD in comparison with adult relatives of normal controls. Such findings may account for the high rates of comorbid anxiety found in children with ADHD, and they suggest a relationship between the two disorders. However, additional studies are needed to address this relationship that include both anxiety disorder and normal control groups. **Method:** The first- (n = 239) and second-degree relatives (n = 1,266) of clinically referred boys with ADHD (n = 49), clinically referred boys with anxiety disorder (n = 46), and controls who have never been psychiatrically ill (NPI controls) (n = 37) were assessed with structured interview and diagnosed according to *DSM-III-R* criteria. Lifetime rates of ADHD and anxiety disorder were then compared for relatives in the three proband groups. **Results:** Female relatives of ADHD probands had significantly higher rates of anxiety disorder than female relatives of NPI controls. However, relatives of anxious probands and NPI controls did not differ for ADHD. Furthermore, no evidence of cosegregation of anxiety disorder with ADHD was found in the relatives of probands in the two patient groups. **Conclusions:** ADHD and anxiety may share common risk factors but appear to be independently transmitted in families. The high rate of anxiety in female relatives of ADHD probands was comparable with that found in relatives of anxious probands and warrants further investigation. *J. Am. Acad. Child Adolesc. Psychiatry,* 1996, 35(8):988–996.

Key Words: attention-deficit hyperactivity disorder, anxiety, family study.

Much of the existing research suggests that attention-deficit hyperactivity disorder (ADHD) and anxiety are unrelated classes of psychiatric disturbance. Indeed, the sociodemographic characteristics and associated clinical features of the two disorders differ in significant ways. Epidemiological investigations place the prevalence of ADHD between 6% and 9% of nonreferred children and adolescents (Anderson et al., 1987; Bird et al., 1988). Little is known about the prevalence of this disorder in adults, but 12-month prevalence estimates in the order of 0.3% have been suggested (see Shaffer, 1994). The majority of those with ADHD are males who frequently exhibit severe disturbances of conduct and mood, learning disabilities, and poor school performance (Anderson et al., 1987; Biederman et al., 1991b; Bird et al., 1993; Faraone et al., 1993; Hinshaw, 1992; Lahey et al., 1988; Munir et al., 1987). The disorder is often chronic, with one third to one half of those affected retaining the diagnosis into adulthood (Lambert, 1988; Manuzza et al., 1991; Weiss et al., 1985).

By contrast, anxiety disorders are more prevalent than ADHD in both nonreferred adults (15%) (Regier et al., 1990) and children (8% to 21%) (Anderson et al., 1987; Kashani et al., 1987, 1988). Also, anxiety disorders are more prevalent among adult women (Regier et al., 1990) but show a roughly equal sex distribution during youth (Anderson et al., 1987, Bird et al., 1988). Furthermore, depression is more commonly associated with anxiety than with behavior disturbances (Anderson et al., 1987; Bird et al., 1993; Costello, 1989; Last et al., 1992; Werry et al., 1987). This may account for the generally favorable psychiatric outcomes observed over time in anxious children (Cantwell and

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Baker, 1989; Keller et al., 1992; Last et al., unpublished).

Despite the sociodemographic and clinical differences between ADHD and anxiety disorder, there is evidence to suggest that the two may be etiologically related and/or share common risk factors. First, roughly one third of referred and nonreferred youths with ADHD have been found to have a lifetime history of anxiety disorder (Anderson et al., 1987; Biederman et al., 1991b, 1993; Bird et al., 1988; Lahey et al., 1988; Last et al., 1987, 1992; Munir et al., 1987; Plizka, 1989; Reeves et al., 1987; Woolston et al., 1989). Second, the presence of a comorbid anxiety disorder suggests a different clinical profile from pure ADHD. Specifically, investigations have found individuals with ADHD and anxiety to be less impulsive, to be more sluggish on memory tasks, to be less responsive to methylphenidate treatment, and to have fewer disturbances of conduct than their pure-ADHD counterparts (Faraone et al., 1993; Plizka, 1989; Taylor et al., 1987; Zahn et al., 1975).

These findings have prompted some to suggest that an ADHD+anxiety subtype with its own unique clinical profile, etiology, and risk factors may exist (Biederman et al., 1991a, 1992). However, comorbidity data alone are not sufficient to establish the validity of ADHD subtypes or an etiological relationship between ADHD and its comorbid disorders. Still, the unique clinical characteristics of youths with ADHD and anxiety suggest that additional investigations of the relationship between these two disorders are needed (Biederman et al., 1991b).

One method for examining the relationship among co-occurring disorders and the validity of disorder subtypes is the family study (Pauls et al., 1986; Reich et al., 1979; Weissman et al., 1986). Specifically, the occurrence of both ADHD and anxiety disorder within families (coaggregation) may point to a common etiology and/or shared risk factors. For example, if ADHD and anxiety are related, then a higher incidence of both disorders would be expected in the relatives of children with either ADHD or anxiety compared with relatives of normal controls (Biederman et al., 1991a, 1992). Furthermore, if ADHD and anxiety disorder tend to co-occur in individual family members (cosegregation), then it is likely that they share a common etiology (Biederman et al., 1991a, 1992).

It is clear from existing family studies employing structured psychiatric interviews and multiple informants that ADHD and anxiety are disorders with strong familial components. In probands with ADHD, roughly one fourth of their first-degree family members also meet criteria for ADHD (lifetime) (Biederman et al., 1990, 1992; Faraone et al., 1991; Frick et al., 1991). This familial rate is clearly higher than that found in the general population, and it differs significantly from rates of ADHD found in the relatives of both psychiatric (5.3% to 18%) (Biederman et al., 1990; Frick et al., 1991) and normal controls (3% to 9%) (Biederman et al., 1990, 1992). Similarly, anxiety disorders also tend to run in families. Roughly 25% to 36% of the first-degree relatives of children with anxiety disorders meet criteria for an anxiety disorder (lifetime) (Fyer et al., 1993; Last et al., 1991; Lenane et al., 1990). Again, the observed rate of anxiety disorder among family members is higher than the base rate for anxiety disorder in the general population and higher in comparison with relatives of subjects with conduct disorder (1.5%) (Lenane et al., 1990), subjects with ADHD (23.5%) (Last et al., 1991), and normal controls (16%) (Fyer et al., 1993, and Last et al., 1991).

However, only recently have researchers begun to examine the coaggregation and cosegregation of ADHD and anxiety disorder in families. Biederman et al. (1991a) compared rates of ADHD and anxiety disorder in the first-degree relatives of 73 males (aged 6 to 17 years) clinically referred for ADHD with those of 26 normal controls referred to a primary care pediatrician. Consistent with the hypothesis that the two disorders share common risk factors, a higher rate of anxiety disorder was found among the relatives of ADHD probands than among relatives of normal controls (23% versus 4.6%, $p < .001$). In addition, the presence of ADHD was associated with a threefold increase in the risk for anxiety disorder in the same relative (11% to 33%, $p < .001$). Thus, it appeared that attention deficit and anxiety disorder were not independently transmitted (Biederman et al., 1991a).

In a second, larger investigation, Biederman et al. (1992) compared rates of ADHD and anxiety in the first-degree relatives of 140 pediatrically referred males with ADHD and of 120 normal controls. Again, a higher rate of anxiety disorder was found in family members of ADHD probands than in controls (25% versus 8%, $p < .001$). However, contrary to their

previous findings, ADHD and anxiety disorders *did not* cosegregate within families. Thus, while the two disorders may share some common risk factors, they appeared to be independently transmitted (Biederman et al., 1992).

The observation that relatives of ADHD probands, particularly parents, have an increased risk for anxiety disorder are consistent with "top-down" studies of mothers with comorbid depression and anxiety. Children of depressed and anxious mothers show higher rates of behavior disorder than children of depressed-only controls (Sylvester et al., 1987; Weissman et al., 1984). Taken together, these family studies provide preliminary evidence of a relationship between ADHD and anxiety disorder.

However, additional investigations are needed because the existing evidence for cosegregation is limited and unclear. Furthermore, no family study to date has employed a pure anxiety control group, in addition to normals, or presented data for second-degree relatives. The addition of a pure anxiety group and data on second-degree relatives may help clarify the relationship between ADHD and anxiety.

In the present study, we extend previous research by examining the familial relationship between ADHD and anxiety in the first- and second-degree relatives of three homogeneous groups: boys with ADHD and no history of depression or anxiety (n = 49), boys with an anxiety disorder and no history of ADHD (n = 46), and controls who have never been psychiatrically ill (NPI controls) (n = 37). Given previous findings by Biederman et al. (1991a, 1992), we anticipated that the first-degree relatives of ADHD probands would have a higher rate of both ADHD and anxiety disorder than the first-degree relatives of NPI controls. To determine whether a similar relationship existed between ADHD and anxiety in relatives of anxious probands, we compared lifetime rates of anxiety disorder for the "pure" anxiety group with those of NPI controls. Finally, we compared rates of anxiety disorder in relatives with ADHD with those of relatives without ADHD to learn whether the two disorders tend to cosegregate.

METHOD

Subjects

Probands. Probands for this investigation originally were recruited for a study of anxiety disorders in children and their families (Last et al., 1991). The original sample included children and adolescents with anxiety disorders (n = 94), children and adolescents with ADHD (n = 58), and NPI controls (n = 87). The focus of this investigation is the 132 male probands who participated in that study, including 49 boys with ADHD, 46 boys with an anxiety disorder, and 37 NPI controls (Table 1). ADHD and anxiety disorder probands were recruited at the same time from general child and anxiety disorder clinics, respectively, at Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine. NPI controls were recruited from the Pittsburgh community via mailings using *Cole's Directory.* Probands in the NPI group were matched on demographic characteristics as closely as possible with children in the anxiety group.

Following diagnostic evaluation at the clinic, participation was offered to families of children with ADHD if they met criteria for a current diagnosis of ADHD, had no history of anxiety disorder or depression (ever), and resided with at least one biological parent. Inclusion criteria for children in the anxiety group were a current *DSM-III-R* diagnosis of anxiety disorder, no history of ADHD (ever), and residence with at least one biological parent. Finally, control subjects from the community (NPI) were offered participation in the study if they had no history of any psychiatric disorder or mental health contact and were residing with at least one biological parent.

Family Members. Subjects included first- and second-degree relatives of children in the three proband groups. The numbers of relatives in the three proband groups were as follows: mothers (ADHD = 49, anxiety = 46, and NPI = 37), fathers (ADHD = 49, anxiety = 46, and NPI = 37), female siblings (ADHD = 14, anxiety = 13, and NPI = 15), male siblings (ADHD = 21, anxiety = 27, and NPI = 17), and second-degree female (ADHD = 223, anxiety = 220, and NPI = 177) and male relatives (ADHD = 225, anxiety = 229, and NPI = 192). Relatives younger than the age of 5 years and half siblings were excluded from all analyses.

Diagnostic Procedures

Probands. Diagnoses were obtained by using a modified version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present Episode) (K-SADS-P) (Chambers et al., 1985). This version of the K-SADS-P (Last, unpublished test) was modified to include comprehensive and detailed sections on all *DSM-III-R* anxiety disorders and allows evaluation of both current and past psychopathology. At the time of intake, all boys and at least one parent were interviewed separately by a trained clinical child psychologist about lifetime psychiatric history. Data from both child and parent interviews were then used to arrive at diagnoses (both current and past) according to *DSM-III-R* criteria (Table 2). In addition, socioeconomic status was assessed at intake with the Hollingshead Four Factor Index of Social Status (Hollingshead, 1975).

Interrater diagnostic agreement was obtained for 47% of the 132 study participants by having a second interviewer score audiotapes of the interviews. The κ coefficients for ADHD, any anxiety disorder, and no psychiatric disorder were .98, .96, and 1.0, respectively. The κ coefficients of agreement for the specific anxiety disorders at intake were as follows: separation anxiety disorder, .92; overanxious disorder, .91; avoidant disorder, .75; panic disorder, .86; social phobia, .95; simple phobia, .73; obsessive-compulsive disorder, .77; and posttraumatic stress disorder, 1.0. In the few instances in which the two interviewers disagreed about the specific diagnoses, the diagnoses of the "live" interviewer were used.

TABLE 1
Proband Sociodemographic Characteristics

	Proband Groups			
	ADHD (n = 49)	Anxiety (n = 46)	NPI (n = 37)	Statistic F/χ^2 (df)
Mean age (years)	9.2	12.1	10.7	10.7 (2,129***)
SD	2.4	3.5	3.1	
Race (% white)	80.4	63.3	67.6	3.6 (2)
Parental marital status (% single/divorced)	47.8	57.1	40.5	2.4 (2)
Socioeconomic status (% low)[a]	43.5	51.0	35.1	2.2 (2)

Note: ADHD = attention-deficit hyperactivity disorder; NPI = never psychiatrically ill controls.
[a] Low = Hollingshead strata of IV or V.
*** $p < .001$, significant post hoc differences between ADHD and anxiety groups.

Family Members. Once the proband was found to meet inclusion criteria for study participation, available first-degree family members were contacted and interviewed directly using the family study method. Adult relatives (≥18 years of age) were interviewed with Structured Clinical Interview for *DSM-III-R*, Nonpatient Version (SCID) (Spitzer, Williams, and Gibbon, unpublished), and with the childhood disorders sections of the modified K-SADS-P. This section of the K-SADS-P was administered to adults to assess for a previous history of the following disorders: overanxious disorder, avoidant disorder, ADHD, conduct disorder, and oppositional defiant disorder. The entire version of the modified K-SADS-P was administered to child and adolescent full siblings. Spouses reported on each other by the family history method (Thompson et al., 1982). Diagnostic information was obtained for first-degree relatives who were not available or refused direct interviews through the family history method. Information on second-degree relatives was obtained from the parents by the family history method.

Direct interviews were administered to almost all of the mothers in the three groups (ADHD = 95.9%, anxiety = 97.8%, and NPI = 97.3%). For fathers, direct interviews were administered to 42.8% (21) of those whose children were in the ADHD group, 39% (18) of the anxiety group, and 56.7% (26) of the NPI group (no significant differences). The smaller percentage of fathers directly interviewed reflected, in part, the high frequency of divorced parents (divorced/separated mothers usually were reluctant to have fathers participate in the study). For full siblings, 57.1% (20) of the ADHD group, 65% (26) of the anxiety group, and 71.9% (23) of the NPI group received direct interviews (no significant differences).

All family interviews were conducted by a psychologist trained in the administration of the SCID, the modified K-SADS-P, and

TABLE 2
Frequency of Psychiatric Disorders in Probands

	Proband Groups			
	ADHD (n = 49)		Anxiety (n = 46)	
DSM-III-R Disorder	Current	Lifetime	Current	Lifetime
ADHD	100.0	100.0	—	—
Oppositional defiant	18.4	28.6	10.8	10.8
Conduct disorder	6.1	12.2	0.0	0.0
Simple phobia	—	—	34.8	45.7
Overanxious disorder	—	—	30.6	30.6
Social phobia	—	—	28.6	36.9
Obsessive-compulsive	—	—	21.7	21.7
Panic disorder	—	—	10.8	13.0
Avoidant disorder	—	—	10.8	15.2
PTSD	—	—	2.2	2.2
Anxiety disorder NOS	—	—	2.2	2.2
Major depression	—	—	4.3	21.7
Dysthymia	—	—	8.7	10.8
Depressive disorder NOS	—	—	2.2	2.2

Note: Values are percentages. Dashes indicate disorders that would have excluded subjects in the two groups from study participation. ADHD = attention-deficit hyperactivity disorder; PTSD = posttraumatic stress disorder; NOS = not otherwise specified.

the family history method who was "blind" to proband diagnoses. Interviewers assigned all applicable *DSM-III-R* diagnoses (current and past) on the basis of all available interview data. A diagnosis of simple phobia was not assigned unless it resulted in clinically significant impairment in the subject's normal routine, social activities, or relationships with others as defined by *DSM-III-R* (American Psychiatric Association, 1987). Interrater reliability coefficients were obtained by a second interviewer, independently scoring audiotapes of interviews for 36% of complete families in the present study (589 complete interviews). The κ coefficients of agreement for anxiety disorders in family members were as follows: any anxiety disorder, .91; generalized anxiety disorder, .94; panic disorder, .83; simple phobia, .96; social phobia, .97; obsessive-compulsive disorder, .84; posttraumatic stress disorder, .94; SAD, .90; avoidant disorder, .87; and overanxious disorder, .91. The κ coefficients of agreement also were high for both childhood ADHD (.87) and no lifetime history of anxiety disorder (.96).

Data Analyses

Reported rates of illness are for lifetime prevalence of disorder (i.e., both past and present occurrences). Subject with a lifetime history of the following disorders were considered to have a positive history of anxiety: panic disorder (with or without agoraphobia), generalized anxiety disorder, social and simple phobias, obsessive-compulsive disorder, posttraumatic stress disorder, overanxious disorder, avoidant disorder, and separation anxiety disorder. Comparison of three groups for continuous measures were done with a one-way analysis of variance with Tukey-b, post hoc comparisons. Rates of psychiatric disorder in the three groups were compared using 3×2 χ^2 analyses. Significant 3×2 χ^2 analyses were followed by 2×2 comparisons. Cosegregation of ADHD and anxiety (hypothesis 3) was examined by comparing rates of anxiety disorder in relatives with ADHD to rates in those without ADHD for the ADHD and anxiety groups using 2×2 χ^2 analysis. The Weinberg shorter method of age correction (Slater and Cowie, 1971) was used for group comparisons of psychiatric disorder in relatives. Since a similar pattern emerged but with inflated percentages (available upon request), only uncorrected rates of disorder are presented.

RESULTS

Table 3 presents lifetime rates for childhood ADHD in the first- and second-degree relatives of boys in the ADHD (n = 49), anxiety (n = 46), and NPI (n = 37) proband groups. Rates of disorder were in the predicted direction; however, few significant differences emerged. ADHD was more frequent among fathers and male siblings (all first-degree male relatives) of ADHD probands than NPI controls but not anxious controls. No differences were observed among the three groups for ADHD in second-degree male relatives. Also, the three groups did not differ in the occurrence of ADHD among female relatives (first- or second-degree).

Table 4 presents rates for anxiety disorder (any) in relatives of probands in the three groups. First-degree female relatives in both the ADHD and anxiety groups had significantly higher rates of anxiety disorder than did first-degree female relatives of NPI controls. In particular, mothers of ADHD boys had greater than a twofold increased risk for anxiety than mothers of NPI boys. Similarly, the rate of anxiety in mothers of boys with anxiety disorders was three times greater than that observed for NPI controls. No significant differences were observed among female siblings alone in the three groups. Significantly higher rates of anxiety disorder were found in the anxiety group compared with ADHD groups for mothers and for all first-degree female relatives. Second-degree female relatives in the ADHD group showed a higher rate of anxiety than their counterparts in the anxiety group.

A somewhat different pattern of differences among the three groups emerged for male relatives. A higher risk for anxiety was found among all first-degree male relatives in the anxiety group compared with NPI controls. However, male relatives in the ADHD group were not at increased risk for anxiety compared with those in the anxiety or NPI groups. Finally, no differences were found among second-degree male relatives in the three proband groups.

To evaluate more fully the familial relationship between ADHD and anxiety disorders in female relatives, rates for specific disorders in mothers and all second-degree female relatives of probands are presented (Table 5). The most frequent anxiety disorders (lifetime) in the mothers of ADHD probands were overanxious disorder, posttraumatic stress disorder, and separation anxiety disorder. Overanxious disorder and social phobia were the most common anxiety disorders in mothers of anxious probands. The "childhood" anxiety disorders were the most frequent anxiety disorder found in second-degree relatives in both the ADHD and anxiety groups. However, no significant differences were found for the three groups for any specific anxiety disorder (either for mothers or second-degree female relatives).

Finally, we examined whether ADHD and anxiety disorders tended to cosegregate in the relatives of probands from the two patient groups. A total of 26 relatives (first- and second-degree) with a lifetime history of ADHD and 447 without such a history were identified. Of those relatives with ADHD, 38.5% (n = 10) also had a lifetime history of anxiety disorder (any). By contrast, 23.5% (n = 105) of relatives without ADHD also had a lifetime history of anxiety disorder

TABLE 3
Lifetime Rates for Childhood ADHD in Relatives

Relationship to Proband	Proband Groups: ADHD n	ADHD %	Anxiety n	Anxiety %	NPI n	NPI %	3 × 2 χ^2
Mothers	3	6.4	1	2.2	0	0.0	0.2
Fathers	3	12.0	0	0.0	0	0.0	5.9†
Female siblings	0	0.0	1	7.7	0	0.0	2.2
Male siblings	4	21.1	2	8.0	0	0.0	4.1
All 1° females	3	5.0	2	3.4	0	0.0	2.5
All 1° males	7	15.9^{a}	2	4.0^{ab}	0	0.0^{b}	8.9*
All 2° females	0	0.0	2	3.2	1	1.9	2.1
All 2° males	6	9.1	4	5.9	1	1.4	4.0

Note: Cells with different superscript letters differ significantly from each other by 2 × 2 χ^2 analysis ($p < .05$). ADHD = attention-deficit hyperactivity disorder; NPI = never psychiatrically ill controls.
† $p = .057$; * $p < .05$.

($\chi^2 = 2.9$, $p = .084$). Thus, in the present study, anxiety disorders did not cosegregate with ADHD in the families of boys with ADHD and boys with anxiety disorder.

DISCUSSION

The purpose of this study was to examine the relationship between ADHD and anxiety disorder in the families of ADHD, anxiety disorder, and NPI probands. This study was unique in that it included both pure anxiety disorder and normal control groups, and also second-degree relatives. Overall, the present findings were mixed with regard to a familial relationship between ADHD and anxiety disorder.

A priori we hypothesized that the relatives of ADHD probands would exhibit an increased risk for both ADHD and anxiety disorder compared with the relatives of NPI controls. The present findings provided only partial support for this hypothesis. Consistent with previous investigations (Biederman et al., 1991a, 1992; Faraone et al., 1991; Frick et al., 1991), higher rates of ADHD were found in the first-degree male relatives of ADHD probands than in the first-degree male relatives of NPI controls. No significant differences were found for female relatives.

It is difficult to evaluate this latter finding as previous investigations have not provided rates of ADHD separately for female and male relatives. However, after controlling for sex, Biederman et al. (1992) continued to observe an increased risk for ADHD in the first-degree relatives of ADHD probands compared with those of normal controls. While the present findings for female relatives may be due to insufficient power

TABLE 4
Lifetime Rates for Anxiety Disorder (Any) in Relatives

Relationship to Proband	Proband Groups: ADHD n	ADHD %	Anxiety n	Anxiety %	NPI n	NPI %	3 × 2 χ^2
Mothers	21	42.9^{a}	30	65.2^{b}	7	18.9^{c}	17.9***
Fathers	7	15.2	11	25.0	4	11.4	2.8
Female siblings	2	15.4	2	15.4	2	13.3	0.1
Male siblings	1	5.6	7	26.9	1	7.1	4.7†
All 1° females	23	37.1^{a}	32	54.2^{b}	9	17.3^{c}	16.2***
All 1° males	8	12.5^{ab}	18	25.7^{a}	5	10.2^{b}	6.3*
All 2° females	35	16.9^{a}	18	9.8^{ab}	10	6.8^{b}	9.1**
All 2° males	10	5.5	14	8.2	8	5.1	1.6

Note: Cells with different superscript letters are significantly different from each other by 2 × 2 χ^2 analysis ($p < .05$). ADHD = attention-deficit hyperactivity disorder; NPI = never psychiatrically ill controls.
† $p = .096$; * $p < .05$; ** $p < .01$; *** $p < .001$.

TABLE 5
Lifetime Rates for Specific Anxiety Disorders in Female Relatives

	Proband Groups						
	ADHD		Anxiety		NPI		
Anxiety Disorder	*n*	%	*n*	%	*n*	%	3 × 2 χ^2
Mothers							
Social phobia	3	6.1	6	13.0	1	2.7	3.4
Simple phobia	1	2.0	1	2.2	0	0.0	1.9
PTSD	7	14.3	3	6.5	1	2.7	4.0
GAD	0	0.0	3	4.3	0	0.0	3.8
OCD	0	0.0	1	2.2	0	0.0	1.9
Panic disorder	0	0.0	0	0.0	0	0.0	—
Anxiety NOS	0	0.0	1	2.2	0	0.0	—
OAD	10	20.8	13	28.9	3	8.3	5.3†
SAD	5	10.9	5	10.4	1	2.8	2.8
Avoidant disorder	3	6.3	5	10.9	0	0.0	4.1
All second-degree females							
Social phobia	1	0.5	1	0.5	0	0.0	0.8
Simple phobia	0	0.0	1	0.6	0	0.0	1.9
PTSD	2	1.1	1	0.6	0	0.0	1.6
GAD	0	0.0	2	1.1	0	0.0	3.7
OCD	0	0.0	0	0.0	0	0.0	—
Panic disorder	0	0.0	0	0.0	0	0.0	—
Anxiety NOS	0	0.0	0	0.0	0	0.0	—
OAD	5	5.5	4	4.6	3	3.8	0.3
SAD	11	11.8	6	6.9	2	2.6	5.3†
Avoidant disorder	4	4.3	2	2.2	0	0.0	4.5

Note: ADHD = attention-deficit hyperactivity disorder; NPI = never psychiatrically ill controls; PTSD = posttraumatic stress disorder; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; OAD = overanxious disorder; SAD = separation anxiety disorder; NOS = not otherwise specified.
† $p < .075$.

to detect differences, population studies suggest that ADHD is a disorder that primarily affects males (Anderson et al., 1987; Bird et al., 1988). Thus, our findings may reflect the low rate of ADHD in females generally.

Previous investigations suggested that anxiety disorders are more prevalent in families of ADHD probands than in families of normal controls (Biederman et al., 1991a, 1992). The present findings also provide partial support for this hypothesis. Female relatives, particularly mothers and second-degree female relatives, showed a two- to threefold increased risk for anxiety disorder compared with NPI controls. Moreover, the maternal rate of anxiety disorder in ADHD probands was comparable with that found in mothers of anxious probands. Indeed, the rate of anxiety in second-degree relatives was significantly higher in the ADHD than in the anxiety group. When considering that the observed rates for anxiety disorders for female relatives of ADHD probands (37.1% to 42.9%) far exceeded those expected from base rates alone, the present findings suggest a relationship between maternal anxiety disorder and ADHD in their male children. It is interesting that analysis of individual anxiety disorders did not differentiate female relatives of ADHD and NPI controls. However, there were very few subjects in both groups with specific anxiety disorders.

By contrast, family members of anxiety disorder probands (male or female) showed no increased risk for ADHD compared with NPI controls. The observed rates for ADHD in family members of anxious probands were consistent with reported prevalence estimates for children (roughly 2% to 8%) (Anderson et al., 1987; Bird et al., 1988), though higher than that expected in nonreferred adults (0.3%) (Shaffer, 1994). Thus, the present findings suggest that ADHD does not aggregate in the families of anxiety disorder probands. As this was the first family study to include a pure anxiety disorder proband group, additional studies are needed to replicate the current findings.

As for the cosegregation of ADHD and anxiety, the present findings do not support the hypothesis that the two disorders are etiologically related. Specifically,

relatives with ADHD did not have significantly higher rates of anxiety disorder than relatives without ADHD. These findings are consistent with those of Biederman et al. (1992), who failed to find any evidence of cosegregation of anxiety disorder with ADHD in families of pure ADHD probands and those with an additional anxiety disorder. To approximate the sample used by Biederman et al. (1992), we reexamined our findings for cosegregation using relatives of pure ADHD boys only. Again, no evidence of cosegregation was found. However, these results must be interpreted in light of the small number of relatives who actually met criteria for a diagnosis of ADHD (n = 26) in both the ADHD and anxiety groups.

In summary, the present investigation adds to a growing body of literature suggesting that ADHD (Biederman et al., 1990, 1992; Faraone et al., 1991; Frick et al., 1991) and anxiety tend to run in families (Fyer et al., 1993; Last et al., 1991; Lenane et al., 1990; Turner et al., 1987) but are independently transmitted. While we await additional investigations, the present data do support previous findings that the male children of anxious mothers are at increased risk for ADHD (Sylvester et al., 1987; Weissman et al., 1984). Whether this finding reflects a genetic or environmental influence is beyond the scope of this study.

Since children with comorbid ADHD and anxiety were excluded from this study, we cannot directly address the validity of an ADHD+anxiety disorder subtype. While an increased risk of anxiety was found in female relatives of ADHD probands, no such relationship was found for ADHD in families of anxiety disorder probands. Thus, while the two disorders may frequently co-occur during childhood and influence the child's overall clinical picture, the present study provided little support for the validity of an ADHD+anxiety subtype based on cosegregation of the two disorders.

The implications of these findings for practicing clinicians are limited but important. First, accurate diagnosis of ADHD in children can be quite difficult, especially where the cardinal symptoms (poor attention, impulsivity, and hyperactivity) are subclinical, and where there are comorbid conditions (e.g., overanxious disorder or oppositional defiant disorder). Evidence of a familial history of ADHD would certainly lend support to a diagnosis of ADHD in the child in such cases. The present findings also suggest that a maternal history of anxiety disorder should also be considered in any assessment of familial risk for ADHD. Second, the presence of a maternal history of anxiety needs to be evaluated in any treatment decisions. High levels of anxiety in the mother may be associated with inconsistent and/or inappropriate responses to problem behaviors in the ADHD child and with poor treatment compliance. Concurrent treatment of the anxious mother may improve treatment outcome with the child and reduce the child's risk for developing a comorbid anxiety disorder over time. With regard to the latter, anxiety disorders show a clear pattern of familial aggregation. Thus, ADHD boys of anxious mothers may show improved long-term response to standard treatments for ADHD with the addition of prophylactic interventions for anxiety as well. Empirical investigations of these issues are needed.

Finally, we wish to mention some limitations of the present investigation. First, our findings are based on clinically referred boys and may not generalize to girls or children in the community. Second, findings for fathers and second-degree relatives in this study were based primarily on family history data rather than direct interviews. Confirmation of our findings with direct interviews for these groups may be warranted. Third, the assessment of childhood psychiatric disorders in adult relatives by the family history method may have underestimated the true prevalence of ADHD and anxiety disorder in the three groups. Future studies should include, where possible, direct interview with all family members. Fourth, because of limited sample size, we did not evaluate the potential mediating influence of environmental factors or additional psychiatric disorders in family members on the aggregation of ADHD and anxiety. Additional studies are needed to address such covariates as socioeconomic status and comorbid depression when evaluating the familial relationship between ADHD and anxiety. Finally, analysis of subsyndromal status of disorders in this sample may have improved the study's generalizability and our understanding of the relationship between ADHD and anxiety.

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