Characteristics and co-morbidity of ADHD sib pairs in the Central Valley of Costa Rica

Jovita Schuler, M.S.[1,2], **Nicholas T. Weiss, M.D., M.A.**[2], **Denise A. Chavira, Ph.D.**[3], **James J. McGough, M.D.**[4], **Monica Berrocal**[5], **Brooke Sheppard**[2], **Evelyn Vaglio**[5], **Eduardo Fournier, M.A.**[5], **Luis Diego Herrera, M.D., M.P.H.**[5], and **Carol A. Mathews, M.D.**[2]

[1]Psychology Institute, University of Zurich, Zurich, Switzerland [2]Department of Psychiatry, University of California, San Francisco, San Francisco, CA [3]Department of Psychiatry, University of California, San Diego, La Jolla, CA [4]Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, Los Angeles, CA [5]Departments of Psychology and Psychiatry, Hospital Nacional de Niños, San Josè, Costa Rica

Abstract

Background—While genetic epidemiological studies demonstrate a substantial degree of genetic predisposition for Attention-Deficit/Hyperactivity Disorder (ADHD), they also suggest that the genetics are complex and may differ between populations or ethnic groups.

Objective—This study describes the phenomenology of siblings with Attention-Deficit/Hyperactivity Disorder (ADHD) from the genetically-isolated population of the Central Valley of Costa Rica.

Methods—Rates of DSM-IV defined ADHD subtypes and co-morbid conditions were calculated in a sample of 157 ADHD-affected children (probands and siblings) recruited for genetic studies using standardized approaches. Sib-sib comparisons and logistic regressions were conducted to identify significant patterns of concordance.

Results—Combined type ADHD (69.5%) was the most common subtype among probands, followed by the inattentive (27.4%), and hyperactive-impulsive (3.2%) subtypes. Anxiety disorders were prevalent (55.9%), as were disruptive behavior disorders (30.9%), and Tourette's disorder (17.0%). Probands and siblings showed high sib-sib concordance for anxiety disorders.

Conclusions—ADHD in Costa Rica is similar in clinical and demographic characteristics to ADHD seen in other parts of the world, although the rates of co-occurring psychiatric disorders differ somewhat from those previously reported in Latin American samples. Comorbid anxiety is prevalent, with high rates of sib-sib concordance, and may represent a distinct, homogeneous subgroup suitable for genetic studies.

Keywords

ADHD; Psychiatric; Genetics; International; Co-morbidity; Sib-pairs

Correspondence to: Carol A. Mathews, Department of Psychiatry, University of California San Francisco, 401 Parnassus Avenue, San Francisco CA 94143; cmathews@lppi.ucsf.edu, phone:415.476.7702, fax: 415.476.7389.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder whose cardinal features are impairing, persistent, and developmentally inappropriate symptoms of inattention, hyperactivity and impulsivity(1). ADHD has a prevalence of 5% to 8% of school-aged youth in North America (2) and is associated with a broad range of negative outcomes for affected individuals, with high rates of co-morbidity and adaptive impairments(3-5) and with significant costs to health care systems and society as a whole(6). For instance, studies of co-morbidity in North American clinical samples have found that about one-half of all children with ADHD will meet criteria for either Conduct Disorder (CD) or Oppositional Defiant Disorder (ODD), one-quarter to one-third will meet criteria for an anxiety disorder, and at least 6% will meet criteria for major depressive disorder (MDD) (7-10).

While susceptibility genes of significant effect have been difficult to identify in ADHD, genetic epidemiological studies have consistently demonstrated a substantial degree of genetic predisposition for the condition(11, 12). However, these studies have also suggested that the genetics of ADHD are complex, and may differ between populations or ethnic groups(13). Therefore, an understanding of the comparative phenomenological and epidemiological aspects of ADHD in different populations worldwide is important in and of itself, but it is also essential for efforts to clarify the genetics of this disorder. In order to determine the generalizability of genetic results obtained in specific populations, it is necessary to examine the epidemiology and phenomenology of the disorder of interest in the study population and to determine whether it can be assessed validly in that setting. Further, detailed descriptions of the phenomenology in a given population can lead to the characterization of phenotypes that are narrower and more homogeneous than ADHD as a whole.

One population of interest for genetic studies is the genetically isolated population of the Central Valley of Costa Rica (CVCR), a mixed urban-suburban-rural area surrounding and including the country's capital city, San José(14). Given that isolated populations have a high degree of genetic homogeneity, their use may simplify the process of identifying disease genes in disorders where multiple genes may play a role(14). The CVCR has been used for genetic mapping studies of several complex traits, including neuropsychiatric disorders such as bipolar disorder, Tourette's disorder, and migraine(14). Despite its importance as a research population, there have not yet been studies examining ADHD phenomenology and co-morbidities in Costa Rica, or in the Central Valley population isolate within Costa Rica.

Preliminary studies of phenomenology and patterns of psychiatric co-morbidity in the CVCR are necessary for two reasons. First, cross-ethnic variation in sex and ADHD subtype distributions as well as psychiatric co-morbidities have been identified, even among Latin American populations(15-17). For instance, Palacio et al. studied 18 families from another Latin American population isolate, the Paisa of Colombia, and found typical rates of co-morbid oppositional defiant disorder (25.4%), major depressive disorder (23.9%), simple phobia (25.4%), other anxiety disorders and substance use, but a strikingly high rate of conduct disorder (50%), and no cases of Tourette's disorder(18). Second, within the CVCR population, previous studies of obsessive-compulsive disorder and Tourette's disorder have found significantly lower rates of co-morbidity and subjective distress in comparison with North American samples, though the basic symptom-level phenomenology and demographic characteristics were similar(19, 20).

The aim of this study was thus to describe the phenomenology and co-morbidities of ADHD in children in Costa Rica in order to further elucidate the presentation of ADHD in Central and Latin America. Additional aims were to compare the clinical presentation of ADHD-affected individuals by age group, to compare probands and their ADHD-affected siblings, and to identify familial patterns of comorbidities. To our knowledge this is the first study of its kind in Costa Rica and only the third study of ADHD co-morbidity in any population isolate, the previous studies having been done in the Paisa community of Colombia (mentioned above)(21, 22) and in Finland(23). We hypothesized that ADHD phenomenology and patterns of comorbidity in Costa Rica would be sufficiently similar to patterns in other studied populations world-wide as to justify subsequent genetic investigations, but that there would be unique aspects due to local genetic and/or cultural factors. In particular, we expected lower overall rates of psychiatric co-morbidity, consistent with previous CVCR findings for OCD and Tourette's disorder. We also hypothesized that ADHD-affected siblings would have similar patterns of comorbid diagnoses (i.e., anxiety vs. tic disorders vs. disruptive behavioral disorders), but would in general be less severely affected (i.e., have fewer comorbid diagnoses).

METHOD

Participants

Study participants were obtained from a clinical sample of children recruited specifically for genetic studies of ADHD. This sample was recruited from the geographical region in Costa Rica around San José or the Central Valley, and all subjects had at least five great-grandparents who could be traced to families native to the region. Subjects were recruited from outpatient clinics, physician referrals, schools, and newspaper advertisements. The study team sought families in which there was at least one child with ADHD (the proband), and then determined whether there was one or more affected siblings who also met inclusion criteria. In some families, three or more siblings were identified who were affected with ADHD. The final sample for this study consisted of 95 probands and 62 siblings affected with ADHD with a mean age of 10.4 (SD=3.5) years (range: 6 to 26). 76% of subjects were between 6 and 12 years of age, and 24% were between 13 and 26; four subjects (all probands) were over age 18. 66% of subjects were male. All analyses were conducted with and without the four participants over 18. As there were no differences in the results, the analyses presented here include all participants, regardless of age. The studies were approved by the relevant institutional review boards in both the United States and Costa Rica. Informed consent by a parent or guardian was obtained for all subjects, and assent by the study subject was obtained where appropriate based on age.

Diagnostic Assessments

All diagnostic assessments were conducted in Spanish. Lifetime occurrence of ADHD and other psychiatric disorders was assessed using the Diagnostic Interview Schedule for Children, DSM-IV Edition (DISC IV), administered to the parents about their children(24, 25) and supplemented with a clinical interview conducted by a child and adolescent psychiatrist with both the parents and the child about the child. Parents and one teacher were also asked to complete the Spanish version of the Swanson, Nolan and Pelham Questionnaire, Version IV (SNAP-IV), and parents were also asked to complete the Child Behavior Checklist (CBCL)(26). In a minority of cases, the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (KSADS)(27) was used in lieu of the DISC-IV. For those four participants who were 18 or over, we followed the accepted ADHD research standard, which is to use the same diagnostic procedures for the adult participants as for the child participants(28-30). Therefore, for the adult participants, lifetime diagnoses were assessed using the same instruments as the child participants; in all cases,

this information was supplemented by clinical interview. Hospital and clinic medical records were obtained when available. Assignment of DSM-IV symptoms and ADHD subtypes were determined from the symptoms endorsed on either the DISC-IV or noted in the clinical interview, supplemented with up to two symptoms from either the parent or teacher rated SNAP IV, consistent with procedures used in other studies(31, 32). Consistent with the DSM-IV diagnostic criteria, impairment from ADHD symptoms was required to be present in at least two settings, and was assessed using the DISC-IV and the clinician interview (primary measures), with teacher assessments used to obtain additional information. As is standard in other ADHD studies, cases where one necessary criterion was marginally absent (i.e., cases where the best estimate/consensus team felt that there was evidence of ADHD, but where impairment was reported in only one area, or where only five of six symptoms were endorsed, or where age of onset could not be determined by age 7) were given a probable diagnosis (N= 18, 11.5%)(23, 29, 30, 33). Of the probable cases, we were unable to establish an age of onset (parents reported "all his life") for six, five had ages of onset between 8 and 10, and seven were either short one symptom criterion or impairment was established, but could only be established in one arena. Given frequently cited elevated rates of specific phobias in epidemiological studies(34, 35) and difficulties with accurately differentiating childhood "normative fears" from "phobias", a more conservative threshold that included at least moderate impairment in functioning plus distress, rather than requiring only distress, was applied to this diagnosis. All available information for each subject was independently reviewed by one psychiatrist and one psychologist (JJM, DC), both of whom are senior investigators with expertise in ADHD and research methods. Best estimate diagnoses were then assigned through consensus agreement according to strict DSM IV criteria using all available clinical information.(36)

Data Analysis

SPSS was used for descriptive statistics (probands only) and to calculate rates for subtypes of ADHD and comorbidities associated with ADHD by age, and for probands versus siblings. Probable as well as definite cases of ADHD were included in the analyses. Chi-square and Fisher's exact tests were used to examine significant differences in prevalence rates between groups (e.g, probands vs. siblings, older vs. younger participants). Linear regression was used to examine the relationship between age as a continuous variable and psychiatric comorbidity. Pairwise correlations were conducted to examine sib-sib concordances for comorbid psychiatric disorders. Heritability estimates for these conditions were determined using the equation $h^2=r/0.5$, where h^2 equals the heritability estimate, r equals the correlation coefficient, and 0.5 equals the kinship coefficient for full siblings. Note that when calculated in this manner, the h^2 does not distinguish between shared genetic and shared environmental effects, and is thus an over estimate. Nevertheless, this measure does serve to give an indication of whether the trait of interest is likely to be heritable in the sample or population being examined. Logistic regression analyses were subsequently conducted to assess demographic and clinical variables that predict concordant co-morbidity in siblings.

RESULTS

ADHD phenomenology

Mean age of onset of ADHD symptoms in this sample was 5.3 years of age (SD=1,7, range 1 to 10 years). Thirty-four percent of the participants were female; there were no significant differences in the age of onset of symptoms between boys and girls. Probands were significantly more likely to be male than were siblings (75% of probands were male, compared to 53% of siblings, $X^2=7.76$, p=0.005). As seen in Table 1, combined type ADHD (ADHD-C) was the most common ADHD subtype in probands, found in 69.5% of subjects,

followed by the predominantly inattentive (ADHD-IA, 27.4%), and then the predominantly hyperactive-impulsive (ADHD-HI, 3.2%) types. There were no significant differences in rates of ADHD-C, ADHD-IA or ADHD-HI between the two age groups (Table 2).

Rates of comorbid psychiatric disorders

Lifetime comorbidities associated with ADHD (for probands only) are also listed in Table 1. Anxiety disorders were the most common class of psychiatric comorbidity seen: 55.9% of probands met criteria for an anxiety disorder, 34.0% met criteria for a tic disorder, 11.7% met criteria for a mood disorder, and 30.9% met criteria for a disruptive behavior disorder other than ADHD. In contrast, oppositional defiant disorder (ODD) was the most common invidivual comorbid disorder observed (26.6%), followed by specific phobia (17.2%), social phobia (17.2%), Tourette's disorder (17.0%), generalized anxiety disorder (14.0%), and separation anxiety (12.9%). Five probands met diagnostic criteria for enuresis, one for substance abuse, and two for tobacco use. Only 16% of probands did not have any associated psychiatric comorbidity.

Age at the time of assessment (analyzed as a continuous variable using linear regression) was significantly associated with the presence of tic disorders (p= 0.04, beta coefficient = 0.02), disruptive behavior disorders other than ADHD (p=0.017, beta coefficient=-0.02), enuresis (p=0.006, beta coefficient=-0.016), and specific phobia p=0.009, beta coefficient=-0.02). Note that a positive beta coefficient indicates higher rates of comorbidities as age increases, and a negative beta coefficient indicates lower rates of comorbidities as age increases. Table 2 compares the rates of anxiety, mood, tic, and disruptive behavior disorders between ADHD-affected children (ages 6-12) and adolescents/young adults (ages 13 and older). In general, children and adolescents had similar rates of comorbid disorders, with the exception of disruptive behavior disorders, were more common in children than in adolescents. This difference was driven primarily by oppositional defiant disorder; 35.9% of the 6-12 year olds had a diagnosis of ODD, compared to 16.2% of the 13-26 year olds (p=0.03).

Comparisons between probands and siblings and sib-sib concordance rates

Siblings did not significantly differ from probands in the rates of any type of comorbid psychiatric disorder with the exception of tic disorders, which were more common among probands (31.9%) than among siblings (11.5%), (p=0.04). Although not statistically significant, siblings were more likely than probands to have no psychiatric comorbidities (16% of probands had no psychiatric comorbidity vs. 26.3% of siblings, p=0.12). When probands and siblings were compared at the individual (family) level (sib-sib comparisons, Table 3), there was a significant concordance between the occurrence of anxiety disorders in probands and in the occurrence of anxiety disorders in their ADHD-affected siblings (correlation=0.41). There was also a trend towards significance for concordance between probands and siblings for mood disorders, although this did not reach statistical significance (correlation=0.25; p=0.07). Only anxiety and mood disorders showed evidence for heritability in these families, with anxiety disorders having a heritability estimate of 0.81 and mood disorders a heritability estimate of 0.49.

To further explore the sib-sib concordance for anxiety disorders, we used logistic regression to determine the odds of a sibling having an anxiety disorder if the ADHD-affected proband had an anxiety disorder. After adjusting for age and gender, siblings were significantly more likely to have an anxiety disorder if the proband had an anxiety disorder (OR = 6.39, 95% CI =1.65-24.7). Adding ADHD subtype (i.e., inattentive or hyperactive type) or any tic disorder in the sibling to this model did not appreciably change the likelihood of having an anxiety disorder (Table 4). In separate analyses, the presence of a co-morbid tic, depressive, or non-

ADHD disruptive behavior disorder in the proband did not make each of those disorders significantly more likely in the siblings (data not shown).

DISCUSSION

The major aim of this study was to describe the phenomenology of ADHD in Costa Rica including patterns of subtype distribution and psychiatric co-morbidity in a cross-sectional clinical sample of children and adolescents with ADHD, as well as among siblings concordant for ADHD. Such information is important both for clinical purposes in Costa Rica, as well as for the design and interpretation of future genetic studies of ADHD to be completed in this population. Strengths of the study include the use of standardized and validated assessments as well as the rigorous best estimating procedure used to assign diagnoses.

Findings from this study support both similarities and differences in these patterns compared to worldwide and Latin American populations. As expected, basic demographic and clinical characteristics of this study sample were similar to what has been previously reported. For example, the gender ratio with a male predominance and the relatively early mean age of onset (approximately 5 years of age) is in line with what has been described previously(37). Similarly, although the assignment of ADHD symptom subtypes has been shown to be dependent to some degree on the type of assessment, the informant, and the age of the participant, the relative distribution of ADHD subtypes in our sample were generally consistent with findings in other populations, in that; a) ADHD-CT was most common and ADHD-HI least common, and; b) ADHD-CT was somewhat more common in younger children (ages 6-12) and ADHDIA somewhat more common in the older age group (ages 13-26)(17, 38-41). Our results converge with these studies, as well as with those that suggest that subtypes change somewhat over time, as pre-school children meeting criteria for ADHD-HI often develop sufficient inattentive-type symptomatology to meet criteria for ADHD-CT later in development(40), and school-aged children who meet criteria for ADHD-CT are somewhat likely to switch into the ADHD-IA category(39).

As in other populations, but in contrast to the reportedly low rates of co-morbidity and symptom severity for OCD and Tourette's disorder in Costa Rica, ADHD was highly associated with other co-morbid psychiatric disorders, particularly anxiety disorders(9, 19, 20, 32). This is not surprising given that a) referred ADHD samples are typically more highly co-morbid than epidemiologic samples and b) sib-pairs with ADHD typically have high levels of co-morbidity, likely reflecting the influence of high genetic loading in families with multiple affected offspring. For example, a study of adults with ADHD ascertained from multiplex families collected for genetic studies of ADHD found high rates of psychiatric comorbidities, including mood, anxiety, substance use, and disruptive behavior disorders(30). Rates of comorbidity were also high even when only probands were considered. Indeed, we found that just 16% of probands and 20% of all participants lacked psychiatric co-morbidities. Consistent with experience elsewhere(9, 18, 32, 39), and similar in particular to the Colombian Paisa population isolate sample mentioned above, common co-morbid disorders in our clinical sample were oppositional defiant disorder (31%), social phobia (20%), specific phobias (15%), separation anxiety (14%), and GAD (11%). In contrast to the Paisa sample and many worldwide populations, we found relatively low rates of conduct disorder and substance use, but relatively high rates of Tourette's disorder (11%) (9, 18, 42). These differences can be partly explained by the relatively young average age of participants as well as by systematic methodologic constraints, but may also reflect specific genetic and/or environmental factors such as differences in reporting, socioeconomic status, and cultural perceptions of given behaviors across samples.

Perhaps our most striking findings were the high rates of anxiety disorders (55% of the overall sample) and the high sib-sib concordance and heritability estimates for anxiety disorders (~40% correlation; 81% heritability). The high rates of anxiety disorders are consistent with previous studies (including the Multimodal Treatment Study of ADHD and the study of multiplex ADHD families) that report rates ranging from 32%-50%(43, 44). Additionally, previous studies also report that such comorbidity is associated with greater attention and school fears as well as lower levels of social competence compared to either group alone (i.e., ADHD-only, or anxiety only)(44). These findings underscore the significant impairment present among children with comorbid ADHD and anxiety and the undeniable vulnerability of this population. Assessment for such comorbidity is essential for effective treatment planning(37). In addition, validated assessments, preferably based on multiple informants, are necessary to examine overlapping symptoms between ADHD and anxiety, such as restlessness and difficulty concentrating, and to consider appropriate differential diagnoses. Our study findings, in particular, the heritability estimates for the commonly co-occurring conditions, also suggest that this sample may contain within it a relatively homogenous subgroup of individuals in which familial factors predispose concurrently to ADHD and anxiety, and who may form a subgroup particularly useful for further genetic investigation, although further investigation is required to determine the relative environmental and genetic contributions, both individual and shared, to these disorders in our families.

Previous research in other populations has more commonly focused on the co-transmission of ADHD with other disruptive behavior disorders rather than on co-transmission with anxiety disorders, though there have been some exceptions(7, 29, 42, 45-47). In the studies that have examined co-morbid anxiety, inheritance patterns have been suggestive of independent transmission of ADHD and anxiety disorders, but the pattern of transmission in families from the CVCR population isolate has yet to be determined(7, 46).

These results are limited by three main factors: 1) the small sample size, which prevents us from drawing strong conclusions regarding the similarities and differences between the probands and siblings; 2) the inclusion of subclinical or probable cases in the analyses, which may artificially lower the rates of comorbid psychiatric disorders, for example; and 3) potential biases in recruitment and assessment. Specifically, this study was conducted using a sample of ADHD-affected individuals and their siblings collected for a genetic study of ADHD. In this sample, 14 probands (14.7%) were recruited from a simultaneously occurring study of Tourette's disorder, clearly inflating the rate of comorbidity for this condition. However, when these subjects were removed from the analysis, the rates of tic disorders in the remaining sample continued to be high at 19.7% (4.2% with Tourette's disorder, 9.1% with chronic motor or vocal tic disorder, and 6.3% with nonspecific tic disorder). This may represent a residual bias related to our ongoing work on tic disorders in this population (the principal investigator of this study in Costa Rica is a well-known expert in TS, potentially leading to a residual referral or diagnostic bias), or may suggest that tic disorders in Costa Rica are actually higher among individuals with ADHD than in the general population. We are unable to distinguish between these possibilities, and further studies in this area are warranted. In addition, we did not systematically assess substance abuse, which may have influenced the low rates of this co-morbidity, although we did consider items on the CBCL addressing substance use as well as the clinical interview conducted by the psychiatrist. This result is more likely, however, attributed to the relatively young age of participants, most of whom had not yet entered the age of risk for substance use. Additionally, given that the vast majority of the participants were children, we did not systematically assess for antisocial personality disorder, which has been reported to be comorbid with ADHD in adults. However, we did assess for lifetime diagnoses of conduct disorder for all participants, which may serve as a proxy for antisocial personality disorder.

In sum, this study suggests that the Costa Rican population of children with ADHD is sufficiently similar to populations described elsewhere that genetic localization derived from it are likely to have broad generalization. However there may also be important local characteristics. In particular, the high concordance between siblings for anxiety and the high overall rates of Tourette's disorder may represent unique and useful findings. Further investigations will seek to determine whether ADHD and co-morbid anxiety disorder does indeed represent a distinct subtype with the two disorders cosegregating among relatives, or whether ADHD and anxiety are transmitted independently in this population(7). If evidence for a distinct subtype is elicited, genetic studies will seek to identify relevant susceptibility genes. Similar investigations of ADHD co-morbid with Tourette's disorder may also prove revealing. From a clinical standpoint, these results clearly demonstrate that that assessment and treatment standards for ADHD developed in North America have applicability in Costa Rica, particularly those standards which take full account of co-morbidity, but that Costa Rican mental health professionals must be particularly vigilant for co-morbid anxiety, both in patients with ADHD and in their affected siblings(48, 49).

Acknowledgments

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Table 1

Subtypes of ADHD and Comorbid Disorders in ADHD-affected Probands

	Probands only (N=95)		Total sample (N=155)	
	Number	%	Number	%
ADHD subtypes				
Combined	66	69.5	101	64.3
Inattentive	26	27.4	49	31.2
Hyperactive	3	3.2	7	4.5
Conduct disorder	4	4.3	9	5.8
ODD	25	26.6	48	31.0
Any disruptive behavior disorder	29	30.9	51	32.9
Major Depression	11	11.7	14	9.0
Dysthymia	0	0	2	1.3
Bipolar I	0	0	0	0
Bipolar II	0	0	0	0
Any mood disorder	11	11.7	15	9.7
GAD	13	14.0	16	10.5
OCD	3	3.2	6	3.9
Social phobia	16	17.2	31	20.1
Specific phobia	16	17.2	23	14.9
Separation anxiety	12	12.9	21	13.6
Agoraphobia	2	2.2	2	1.3
Any anxiety disorder	52	55.9	85	55.2
Tourette's disorder	16	17.0	17	11.0
CMVT	5	5.3	10	6.5
Nonspecific	9	9.6	10	6.5
Any tic disorder	33	34.0	37	23.9
Enuresis	5	5.3	10	6.5
Substance abuse	1	1.1	1	0.7
Tobacco	2	2.3	2	1.4
No comorbidities	15	16.0	31	20.0

Note: ADHD = attention deficit hyperactivity disorder; ODD = oppositional defiant disorder; GAD = generalized anxiety disorder; OCD = obsessive compulsive disorder; CMVT = chronic motor/vocal tics. Total sample for ADHD subtypes was 157. Two siblings did not have available data on comorbid psychiatric conditions.

Table 2

Subtypes of ADHD and comorbidities associated with ADHD by age

ADHD subtypes	Ages 6-12 N=119		Ages 13-26 N=37		X²	P value
	N	%	N	%		
Combined	80	67.2	20	54.1	2.13	0.15
Inattentive	35	29.4	14	37.8	0.03	0.34
Hyperactive	5	4.2	2	5.4	0.10	0.76
Any disruptive behavior disorder	45	38.5	6	16.2	6.28	0.01
Any mood disorder	12	10.3	3	8.1	0.15	0.70
Any anxiety disorder	66	56.4	19	52.8	0.15	0.70
Any tic disorder	25	21.4	12	32.4	0.84	0.36
No comorbidities	21	18.0	9	24.3	0.73	0.39

Note: ADHD = attention deficit hyperactivity disorder.

Table 3

Sib-sib comparisons for psychiatric diagnostic categories between probands and siblings

	Pairwise correlation	P value	H^2
ADHD Inattentive	0.084	0.54	0.168
ADHD hyperactive/impulsive	-0.041	0.76	0.082
ADHD combined	0.016	0.91	0.032
Any disruptive behavior disorder (except ADHD)	0.01	0.95	0.020
Any mood disorder	0.245	0.07	0.490
Any anxiety disorder	0.407	0.002	0.814
Any tic disorder	0.143	0.29	0.286

H^2 = estimated heritability

Table 4

Demographic and clinical diagnoses in proband associated with any anxiety disorder in the sibling.

	OR	95% CI	P value
Gender	0.62	0.11-3.39	0.58
Age	1.49	1.07-2.10	0.02
ADHD Inattentive subtype	0.85	0.37-1.97	0.70
ADHD Hyperactive-Impulsive subtype	0.34	0.32-3.72	0.38
Any Tic disorder	0.54	0.11-2.59	0.44
Any Anxiety Disorder	6.13	1.52-24.83	0.01

OR = Odds ratio; 95% CI= 95% confidence interval