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EXAMINING THE NATURE OF THE COMORBIDITY BETWEEN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND POSTTRAUMATIC STRESS DISORDER

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Abstract

Objective—This study sought to address the link between attention-deficit/hyperactivity disorder (ADHD) and posttraumatic stress disorder (PTSD) in youth by providing a comprehensive comparison of clinical correlates of ADHD subjects with and without PTSD across multiple non-overlapping domains of functioning and familial patterns of transmission.

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DECLARATION OF INTEREST

Dr. Joseph Biederman is currently receiving research support from the following sources: Elminda, Janssen, McNeil, and Shire. In 2012, Dr. Joseph Biederman received an honorarium from the MGH Psychiatry Academy and The Children's Hospital of Southwest Florida/Lee Memorial Health System for tuition-funded CME courses. In 2011, Dr. Joseph Biederman gave a single unpaid talk for Juste Pharmaceutical Spain, received honoraria from the MGH Psychiatry Academy for a tuition-funded CME course, and received honoraria for presenting at international scientific conference on ADHD. He also received an honorarium from Cambridge University Press for a chapter publication. Dr. Biederman received departmental royalties from a copyrighted rating scale used for ADHD diagnoses, paid by Eli Lilly, Shire and AstraZeneca; these royalties are paid to the Department of Psychiatry at MGH. In 2010, Dr. Joseph Biederman received a speaker's fee from a single talk given at Fundación Dr. Manuel Camelo A.C. in Monterrey Mexico. Dr. Biederman provided single consultations for Shionogi Pharma Inc. and Cipher Pharmaceuticals Inc.; the honoraria for these consultations were paid to the Department of Psychiatry at the MGH. Dr. Biederman received honoraria from the MGH Psychiatry Academy for a tuition-funded CME course. In previous years, Dr. Joseph Biederman received research support, consultation fees, or speaker's fees for/from the following additional sources: Abbott, Alza, AstraZeneca, Boston University, Bristol Myers Squibb, Celltech, Cephalon, Eli Lilly and Co., Esai, Fundacion Areces (Spain), Forest, Glaxo, Gliatech, Hastings Center, Janssen, McNeil, Medice Pharmaceuticals (Germany), Merck, MMC Pediatric, NARSAD, NIDA, New River, NICHD, NIMH, Novartis, Noven, Neurosearch, Organon, Otsuka, Pfizer, Pharmacia, Phase V Communications, Physicians Academy, The Prechter Foundation, Quantia Communications, Reed Exhibitions, Shire, the Spanish Child Psychiatry Association, The Stanley Foundation, UCB Pharma Inc., Veritas, and Wyeth.

In the past year, Dr. Faraone received consulting income and/or research support from Shire, Otsuka and Alcobra and research support from the National Institutes of Health (NIH). In previous years, he received consulting fees or was on Advisory Boards or participated in continuing medical education programs sponsored by: Shire, McNeil, Janssen, Novartis, Pfizer and Eli Lilly. Dr. Faraone receives royalties from books published by Guilford Press: *Straight Talk about Your Child's Mental Health* and Oxford University Press: *Schizophrenia: The Facts*. Dr. Bhide, Mr. Petty, and Ms. Woodworth have no interests to declare.

Method—Participants were 271 youth with ADHD and 230 controls without ADHD of both sexes along with their siblings. Participants completed a large battery of measures designed to assess psychiatric comorbidity, psychosocial, educational, and cognitive parameters.

Results—PTSD was significantly higher in ADHD probands vs. controls (5.2% vs. 1.7%, $\chi^2_{(1)}=4.36$, $p=0.04$). Irrespective of the comorbidity with PTSD, ADHD subjects had similar ages at onset of ADHD, similar type and mean number of ADHD symptoms, and similar ADHD-associated impairments. PTSD in ADHD probands was significantly associated with a higher risk of psychiatric hospitalization, school impairment, poorer social functioning and higher prevalences of mood, conduct disorder, and anxiety disorders. The mean onset of PTSD (12.6 years) was significantly later than that of ADHD and comorbid disorders (all $p<0.05$). Siblings of ADHD and ADHD+PTSD probands had higher prevalences of ADHD vs. siblings of controls (35% vs. 18%, $z=4.00$, $p<0.001$ and 67% vs. 18%, $z=4.02$, $p<0.001$, respectively) and siblings of ADHD+PTSD probands had a significantly higher prevalence of PTSD compared to the siblings of ADHD and control probands (20% vs. 3% and 3%, $z=2.99$, $p=0.003$ and $z=2.07$, $p=0.04$, respectively).

Conclusion—Findings indicate that the comorbidity with PTSD in ADHD leads to greater clinical severity as regards psychiatric comorbidity and psychosocial dysfunction. ADHD is equally familial in the presence of PTSD in the proband indicating that their co-occurrence is not due to diagnostic error.

Keywords

Attention deficit disorder (ADD); attention-deficit/hyperactivity disorder (ADHD); post-traumatic stress disorder (PTSD); comorbidity

INTRODUCTION

A recent literature has begun to document a robust link between attention-deficit/hyperactivity disorder (ADHD) and posttraumatic stress disorder (PTSD). A strong association between ADHD and PTSD has been identified in clinical and epidemiological samples of adults. Adler et al. (1) found an increased risk for ADHD in combat veterans with PTSD and suggested that ADHD may be a risk factor for the development of PTSD. Gurvits et al. (2) found that, 30% of both male and females with PTSD had ADHD symptoms in childhood, compared to only 11% of the adults without PTSD. Furthermore, PTSD Scale scores were significantly correlated ($r = .42$) with mean childhood ADHD scores as assessed by Wender Utah Rating Scale (2). Kessler et al. (3) reported a bidirectional and significant risk between ADHD and PTSD in a large epidemiological sample, which suggests that the association between ADHD and PTSD cannot be attributed to referral bias.

Recently, Antshel et al. (Post-Traumatic Stress Disorder in Adult Attention Deficit Hyperactivity Disorder: Clinical Features and Familial Transmission. Submitted manuscript) addressed the link between ADHD and PTSD in 201 adults with ADHD and 123 controls without ADHD and found a significantly increased risk for PTSD among ADHD versus controls. These investigators also documented that ADHD subjects with PTSD had higher rates of psychiatric comorbidity than controls and similarly elevated rates of both PTSD and ADHD in first-degree relatives that significantly differed from those in controls.

Similarly, pediatric studies have also documented that youth with ADHD are more likely than those without ADHD to develop PTSD and vice versa (4–6). A recent longitudinal follow-up study of children with ADHD grown up of both sexes also documented a significant risk for PTSD in youth ADHD when compared with controls without this

disorder (Biederman et al. Is ADHD a risk for posttraumatic stress disorder (PTSD)? Results from a large longitudinal study of referred children with and without ADHD. Submitted manuscript).

Yet concerns remain as to whether children with symptoms of both ADHD and PTSD suffer from ADHD or whether their symptoms are secondary to PTSD. Because both ADHD and PTSD are familial disorders (7–10), one way to help clarify this important question is to examine patterns of familial transmission between the two disorders. If children with ADHD plus PTSD truly have ADHD, then patterns of familiarity with ADHD should be similar in children with ADHD irrespective of the presence or absence of PTSD in the proband child. Likewise, we would also expect that the symptomatic picture of ADHD would be similar in ADHD children irrespective of the presence or absence of PTSD in the proband child. Finally, if children that meet criteria for both ADHD and PTSD truly suffer from ADHD and their symptomatic picture is not secondary to PTSD, we would expect that ADHD would precede the onset of PTSD and not follow it. To the best of our knowledge, these issues have never before been adequately addressed in the PTSD or ADHD literature.

A better understanding of the relationship between ADHD and PTSD has important clinical, scientific and public health implications. If ADHD puts children at risk for developing PTSD, such information would provide valuable information to clinicians caring for children with ADHD by alerting them that ADHD may predispose these children to develop PTSD after being exposed to traumatic experiences. It would also alert clinicians about the ways in which children with comorbid ADHD and PTSD may differ from those with ADHD alone, which could impact diagnosis and service delivery. Considering the high prevalence of ADHD, and its propensity for impulsivity and accidents, children with ADHD should be considered a high risk population for the development of PTSD. From the scientific perspective, this knowledge could advance research efforts to gain insight into the pathophysiology of some forms of PTSD linked to ADHD.

Aims of the study

To examine the association between attention-deficit/hyperactivity disorder (ADHD) and attention-deficit/hyperactivity disorder (PTSD) by testing the following hypotheses: i) ADHD plus PTSD will be associated with more dysfunction than ADHD alone; ii) ADHD symptoms will be similar in ADHD subjects with and without PTSD; iii) relatives of ADHD plus PTSD patients will be at a risk for ADHD; iv) PTSD will onset after ADHD. To the best of our knowledge, this study is the first comprehensive evaluation of the implications of PTSD in pediatric ADHD.

MATERIAL AND METHODS

Subjects

Subjects were youth probands of both sexes and their siblings derived from two identically designed, longitudinal, case-control family studies conducted at the Clinical and Research Programs in Pediatric Psychopharmacology and Adult ADHD at the Massachusetts General Hospital (MGH). Detailed study methodology has been previously reported (11, 12). Briefly, these studies included male and female youth probands with and without DSM-III-R ADHD and their first-degree relatives (hereafter referred to as the Boys and Girls ADHD study, respectively) ascertained from pediatric and psychiatric sources. For both studies, potential probands were excluded if they had been adopted, if their nuclear family was not available, if they had major sensorimotor handicaps (paralysis, deafness, blindness), if they had psychosis or autism, or if they were unable to participate in the assessments due to language barriers or an estimated IQ < 80. After a complete description of the study, parents

provided written informed consent for their children, and children and adolescents provided written assent. The IRB at MGH approved this study.

We used a three-stage ascertainment procedure to select probands (13, 14). For ADHD subjects, the first stage was their referral, which resulted in a clinical diagnosis of ADHD. The second stage confirmed the diagnosis of ADHD through a telephone questionnaire administered to the mother. The third stage was a diagnostic assessment with a structured interview. Only patients who received a positive diagnosis at all three stages were included. Controls were similarly selected through a three-stage procedure. First, we ascertained them from consecutive referrals to medical clinics for routine physical examinations at both the psychiatric and pediatric sources. In stage two, the control mothers responded to the DSM-III-R ADHD telephone questionnaire about their children. Eligible controls meeting study entry criteria were recruited for the study and received the third stage, a diagnostic assessment with a structured interview. Only subjects classified as not having ADHD at all three stages were included in the control group.

We used data from male and female probands from both studies who were assessed for PTSD at least once ($n=243$ probands from the Boys study and $n=258$ from the Girls study). Siblings of these probands were also assessed ($n=355$ siblings from the Boys study and $n=333$ from the Girls study). In the Boys study (11), PTSD was assessed at the four- and ten-year follow-ups. In the Girls study (15), PTSD was assessed at baseline and at five- and eleven-year follow-ups. The mean age of the probands and their siblings at last assessment was 21.2.

Assessment Procedures

Psychiatric assessments relied on the Kiddie Schedule for Affective Disorders and Schizophrenia- Epidemiologic Version (K-SADS-E) (16) for subjects less than 18 years of age and the Structured Clinical Interview for DSM-III-R (SCID) (17) (supplemented with modules from the K-SADS-E to assess childhood diagnoses) for subjects aged 18 and older. Diagnoses were based on direct interviews with the mothers and the offspring, except for children <12 years that were not interviewed directly. Combining data from direct and indirect interviews, we considered a diagnosis positive if it was endorsed in either interview. All interviews conducted were blind to the subject's referral source or diagnostic status (ADHD or control, proband or sibling). Diagnoses were considered positive if DSM-III-R criteria were unequivocally met. A committee of board-certified child and adult psychiatrists, who were blind to the subject's ascertainment status and all other data, resolved diagnostic uncertainties. Diagnoses presented for review were considered positive only if a consensus was achieved that criteria were met to a degree that would be considered clinically meaningful.

All interviewers had undergraduate degrees in psychology and were trained to high levels of inter-rater reliability. First, they underwent several weeks of classroom style training, learning interview mechanics, diagnostic criteria, and coding algorithms. Then, experienced raters and clinicians observed interviewers. They subsequently conducted at least six practice (non-study) interviews and at least two study interviews while being observed by senior interviewers. The principal investigator (JB) supervised the interviewers throughout the study. We computed kappa coefficients of agreement by having child and adult psychiatrists and clinical psychologists diagnose subjects from audio taped interviews. Based on 500 assessments from interviews of children and adults, the median kappa coefficient was 0.98. Kappa coefficients for individual diagnoses included: ADHD (0.88), separation anxiety (1.0), agoraphobia (1.0), and panic (0.95). Socio-economic status (SES) was measured with the 5-point Hollingshead scale (18), using the occupational and educational status of the parents.

Statistical Analysis

First, we examined demographic characteristics in non-ADHD controls and ADHD probands with and without PTSD using logistic, linear, or ordered logistic regression, depending on the distribution of the dependent variable. We controlled for any demographic confounder that reached significance at the 0.10 alpha level. We compared the three groups on psychiatric disorders and neuropsychological testing using logistic and linear regression, and we compared the two ADHD groups on characteristics of ADHD. Across all models, we used robust Huber-White estimates of variance to account for the non-independence among subjects due to the correlation between family members. All tests were two-tailed and alpha was set at 0.05. We calculated all statistics using STATA, version 12.0.

RESULTS

The prevalence of PTSD was significantly higher in ADHD probands compared to control probands (5.2% vs. 1.7%, $\chi^2_{(1)}=4.36$, $p=0.04$) (3 car accidents, 3 witnessed abuse, 5 sexual abuse/rape and 3 physical abuse). ADHD probands were younger and had lower socioeconomic status (SES) than controls (Table 1). Therefore, all subsequent analyses controlled for proband age and family SES.

At baseline, the two ADHD groups had similar ages at onset of ADHD, similar mean number of symptoms, and similar ADHD-associated impairments (Table 2). They also had a similar prevalence of individual ADHD symptoms (all $p>0.20$). However, the presence of PTSD in ADHD probands was significantly associated with a higher risk of psychiatric hospitalization, a higher likelihood to have repeated a grade or been placed in a special classes and with poorer social functioning as measured by the SAICA, in particular having problems with peers (Table 2).

As can be seen in Figure 1, with the exception of alcohol abuse and dependence, both ADHD groups had significantly higher prevalences of all psychiatric disorders assessed. However, comorbid PTSD in ADHD probands was selectively associated with higher prevalences of major depressive disorder, bipolar disorder, conduct disorder, separation anxiety disorder, generalized anxiety disorder, agoraphobia, and panic disorder.

Both ADHD groups had significantly higher rates of both types of emotional regulation deficits as defined through the CBCL (CBCL-Deficient Emotional Self-Regulation: Controls=1.8%, ADHD=35.6%, ADHD+PTSD=27.3%; CBCL-Severe Dysregulation: Controls=0%, ADHD=17.1%, ADHD+PTSD=45.3%; all ADHD versus Control comparisons $p<0.001$). Although the ADHD+PTSD had a higher rate of CBCL-Severe Dysregulation compared to the ADHD group, it failed to reach our a priori threshold for statistical significance.

As can be seen in Figure 2A, the mean onset of PTSD (12.6 years, $SD=6.5$, range 3 to 25) was significantly later than that of ADHD, social phobia, separation anxiety disorder, oppositional defiant disorder, and major depressive disorder (all $p<0.05$). In fact the onset of the overwhelming majority of comorbid disorders occurred before the onset of PTSD, with the exception of substance use disorders (Figure 2B).

With the exception of PTSD being associated with significantly fewer categories completed (3.5 ± 2.1 vs. 4.9 ± 1.7 , $p<0.05$) and more non-perseverative errors on the Wisconsin Card Sorting Test (26.8 ± 15.5 vs. 17.2 ± 13.2 , $p<0.05$), there were no other meaningful differences in neuropsychological test scores (all $p>0.05$).

Familial Risk Analysis

As shown in Figure 3, siblings of the ADHD and ADHD+PTSD probands had higher prevalences of ADHD compared to that of siblings of controls (Figure 3A, 35% vs. 18%, $z=4.00$, $p<0.001$ and 67% vs. 18%, $z=4.02$, $p<0.001$, respectively). In addition, siblings of ADHD+PTSD probands had a significantly higher prevalence of ADHD compared to siblings of other ADHD probands ($z=2.87$, $p=0.004$). Siblings of ADHD+PTSD probands also had a significantly higher prevalence of PTSD compared to the siblings of ADHD and control probands (Figure 3B, 20% vs. 3% and 3%, $z=2.99$, $p=0.003$ and $z=2.07$, $p=0.04$, respectively). The rates of PTSD in siblings did not differ in siblings of ADHD and control probands.

DISCUSSION

Our results from this large, controlled family study of youth with and without ADHD confirm results from prior studies reporting that ADHD is associated with PTSD. Although ADHD+PTSD probands did not differ from other ADHD probands in regards to the clinical features of ADHD, the comorbid condition of ADHD+PTSD led to greater clinical severity in regard to other psychiatric comorbidities and psychosocial dysfunction. Familial risk analysis suggests that ADHD and PTSD breed true in families.

The ADHD probands with and without PTSD did not differ in their severity of inattentive or hyperactive-impulsive symptoms. This suggests that the development of PTSD in the ADHD+PTSD group cannot be simply attributed to higher levels of these ADHD symptom domains. Despite these similarities in the clinical features of ADHD proper, probands with PTSD showed greater severity as regards patterns of psychiatric comorbidity such that the ADHD+PTSD group had higher lifetime rates of almost all psychiatric disorders.

Our findings documenting higher levels of morbidity and dysfunction associated with PTSD in youth with ADHD when compared with other youth with ADHD without this comorbidity are highly consistent with findings in adult samples. Our recent study of adult ADHD also documented higher rates of psychiatric comorbidity and psychosocial dysfunction in ADHD adults who developed PTSD (Antshel et al. Post-Traumatic Stress Disorder in Adult Attention Deficit Hyperactivity Disorder: Clinical Features and Familial Transmission. Submitted manuscript).

Our finding that, with few exceptions, the onset of ADHD and other comorbid disorders preceded significantly the onset of PTSD suggests that ADHD and associated comorbid disorders are antecedent risk factors for the development of PTSD in youth. Considering that effective treatments are widely available for the treatment of ADHD and many comorbid psychiatric disorders, their identification and treatment could mitigate the development of PTSD in youth with ADHD. Partial support for this hypothesis derives from our previous work documenting that treatment for ADHD with stimulants significantly decreases the subsequent development of anxiety disorders, including PTSD, in youth with ADHD (19). Considering the severity and morbidity associated with PTSD, confirmation of this hypothesis could have large clinical, scientific and public health relevance.

Because prior studies of ADHD and PTSD show that both exhibit genetic transmission (7–10), our familial transmission data provides unique insights into the nature of the association between these disorders. These data show that the relatives of ADHD probands with and without PTSD had significantly elevated rates of ADHD than controls. This familial transmission data address the idea that ADHD symptoms among PTSD patients are misdiagnosed due to clinical features of PTSD that might confound an ADHD diagnosis such as hyperarousal and inattention (20–22). If PTSD caused an ADHD-like syndrome that

is misdiagnosed as ADHD, we would not have expected to find an elevated prevalence of ADHD among ADHD+PTSD probands. The idea that ADHD among PTSD patients is a mimic of ADHD is further contradicted by our finding that that age at onset of PTSD was typically subsequent to the age at onset of ADHD.

Our family study data also suggest that ADHD+PTSD may be a more severe familial variant of ADHD. This inference derives from the much greater rates of ADHD among relatives of ADHD+PTSD compared with ADHD probands. For example, compared with relatives of ADHD probands, relatives of ADHD+PTSD probands had more than twice the prevalence of ADHD. The finding that rates of PTSD were only increased in relatives of probands with PTSD and not in relatives of ADHD probands indicates that PTSD breeds true in families. This finding in our pediatric sample is partially discrepant with our study of adult probands that found elevated rates of PTSD in relatives irrespective of PTSD status in the ADHD proband, a finding more compatible with the hypothesis that in adults, ADHD and PTSD share familial etiological risk factors. More work is needed with longer follow up time of our longitudinal pediatric sample to re-examine the familial transmission of ADHD and PTSD.

Although prior family-genetic studies of PTSD have not assessed ADHD, Koenen et al.'s (8, 9) and Sartor et al.'s (10) twin studies found shared heritability between PTSD and major depression, which is frequently comorbid with ADHD. Twin studies are needed to determine if the familial co-transmission of ADHD and PTSD can be attributed to genetic or environmental familial risk factors.

Our work has several important implications. Clinicians who treat youth with ADHD should be alert to the fact that their ADHD patients are at high risk for PTSD. Moreover, among ADHD patients, the presence of PTSD signals a more complicated course and outcome. We found that many psychiatric disorders were more common among ADHD youth with PTSD compared with other ADHD youth. Because many of these disorders are treatable, clinicians should screen for these conditions among ADHD+PTSD youth. Of particular importance, the onset of drug and alcohol use disorders tends to onset after the onset of PTSD. Thus, ADHD youth with PTSD should be carefully monitored for substance use. For clinicians who focus on the treatment of PTSD, it would be prudent to assess for ADHD and treat the associated ADHD once adequate symptom stabilization and safety is achieved for the PTSD. Our data also suggest that ADHD symptoms should not be viewed as a complication of PTSD. Clinicians should also be alert to the fact that if they are treating a patient with ADHD+PTSD, the relatives of these patients are at particularly high risk for both ADHD and PTSD. The presence of these disorders in parents could complicate the treatment of ADHD youth.

This study has also some limitations. Firstly, the number of PTSD subjects and their relatives was relatively small. Although this would not have caused spurious findings of statistical significance, it did limit our power to detect some effects. We only had PTSD data for probands and siblings, precluding our ability to examine rates of PTSD in all first-degree relatives. Additionally, we lacked a PTSD only comparison group that would have been ideal for establishing the co-transmission of the two disorders. Since our sample was referred and overwhelmingly Caucasian, our findings may not generalize to community samples or other ethnic groups. Although our interviewers were blind to the diagnosis of the probands, parents were not. Another potential source of bias stems from the lack of direct psychiatric interviews with children younger than twelve; this may have decreased the sensitivity of some diagnoses. This may be especially the case for "internalizing" disorders such as anxiety and depression. However, we found high rates of both these disorders in our study. Also, children younger than 12 have limited expressive and receptive language

abilities; they cannot easily sequence events in time, and have difficulties with abstraction. Thus, there is a real question about whether their self-perceptions, memories, feelings, and reported behavior can be reliably assessed through self-report, especially as regards lifetime history of psychopathology (23). Although limited, studies of interview techniques for children under the age of 12 suggest that their responses are unreliable (24). Another concern is that interviews with mothers about their children may have been subject to a halo effect (i.e., a bias toward reporting a second illness in the presence of another). This could have led to an overestimation of the comorbidity between ADHD and other disorders.

Although diagnoses were made by a committee of Board Certified child and adolescent psychiatrists, some caution in their interpretation is warranted. First, the diagnoses were based on the child's lifetime history of psychopathology. The formulation of such diagnoses is a difficult process, especially in the context of comorbidity. However, in our own work, lifetime diagnoses have shown excellent inter-rater reliability (see Methods) and good to excellent test-retest reliability over a one year period (25). Although our results are likely to generalize to many of the ADHD children seen in pediatric and psychiatric settings, we do not know if our results will generalize to ADHD children in the general population.

Despite these limitations, our study adds to our understanding of the association between PTSD and ADHD in youth, and provides new insights as to the clinical ramifications of this association for affected patients as well as their families. Our data suggest that among ADHD patients, PTSD is not caused by excessive hyperactive-impulsive or inattentive symptoms and that ADHD symptoms are not sequelae of PTSD. Instead, our work suggests that ADHD and PTSD breed true in families and that the accumulation of these factors in ADHD+PTSD patients leads to a more severe course and outcome.

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Significant Outcomes

- Attention-deficit/hyperactivity disorder (ADHD)+ post-traumatic stress disorder (PTSD) probands did not differ from other ADHD probands as regards the clinical features of ADHD.
- The comorbid condition of ADHD+PTSD led to greater clinical severity as regards to other psychiatric comorbidities and psychosocial dysfunction.
- Familial risk analysis suggests that ADHD and PTSD breed true in families.

Limitations

- The number of PTSD subjects and their relatives was relatively small, limiting the power to detect some effects.
- PTSD data was available for probands and siblings, precluding the ability to examine rates of PTSD in all first-degree relatives.
- We lacked a PTSD without ADHD group that would have been ideal for establishing the co-transmission of the two disorders.

Figure 1.
Lifetime Prevalences of Psychiatric Disorders in Probands

Figure 2.

Ages of Onset of Comorbid Disorders in Relation to PTSD

A. Mean ages of onset

B. Percent of Comorbid disorder with Onset Before the onset of PTSD

A. Rates of ADHD

B. Rates of PTSD group

A: vs. Controls, B: vs. ADHD, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Figure 3.
Familial Risk Analysis of ADHD and PTSD: Rates in Siblings

Table 1

Sociodemographics Characteristics

	Probands			Test statistic	p-value
	Controls N=230	ADHD N=257	ADHD+PTSD N=14		
Baseline age	11.9 ± 3.3	10.9 ± 3.2 ^a	10.5 ± 3.4	F _(2,498) =5.65	0.004
Last assessment age	21.6 ± 4.3	20.1 ± 4.7 ^a	21.1 ± 3.4	F _(2,498) =7.58	<0.001
% Male	112 (49)	126 (49)	5 (36)	χ ² ₍₂₎ =0.95	0.62
% Caucasian	216 (94)	249 (97)	14 (100)	χ ² ₍₂₎ =3.22	0.20
Baseline socioeconomic status	1.6 ± 0.8	1.8 ± 0.9 ^a	2.4 ± 1.4 ^a	χ ² ₍₂₎ =11.82	0.003
Siblings					
	N=303	N=365	N=15		
Last assessment age	20.9 ± 6.5	20.4 ± 7.2	19.3 ± 5.5	F _(2,422) =0.60	0.55
% Male	158 (52)	197 (54)	8 (53)	χ ² ₍₂₎ =0.21	0.90

^a p<0.05 vs. Controls

ADHD characteristics, treatment history, educational functioning, and social adjustment inventory for children and adolescents (SAICA) in probands

Table 2

	Controls (N=230)	ADHD (N=257)	ADHD+PTSD (N=14)	Test Statistic	p-value
	N (%) or Mean $\pm$ SD	N (%) or Mean $\pm$ SD	N (%) or Mean $\pm$ SD		
ADHD characteristics					
ADHD age of onset (years)	--	3.1 $\pm$ 2.3	3.3 $\pm$ 2.6	z=0.04	0.97
ADHD onset before PTSD	--	--	13 (93)		
ADHD impairment					
Mild	--	16 (6)	0 (0)	Exact	0.99
Moderate	--	134 (52)	7 (50)	z=-0.01	0.99
Severe	--	106 (41)	7 (50)	z=0.31	0.75
ADHD total symptoms	--	11.6 $\pm$ 1.9	12.3 $\pm$ 1.8	z=0.78	0.43
Treatment history					
None	132 (57)	11 (4)	0 (0)	Exact	<0.001
Counseling	66 (29)	10 (4) ^a ^{***}	1 (7)	$\chi^2_{(1)}=38.66$	<0.001
Medication	5 (2)	30 (12)	0 (0)	Exact	<0.001
Counseling+medication	25 (11)	164 (64) ^a ^{***}	5 (36) ^a ^{**}	$\chi^2_{(2)}=115.83$	<0.001
Hospitalization	2 (1)	42 (16) ^a ^{***}	8 (57) ^a ^{***b} ^{**}	$\chi^2_{(2)}=27.88$	<0.001
School Failure					
Tutoring	98 (43)	225 (88) ^a ^{***}	13 (93) ^a ^{**}	$\chi^2_{(2)}=95.95$	<0.001
Placement in special class	6 (3)	100 (39) ^a ^{***}	11 (79) ^a ^{***b} [*]	$\chi^2_{(2)}=58.08$	<0.001
Repeated grade	23 (10)	87 (34) ^a ^{***}	11 (79) ^a ^{***b} [*]	$\chi^2_{(2)}=41.41$	<0.001
SAICA Scale					
Total score	1.6 $\pm$ 0.3	2.0 $\pm$ 0.4 ^a ^{***}	2.3 $\pm$ 0.4 ^a ^{***b} [*]	F _(2,475) =98.73	<0.001
School behavior problems	1.6 $\pm$ 0.6	2.7 $\pm$ 0.8 ^a ^{***}	3.0 $\pm$ 0.6 ^a ^{***}	$\chi^2_{(2)}=156.66$	<0.001
Spare time activities	1.8 $\pm$ 0.5	2.0 $\pm$ 0.6 ^a ^{***}	2.3 $\pm$ 0.8 ^a ^{**}	$\chi^2_{(2)}=21.29$	<0.001
Spare time problems	1.4 $\pm$ 0.6	2.2 $\pm$ 0.8 ^a ^{***}	2.7 $\pm$ 0.9 ^a ^{***}	$\chi^2_{(2)}=108.41$	<0.001
Activities with peers	1.7 $\pm$ 0.6	2.1 $\pm$ 0.7 ^a ^{***}	2.1 $\pm$ 0.8	$\chi^2_{(2)}=28.57$	<0.001

	Controls (N=230)	ADHD (N=257)	ADHD+PTSD (N=14)	Test Statistic	p-value
	N (%) or Mean $\pm$ SD	N (%) or Mean $\pm$ SD	N (%) or Mean $\pm$ SD		
Problems with peers	1.4 $\pm$ 0.5	2.1 $\pm$ 0.8 ^{a***}	2.8 $\pm$ 0.9 ^{a***b**}	$\chi^2_{(2)}=103.29$	<0.001
Boy-girl relationship	2.3 $\pm$ 0.7	2.4 $\pm$ 0.8	2.0 $\pm$ 0.8	$\chi^2_{(2)}=1.12$	0.57
Problems with opposite sex	1.3 $\pm$ 0.5	1.5 $\pm$ 0.8 ^{a*}	1.8 $\pm$ 1.0	$\chi^2_{(2)}=6.50$	0.04
Relationship with siblings	1.7 $\pm$ 0.7	1.9 $\pm$ 0.8 ^{a***}	1.9 $\pm$ 0.8	$\chi^2_{(2)}=12.78$	0.002
Problems with siblings	1.5 $\pm$ 0.7	2.0 $\pm$ 0.8 ^{a***}	2.4 $\pm$ 0.7 ^{a**}	$\chi^2_{(2)}=39.02$	<0.001
Relationship with mother	1.4 $\pm$ 0.6	1.6 $\pm$ 0.7 ^{a***}	1.3 $\pm$ 0.7	$\chi^2_{(2)}=14.04$	<0.001
Relationship with father	1.6 $\pm$ 0.7	1.8 $\pm$ 0.8 ^{a**}	2.3 $\pm$ 1.2 ^{a**}	$\chi^2_{(2)}=14.58$	<0.001
Problems with parents	1.3 $\pm$ 0.5	2.0 $\pm$ 0.8 ^{a***}	2.4 $\pm$ 0.7 ^{a***}	$\chi^2_{(2)}=104.93$	<0.001

^a vs. Controls,

^b vs. ADHD

* p<0.05,

** p<0.01,

*** p<0.001