Scandinavian Journal of Child and Adolescent Psychiatry and Psychology
Vol. 4(2):77-87 (2016)

SJCAPP

Research Article **Open Access**

Are Autistic Traits in Youth Meaningful? A Replication study in Non-referred Siblings of Youth with and without Attention-Deficit/Hyperactivity Disorder

Joseph Biederman[1-3], Maura Fitzgerald[1,2], Stephen V. Faraone[4,5], Ronna Fried[1-3], K. Yvonne Woodworth[1,2], Alexandra Saunders[1,2], Kristina Conroy[1,2], Gagan Joshi[1-3]

[1]Clinical and Research Programs in Pediatric Psychopharmacology and Adult ADHD, Massachusetts General Hospital, Boston, MA, USA
[2]Alan and Lorraine Bressler Clinical and Research Program for Autism Spectrum Disorder, Massachusetts General Hospital, Boston, MA, USA
[3]Department of Psychiatry, Harvard Medical School, Boston, MA, USA
[4]Departments of Psychiatry and of Neuroscience and Physiology, SUNY Upstate Medical University, Syracuse, NY, USA
[5]K.G.Jebsen Centre for Psychiatric Disorders, Department of Biomedicine, University of Bergen, Bergen,Norway

***Corresponding author:** jbiederman@partners.org

Abstract

Background: We previously described the high prevalence and burden of significant autistic traits (ATs) in youth with attention-deficit/hyperactivity disorder (ADHD). These traits are associated with significantly greater impairment in psychopathological, interpersonal, educational, and neuropsychological functioning. Because the sample consisted of referred ADHD youth, uncertainty remained regarding whether these findings are generalizable to non-referred populations of youths with and without ADHD.
Objective: The aim of the current study was to assess the prevalence and implications of ATs in a non-referred population of siblings of probands with and without ADHD.
Method: Participants were non-referred siblings of probands with ADHD (N = 257) and control probands (N = 234) of longitudinal, case-control family studies conducted at Massachusetts General Hospital. Assessments included measures of psychiatric, psychosocial, educational, and cognitive functioning. The presence of significant ATs was operationalized using the Child Behavior Checklist AT profile, which consists of combined aggregate T-scores of ≥ 195 on the Withdrawn, Social, and Thought Problems subscales.
Results: ATs were significantly more prevalent among the siblings of probands with ADHD as compared with siblings of control probands (6% vs. 1%; $P = .02$). Siblings of probands with ADHD with a positive AT profile (N = 15) were significantly more impaired than those without an AT profile (N = 242) with regard to psychopathological, interpersonal, educational, and neuropsychological functioning.
Conclusions: The current study reports a higher-than-expected prevalence of ATs in a non-referred sample of siblings of youth with ADHD, which is consistent with previous findings regarding ATs in a referred sample of youth with ADHD. The presence of ATs is associated with higher levels of morbidity and dysfunction.

Keywords: attention-deficit/hyperactivity disorder (ADHD); autistic trait (AT); youth

Introduction

Both attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) have strong heritable components. Although their underlying etiologies are yet to be fully elucidated, evidence from twin and family studies indicate shared heritability (1,2). Individuals with ADHD may manifest different forms of ASD, from a fully developed syndromic form to a milder form of ASD symptomatology that involves the exhibition of

autistic traits (ATs). However, in contrast with the well-developed literature addressing ASD, much less is known about the morbidity and dysfunction associated with ATs for individuals with and without ADHD.

Recent studies have shown that symptoms of autism or ATs appear in 20% to 30% of children with ADHD (3-5). Children with ADHD and ATs appear to be more impaired and dysfunctional than children with ADHD and no ATs. With these literature findings in mind, we assessed the prevalence and correlates of ATs in youth with and without ADHD, with a diagnosis of autism being exclusionary (6). ATs were operationalized with the use of a profile from the Child Behavior Checklist (CBCL) by using extreme values from the sums of the Withdrawn, Social, and Thought Problems T-scores (7).

In the prior study, a positive AT profile was significantly more prevalent among children with ADHD as compared with control children (18% vs. 0.87%; $p < .01$). Children with ADHD with positive AT profiles were significantly more impaired than other children with ADHD and control children with regard to psychopathology and interpersonal, school, family, and cognitive functioning. However, because our results and the results of previous reports examined ATs in referred samples of children with ADHD (3-5), it remains unknown whether these findings can be generalized to non-referred samples of children with and without ADHD. Studies of such samples would allow clinicians to identify children at high risk for adverse outcomes in multiple domains of functioning. This information could further lead to the development of appropriate intervention strategies aimed at mitigating the adverse outcomes associated with ATs.

The aim of the current study was to examine both the prevalence and correlates of ATs in non-referred youth with and without ADHD. To this end, we used data from an existing large-scale sample of non-referred siblings of probands with and without ADHD. On the basis of the findings in probands, we hypothesized that ATs would be identifiable in non-referred siblings and that the presence of ATs would be associated with higher levels of morbidity and dysfunction.

Methods

Subjects

Subjects were youth of both sexes who had been enrolled in longitudinal case-control family studies conducted at Massachusetts General Hospital (8,9). These studies included probands between the ages of 6 and 18 years with (N = 280) and without (N = 242) ADHD according to *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised,* criteria as determined by pediatric and psychiatric sources. Adoption, unavailable nuclear family, major sensorimotor handicaps, psychosis, autism, language barriers, estimated intelligence quotients of less than 80 were exclusionary for both probands with ADHD and control probands. Parents provided written informed consent, and children and adolescents provided written assent. The institutionnal review board at Massachusetts General Hospital approved the study. The present analysis relied on the non-referred siblings of these probands (N = 395 siblings of probands with ADHD; N = 317 siblings of control probands). Siblings with estimated intelligence quotients of less than 80 were excluded from the present analysis.

Assessment Procedures

We used an empirically derived profile from the CBCL to define ATs (CBCL-AT) by using a cutoff of 195 or more from the combined T-scores of the Withdrawn, Social Problems, and Thought Problems subscales. We previously reported that this profile correctly classified 78% of all subjects with ASD in a psychiatrically referred sample of youth with and without ASD (7). CBCL emotional dysregulation profiles were created from the combined T-scores of the Anxiety/Depression, Aggression, and Attention subscales. Deficient emotional self-regulation was defined as a combined T-score of 180 or more but less than 210; severe emotional dysregulation was defined as a combined T-score of 210 or more.

Psychiatric assessments relied on the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiological Version (K-SADS-E) (10,11). Indirect interviews were conducted with each subject's parent or guardian, usually the mother. Direct interviews were conducted with subjects who were at least 12 years old. After combining data from direct and indirect interviews, a diagnosis was considered positive if it was endorsed in either interview.

Interviews were administered by highly trained and closely supervised raters with bachelor's or master's degrees in psychology or related fields. Raters were blinded to the referral source and the proband's diagnostic status (i.e., ADHD vs. control). On the basis of 500 assessments obtained via interviews of children and adults, the median κ coefficient of agreement between a rater and an experienced clinician was 0.98.

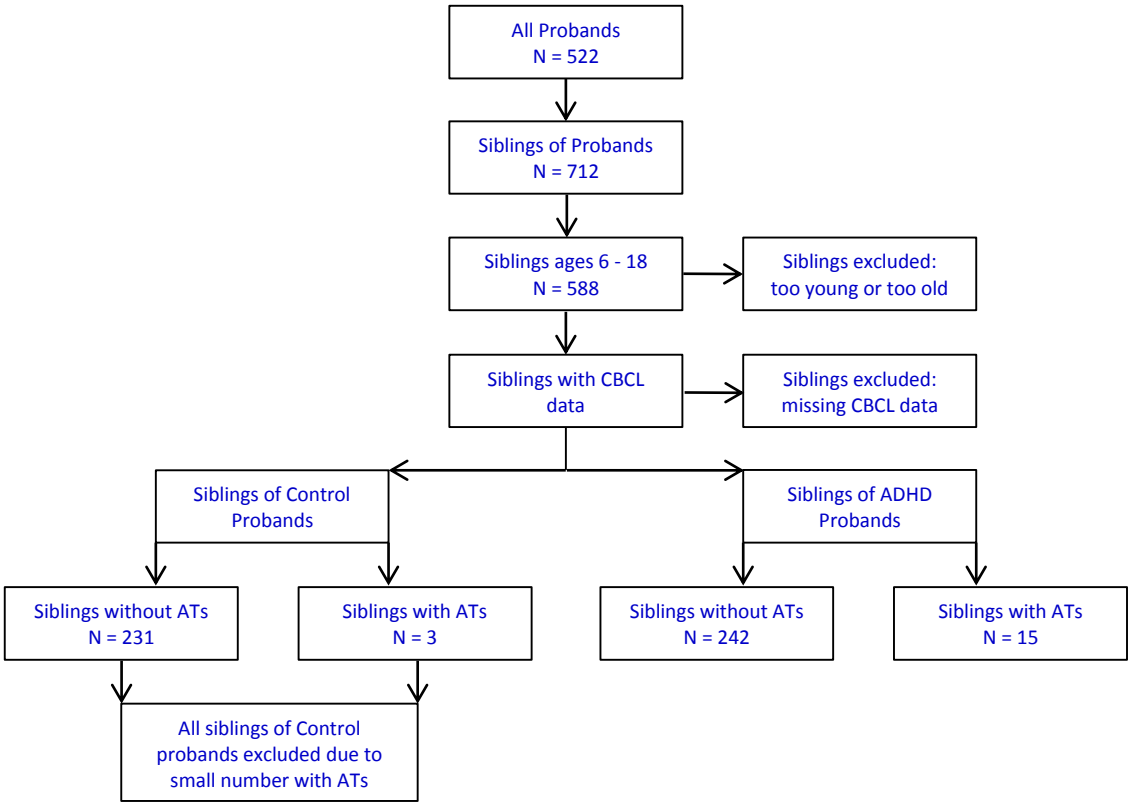
The parent or guardian also provided information about pregnancy and delivery history and the child's infancy. Socioeconomic status (SES) was established using categories delineated by Hollingshead (12). The Global Assessment of Functioning (GAF) scale was used to measure overall adaptive functioning (13,14).

Interpersonal and psychosocial functioning was assessed with the use of the Social Adjustment Inventory for Children and Adolescents (SAICA) (15). To better gauge social difficulties, we computed an index of social dysfunction that we previously called *Social Disability*. This index was computed with the use of methodology recommended by Reynolds (16); it was previously implemented by our team to assess learning disabilities on the basis of the discrepancy between the expected SAICA scaled score (derived from the estimated full-scale intelligence quotient) and the actual SAICA scaled score (17).

To evaluate school functioning, three indices of school difficulties were used: placement in special classes, extra tutoring, and repeated grades as reported by the parent or guardian.

Intellectual functioning was assessed through the Vocabulary, Block Design, Digit Span, Digit Symbol, Digit Coding, and Arithmetic subtests of the Wechsler Intelligence Scale for Children–Revised (WISC-R) (18). By using procedures suggested by Sattler (19), we estimated the full-scale intelligence quotient from the Block Design and Vocabulary subtests of the WISC-R using age-corrected scaled scores. We computed the Freedom from Distractibility intelligence quotient using the Digit Span, Digit Coding, and oral Arithmetic subscales of the WISC-R. Reading and arithmetic achievement were assessed using subtests of the Wide Range Achievement Test–Revised (WRAT-R) (20).

FIGURE 1. PRISMA diagram. Siblings were excluded if they were not 6 – 18 years old or if they were missing CBCL data. Our final sample was restricted to the siblings of ADHD probands because only 3 siblings of control probands had ATs



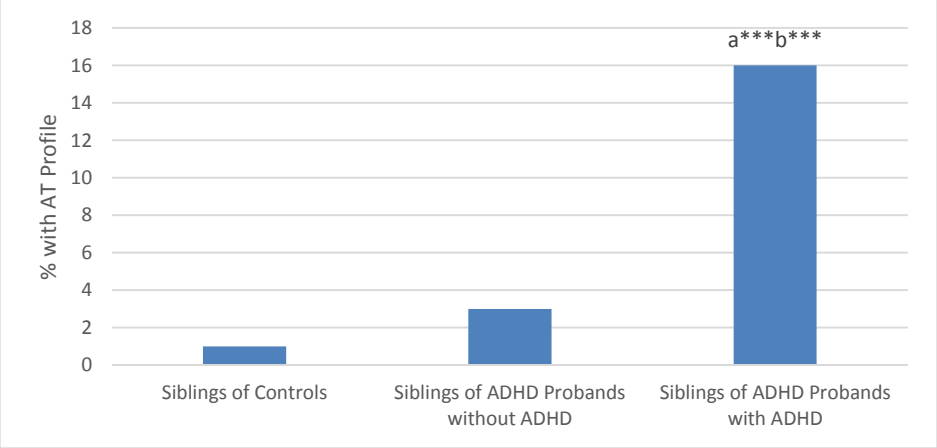
Statistical Analyses

All analyses were performed using regression models with robust standard errors to account for the non-independence of siblings. Differences in sociodemographic characteristics were assessed with the use of linear regression for continuous outcomes and logistic regression for binary outcomes. We controlled for any demographic confounder that reached significance at the 0.05 alpha level. Rates of ATs in siblings of probands with ADHD and control probands were analyzed using logistic regression. Analyses for psychiatric disorders, emotional dysregulation, school functioning, social disability, and perinatal complications were performed using exact logistic regression with permutation testing to deal with the issues of small expected numbers and non-independence. Analyses of the CBCL, GAF, SAICA, WISC-R, and WRAT-R items were performed with the use of linear regression. All tests were two-tailed, with the alpha set at 0.05. We calculated all statistics using Stata software version 14.0 (StataCorp, College Station, TX).

Results

Although there were 712 siblings in total, 221 siblings were excluded because they did not meet the age criteria of 6 to 18 years or because they were missing CBCL information (Figure 1). Thus, our final sample included 257 siblings of probands with ADHD and 234 siblings of control probands. Siblings had mean ± standard deviation ages of 10.7 ± 3.2 years and SES scores of 1.8 ± 0.9. Of the 230 subjects who reported their race, 94% were Caucasian.

FIGURE 2. Rate of ATs in siblings of Control probands (n = 234), siblings of ADHD probands without ADHD (n = 201), and siblings of ADHD probands with ADHD (n = 56). [a] Compared to siblings of Control [b]



As shown in Figure 2, rates of ATs were lowest among the siblings of control probands, intermediate among siblings of probands with ADHD without ADHD, and highest among siblings of probands with ADHD with ADHD. Siblings of probands with ADHD had significantly higher rates of ATs as compared with siblings of control probands (6% vs. 1%; $\chi^2 = 5.92$; $p = .02$). Because only three siblings of control probands had positive AT profiles, analyses were limited to siblings of probands with ADHD with ATs (n = 15) and without ATs (n = 242).

TABLE 1. Sociodemographic Characteristics

Characteristic	Sibling without ATs N = 242	Siblings with ATs N = 15	Test Statistic	*p*-Value
Age	10.6 ± 3.2	9.9 ± 3.4	$t_{(174)} = -0.83$	0.41
Sex (Male)	123 (51)	11 (73)	$X^2 = 3.03$	0.08
SES	1.9 ± 0.9	2.3 ± 0.9	$X^2 = 4.86$	0.03

Data are presented as mean ± SD or *n* (%)

TABLE 2. Pregnancy and Infancy Characteristics

	Sibling without ATs N = 222	Siblings with ATs N = 15	Test Statistic	*p*-Value
Pregnancy Characteristics				
Excessive nausea	48 (22)	3 (20)	Exact	0.30
Infection	26 (12)	5 (33)	Exact	<0.001
High blood pressure	37 (17)	4 (27)	Exact	0.002
Accidents	6 (3)	0 (0)	Exact	0.04
Family Problems	31 (14)	5 (33)	Exact	<0.001
Medications	55 (25)	7 (47)	Exact	<0.001
Smoking (3 mo. at gestation)	32 (14)	5 (33)	Exact	0.002
Infancy Characteristics				
Switch formulas	18 (8)	7 (47)	Exact	<0.001
Crying infant	28 (13)	5 (33)	Exact	0.003
Stiffened infant	5 (2)	2 (13)	Exact	<0.001

Data are presented as mean ± SD or *n* (%)

Sociodemographic Characteristics

The siblings with ATs were of similar age and sex as the siblings without ATs but were of a more disadvantaged SES status. Siblings with ATs scored an average of 2.3 on the Hollingshead measure of SES as compared with a score of 1.9 for siblings without ATs (Table 1). Therefore, all subsequent analyses corrected for SES.

Patterns of Psychiatric Comorbidity and Psychopathology

The average number of psychiatric disorders was significantly higher for siblings with ATs as compared with siblings without ATs ($t_{(174)} = 3.68$; $p < .001$; Figure 3, *A*). As compared with siblings without ATs, siblings with ATs had a significantly higher prevalence of ADHD, other disruptive behavior disorders, mood disorders, multiple (two or more) anxiety disorders, language disorders, and elimination disorders ($p < .005$ for all; see Figure 3, *B*). Likewise, individual and composite scores on all CBCL clinical scales as well as the two CBCL emotional dysregulation profiles were significantly more impaired among siblings with ATs as compared with those without ATs ($p \leq .001$ for all; see Figure 3, *C* and *D*).

Psychosocial Functioning

As compared with siblings without ATs, siblings with ATs had significantly more impaired GAF scores ($t_{(174)} = -4.75$; $p < .001$; Figure 4, *A*), significantly more impaired scores on the CBCL social and school competence scales ($p < .001$ for both; see Figure 4, *B*), significantly more impaired SAICA scaled scores on 7 of the 10 subscales ($p < .05$ for all; see Figure 4, *C*), and a significantly higher prevalence of social disability (Exact; $p = .001$; see Figure 4, *D*).

School Functioning

Siblings with ATs were significantly more likely to receive tutoring ($\chi^2 = 10.69$; $p = .001$) and to be placed in special classes (Exact; $p < .001$) as compared with siblings without ATs (Figure 5, *A*).

Neuropsychological Functioning

Siblings with ATs had lower composite cognitive and achievement WISC-R and WRAT-R scores than siblings without ATs (see Figure 5, *B*) as well as lower scores on the five WISC-R subscales (see Figure 5, *C*). However, these differences failed to reach our a priori threshold for statistical significance.

FIGURE 3. Rates of psychopathology in siblings with and without ATs. A. Average number of psychiatric disorders. B. Comorbid disorders. C. Clinical CBCL. D. CBCL emotional dysregulation profiles. ª Compared to siblings without ATs. *$p<0.05$, **$p<0.005$, ***$p<0.001$

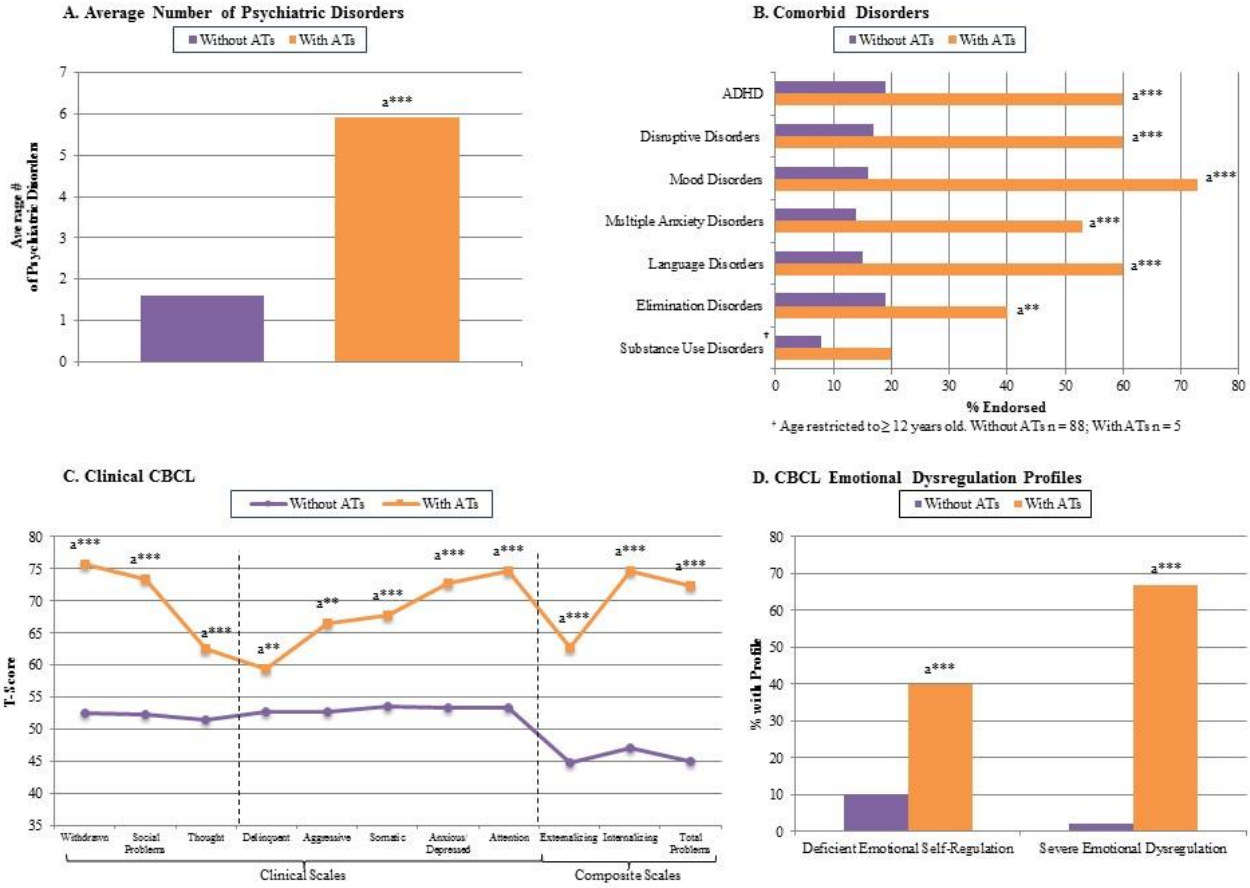


FIGURE 4. Social functioning in siblings with and without ATs. A. GAF score. B. CBCL social functioning scale. C. SAICA individual item scores. D. Social disability. • Compared to siblings without ATs. *$p<0.05$, **$p<0.005$, ***$p<0.001$

† Smaller sample sizes:
B. CBCL–Activities: Without ATs n = 234, With ATs n = 13; Social: Without ATs n = 207, With ATs n = 14; School: Without ATs n = 229, With ATs n = 10; Total Competence: Without ATs n = 181, With ATs n = 10.
C. SAICA—Relationship with Father: Without ATs n = 203, With ATs n = 9
D. Social Disability: Without ATs n = 204, With ATs n = 9

FIGURE 5. School functioning in siblings with and without ATs. • Compared to siblings without ATs. *$p<0.05$, **$p<0.005$, ***$p<0.001$

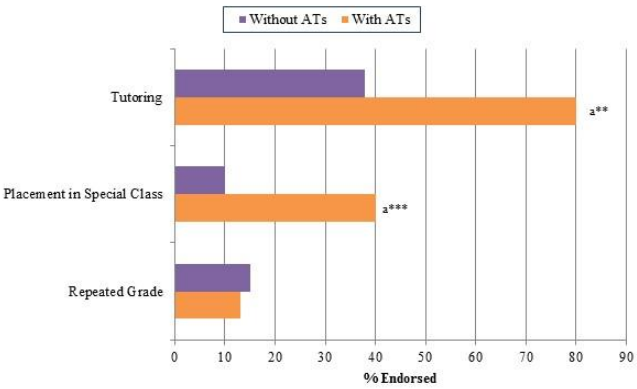
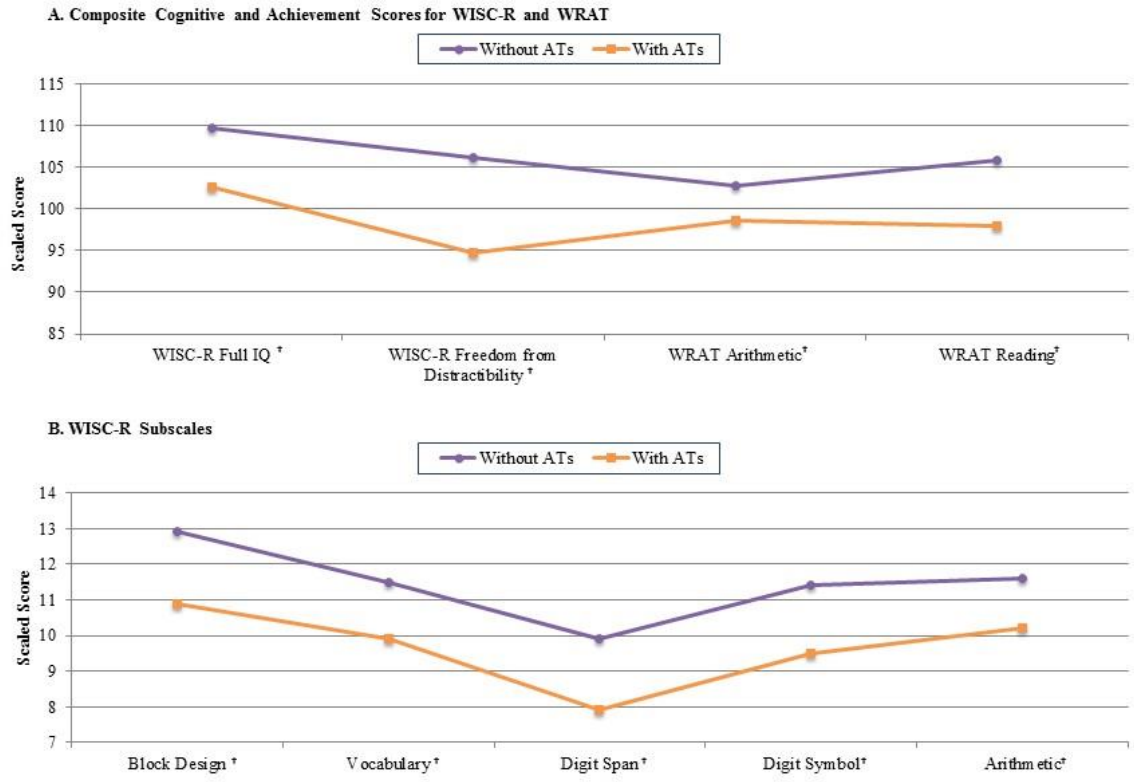


FIGURE 6. Neuropsychological functioning in siblings. A. Composite cognitive and achievement scores for WISC-R and WRAT. B. WISC-R subscales



† Smaller sample sizes:
A. Composite Scores WISC-R & WRAT—Full IQ: Without ATs n = 228, With ATs n = 13; Freedom from Distractibility: Without ATs n = 206, With ATs n = 10; Arithmetic: Without ATs n = 233, With ATs n = 13; Reading: Without ATs n = 107, With ATs n = 10
B. WISC-R Subscales—Block Design, Digit Span, Digit Symbol: Without ATs n = 207, With ATs n = 10; Vocabulary: Without ATs n = 207, With ATs n = 9; Arithmetic: Without ATs n = 206, With ATs n = 10

Perinatal Complications

Rates of all but two pregnancy and infancy characteristics were significantly higher among siblings with ATs as compared with siblings without ATs ($p < .005$ for all), and the rate of accidents during pregnancy was significantly lower among siblings with ATs (Exact; $p = .04$; Table 2).

Discussion

Our findings reveal that ATs can be identified in a sizeable number of non-referred children, particularly in those with ADHD. The results also show that the presence of ATs heralds a significantly more compromised clinical presentation that is characterized by higher rates of psychopathological, neuropsychological, and interpersonal deficits as compared with children without these traits. These results in non-referred youth are highly consistent with the findings of previous reports (3-5) and with our findings from probands with ADHD (21). Thus, these results provide further support for the clinical relevance of ATs, irrespective of referral status.

Non-referred youth with ATs exhibited significantly higher rates of comorbid psychopathology as compared with those without ATs as expressed by the significantly higher mean number of comorbid psychiatric disorders; the significantly higher rates of disruptive behavior, mood, anxiety, language, and elimination disorders; the marked impairments noted in all individual and composite CBCL clinical scales; and higher rates of emotional dysregulation. These findings are highly consistent with those previously reported for referred probands with ADHD with ATs and therefore stress the heavy burden of psychopathology associated with ATs in both referred and non-referred youth. These findings are also in line with the prevailing literature, which highlights higher-than-expected rates of major psychiatric disorders among youth with ASD (22-24).

Also consistent with previously reported findings in probands with ADHD (6) is that non-referred siblings with ATs experienced greater social and interpersonal deficits as manifested by significantly worse GAF scores, significantly more impaired CBCL social and school competence scores, significantly more impaired SAICA scores, and

higher rates of social disability as compared with siblings without ATs. Taken together, these findings provide further evidence that ATs severely affect the social functioning of afflicted children, irrespective of referral status.

Although the results did not reach our a priori threshold for statistical significance, we found that non-referred siblings with ATs had similarly lower full-scale intelligence quotients, Freedom from Distractibility intelligence quotients, and Block Design and Digit Symbol WISC-R scores as well as lower WRAT-R reading and arithmetic scores. These findings, which mirror what we reported for probands with ADHD, suggest that neurocognitive functioning is compromised in the presence of ATs.

Also in line with the findings reported for probands with ADHD is that non-referred children with ATs had higher rates of most pregnancy and infancy complications as compared with those of other children without ATs. These findings further support the hypothesis that perinatal complications alone—or in combination with genetic risk factors—could account for the development of ATs in some children.

Extending findings related to ATs to non-referred children has important clinical and scientific implications. Documenting the broad and severe spectrum of morbidity and dysfunction associated with ATs in non-referred youth supports the clinical relevance of ATs independent of referral status. Considering how easy it is to screen for ATs with the use of the CBCL, clinicians in the community have access to a rapid, inexpensive, and informative tool to screen children in clinical practice. Significant morbidity and dysfunction are associated with ATs, so the ability to identify children with ATs may facilitate the development of appropriate interventions that target afflicted children. This knowledge will help to inform future research aimed at identifying distinct genetic, neural, and therapeutic targets related to ATs.

The present study contains several strengths. Most notably, it relies on a large number of non-referred youth and an operationalized definition of ATs that is based on a unique profile of the empirically derived CBCL for the identification of ATs, which can be easily used in the clinical setting.

However, our findings need to be viewed in light of certain limitations. Despite the strength of the findings, our sample of non-referred siblings with ATs was relatively small. Although ATs were more strongly associated with ADHD, the sample size was too small to allow for a separate analysis limited to siblings with ADHD. Because we lacked an adequate sample of siblings of control probands with ATs, the analysis was limited to siblings of probands with ADHD. Although autism was excluded in the probands, it was not systematically ruled out in the siblings, thereby allowing for the possibility that some of the children may have had undiagnosed ASD. Although this analysis was limited to the siblings of probands with ADHD with and without ATs, we have previously documented the high discriminant validity of the CBCL-AT profile for the identification of ASD in a psychiatrically referred population of youth. (5) It is also notable that the presence of ATs in the siblings of children with ADHD was associated with lower SES, even though the analysis was controlled for social class. The present findings are in line with our previous report of poorer SES being more highly associated with children with ADHD with ATs than without ATs (6). Our findings are consistent with those of the prevailing literature, which suggest a higher association of ASD with low SES (25). Furthermore, we found a lower rate of accidents during pregnancy among siblings with ATs. This was an unexpected finding, so additional studies are needed to verify this result. Finally, our sample was largely Caucasian, but our findings may not generalize to other ethnic groups.

Despite these considerations, our work shows that ATs can be identified in a sizeable minority of non-referred children and that these children are at high risk for significant morbidity and disability. More work is needed to replicate these findings and to further examine their prognostic usefulness.

Clinical Significance

The current findings suggest that elevated scores on the CBCL-AT subscale may indicate a need to clinically assess a child for ASD and ADHD; mood, anxiety, and disruptive behavior disorders; emotional dysregulation; and impaired social and school functioning.

Authors' Disclosures:
Dr. Joseph Biederman is currently receiving research support from the following sources: the US Department of Defense, the US Food and Drug Administration, Ironshore, Lundbeck, Magceutics Inc., Merck, Pamlab, Pfizer, Shire Pharmaceuticals Inc., SPRITES, Sunovion, Vaya Pharma/Enzymotec, and the National Institutes of Health. In 2015, Dr. Biederman received honoraria from the Massachusetts General Hospital (MGH) Psychiatry Academy for tuition-funded continuing medical education (CME) courses. He has a US patent application pending (Provisional Number #61/233,686) through MGH corporate licensing for a method to prevent stimulant abuse. In 2014, Dr. Biederman received honoraria from the MGH Psychiatry Academy for tuition-funded CME courses. He received research support from the American Academy of Child and Adolescent Psychiatry, Alcobra,

Forest Research Institute, and Shire Pharmaceuticals Inc. Dr. Biederman received departmental royalties from a copyrighted rating scale used for ADHD diagnoses paid by Ingenix, Prophase, Shire, Bracket Global, Sunovion, and Theravance; these royalties were paid to the Department of Psychiatry at MGH. In 2013, Dr. Biederman received an honorarium from the MGH Psychiatry Academy for a tuition-funded CME course. He received research support from the American Professional Society of ADHD and Related Disorders, ElMindA, McNeil, and Shire. Dr. Biederman received departmental royalties from a copyrighted rating scale used for ADHD diagnoses paid by Shire and Sunovion; these royalties were paid to the Department of Psychiatry at MGH. In 2012, Dr. 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.

Dr. Stephen Faraone has received income, potential income, travel expenses, and/or research support from Arbor, Pfizer, Ironshore, Shire, Akili Interactive Labs, CogCubed, Alcobra, VAYA Pharma, Neurovance, Impax, and NeuroLifeSciences during the past year. With his institution, he has US patent no. US20130217707 A1 for the use of sodium-hydrogen exchange inhibitors in the treatment of ADHD. In previous years, he received income or research support from Shire, Alcobra, Otsuka, 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)*, Oxford University Press *(Schizophrenia: The Facts)*, and Elsevier *(ADHD: Non-Pharmacologic Interventions)*.

Dr. Ronna Fried is currently receiving research support from Lundbeck. In 2015, Dr. Fried received honoraria from the MGH Psychiatry Academy for tuition-funded CME courses. During previous years, Dr. Fried received research support from the National Institutes of Health and Shire.

Dr. Gagan Joshi is supported by the National Institute of Mental Health of the National Institutes of Health under award no. K23MH100450. He receives research support from Pfizer and the Simons Center for the Social Brain as a principal investigator for investigator-initiated studies. In addition, he receives research support from Duke University, Forest Research Laboratories, and Sunovion Pharmaceuticals as a site principal investigator for multi-site trials. He is a co-investigator for clinical trials sponsored by the US Department of Defense, Pamlab, and Schering-Plough Corporation. He received an honorarium from the Governor's Council for Medical Research and Treatment of Autism in New Jersey for grant review activities, and he received speaker's honorariums from the American Academy of Child and Adolescent Psychiatry, MGH Psychiatry Academy, and the Medical Society of Delaware.

Ms. Maura Fitzgerald, Ms. Yvonne Woodworth, Ms. Alexandra Saunders, and Ms. Kristina Conroy do not have any disclosures to declare.

Acknowledgments:
The data acquisition from which this analysis was derived was funded by National Institute of Mental Health grants MH-41314, HD036317, and MH050657 to Dr. Joseph Biederman. The manuscript and the analysis of the data were indirectly supported by the Pediatric Psychopharmacology Research Council Fund and the Saylor family fund supporting research in autism. Dr. Gagan Joshi is supported by the National Institute of Mental Health of the National Institutes of Health under award no. K23MH100450. Professor Faraone is supported by the K.G. Jebsen Centre for Research for Neuropsychiatric Disorders, University of Bergen, Bergen, Norway; the European Union's Seventh Framework Programme for Research, Technological Development, and Demonstration under grant agreement no. 602805, and National Institute of Mental Health grant nos. R13MH059126 and R01MH094469.

Rerences

1. Lundstrom S, Reichenberg A, Melke J, et al. Autism spectrum disorders and coexisting disorders in a nationwide Swedish twin study. J Child Psychol Psychiatry 2015;56(6):702-10.
2. Sandin S, Lichtenstein P, Kuja-Halkola R, Larsson H, Hultman CM, Reichenberg A. The familial risk of autism. JAMA 2014;311(17):1770-7.
3. Grzadzinski R, Di Martino A, Brady E, et al. Examining autistic traits in children with ADHD: does the autism spectrum extend to ADHD? J Autism Dev Disord 2011;41(9):1178-91.
4. Kochhar P, Batty MJ, Liddle EB, et al. Autistic spectrum disorder traits in children with attention deficit hyperactivity disorder. Child Care Health Dev 2011;37(1):103-10.
5. Mulligan A, Anney RJ, O'Regan M, et al. Autism symptoms in attention-deficit/hyperactivity disorder: a familial trait which correlates with conduct, oppositional defiant, language and motor disorders. J Autism Dev Disord 2009;39(2):197-209.
6. Kotte A, Joshi G, Fried R, et al. Autistic traits in children with and without ADHD. Pediatrics 2013;132(3):e612-22.
7. Biederman J, Petty CR, Fried R, et al. Child behavior checklist clinical scales discriminate referred youth with autism spectrum disorder: a preliminary study. J Dev Behav Pediatr.2010;31(6):485-90.
8. Biederman J, Monuteaux MC, Mick E, et al. Young adult outcome of attention deficit hyperactivity disorder: a controlled 10-year follow-up study. Psychol Med 2006;36(2):167-79.
9. Biederman J, Monuteaux M, Mick E, et al. Psychopathology in females with attention-deficit/hyperactivity disorder: a controlled, five-year prospective study. Biol Psychiatry 2006;60(10):1098-105.
10. Orvaschel H. Schedule for Affective Disorders and Schizophrenia for School-Age Children Epidemiologic Version. 5th ed. Ft. Lauderdale: Nova Southeastern University, Center for Psychological Studies; 1994.
11. Orvaschel H. Psychiatric interviews suitable for use in research with children and adolescents. Psychopharmacol Bull 1985;21(4):737-45.
12. Hollingshead AB. Four Factor Index of Social Status. New Haven, CT: Yale Press; 1975.
13. Endicott J, Spitzer RL, Fleiss JL, Cohen J. The global assessment scale. A procedure for measuring overall severity of psychiatric disturbance. Arch Gen Psychiatry 1976;33(6):766-71.

14. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th ed). Washington, D.C.: American Psychiatric Association; 1994.

15. John K, Gammon GD, Prusoff BA, Warner V. The Social Adjustment Inventory for Children and Adolescents (SAICA): Testing of a new semistructured interview. J Am Acad Child Adolesc Psychiatry 1987;26(6):898-911.

16. Reynolds CR. Critical measurement issues in learning disabilities. J Spec Educ 1984;18(4):451-75.

17. Faraone SV, Biederman J, Lehman BK, et al. Intellectual performance and school failure in children with attention deficit hyperactivity disorder and in their siblings. J Abnorm Psychol 1993;102(4):616-23.

18. Wechsler D. Manual for the Wechsler Intelligence Scale for Children-Revised. New York: The Psychological Corporation; 1974.

19. Sattler J. Psychological Assessment. Fourth ed. New York: McGraw-Hill; 1988.

20. Jastak JF, Jastak S. The wide range achievement test-revised. Wilmington, Delaware: Jastak Associates; 1985.

21. Uchida M, Faraone SV, Joshi G, et al. How prevalent are autistic traits among children with attention-deficit/hyperactivity disorder? A qualitative review of the literature. Scand J Child Adolesct Psychiatr Psychol 2013;1(1):33-40.

22. Joshi G, Petty C, Wozniak J, et al. The heavy burden of psychiatric comorbidity in youth with autism spectrum disorders: a large comparative study of a psychiatrically referred population. J Autism Dev Disord 2010;40(11):1361-70.

23. Joshi G, Wozniak J, Petty C, et al. Psychiatric comorbidity and functioning in a clinically referred population of adults with autism spectrum disorders: a comparative study. J Autism Dev Disord 2013;43(6):1314-25.

24. Joshi G, Faraone SV, Wozniak J, et al. Examining the clinical correlates of autism spectrum disorder in youth by ascertainment source. J Autism Dev Disord 2014;44(9):2117-26.

25. Rai D, Lewis G, Lundberg M, et al. Parental socioeconomic status and risk of offspring autism spectrum disorders in a Swedish population-based study. J Am Acad Child Adolesc Psychiatry 2012;51(5):467-76 e6.