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To cite this article: Adrienne P. Borschuk PhD, Casey Rodweller BS & Cynthia F. Salorio PhD (2017): The influence of comorbid asthma on the severity of symptoms in children with attention-deficit hyperactivity disorder, Journal of Asthma, DOI: [10.1080/02770903.2017.1306549](https://doi.org/10.1080/02770903.2017.1306549)

To link to this article: <http://dx.doi.org/10.1080/02770903.2017.1306549>



Published online: 01 May 2017.



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The influence of comorbid asthma on the severity of symptoms in children with attention-deficit hyperactivity disorder

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ABSTRACT

Objective: The current study examined the association between asthma and attention-deficit hyperactivity disorder (ADHD) symptoms in a clinical pediatric sample. **Methods:** Demographic and neuropsychological data for children with a billing diagnosis of ADHD were extracted from a clinical database. Families completed standard rating scales. Seventy-one patients with a co-morbid asthma diagnosis were identified and matched by age to a group of 71 patients with only ADHD. **Results:** Children with asthma and ADHD were more likely to display clinically elevated levels of hyperactivity, externalizing behaviors, anxiety, and hyperactive/impulsive behaviors compared to children with ADHD alone. Boys with asthma and ADHD had more symptoms than boys with only ADHD of somatization and emotional internalizing, while girls with asthma and ADHD had more symptoms of hyperactivity/impulsivity, conduct problems, anxiety, and emotional internalizing compared to girls with only ADHD. **Conclusions:** Findings suggest that in children with ADHD, co-morbid asthma is associated with increased behavioral and internalizing symptoms, with distinct gender differences present. Increased behavioral and internalizing symptoms seen in children with both asthma and ADHD may be due to the burden of their medical condition. No difference was found on cognitive variables, suggesting chronic hypoxia may be less influential in explaining these differences. Future research should determine the specific mechanisms of these differences.

ARTICLE HISTORY

Received 30 November 2016

Revised 20 February 2017

Accepted 9 March 2017

KEYWORDS

ADHD; asthma;
attention-deficit
hyperactivity disorder;
emotional functioning;
pediatrics

Introduction

Attention-deficit hyperactivity disorder (ADHD) and asthma are two of the most common disorders diagnosed in childhood. The most recent data indicate prevalence rates of 9.5 and 8.6% for ADHD and asthma, respectively, in children under the age of 18 [1, 2]. Shared risk factors of these conditions include family history of the condition, low birth weight, intrauterine growth restriction, and low socioeconomic status [3–5].

ADHD and asthma are often comorbid conditions. Research suggests that asthma in very early life increases the risk of the development of ADHD [6, 7], and lifetime prevalence rates of asthma in children with ADHD are estimated to be 36.6% [8]. Children with asthma are almost twice as likely to also have ADHD compared to children without asthma [9]. Mechanisms of this connection are unclear. Longitudinal studies suggest that asthma precedes the development of ADHD [7], and genetic inheritance of the disorders does not seem to be linked [10]. African-American children are more likely to be diagnosed with asthma [11] and ADHD [12] compared

to any other race; there is no research on ethnic or racial disparities in comorbid diagnoses. While boys tend to be diagnosed with ADHD alone more frequently than girls, rates of comorbid asthma and ADHD diagnoses are comparable between genders [13, 14]. Research has identified that premature birth and prenatal stress are linked to comorbid ADHD and asthma [13]. While there is some support for an immunological hypothesis linking maternal autoimmune disease to ADHD in offspring [15], there is no known immunological hypothesis connecting comorbid asthma and ADHD.

It is hypothesized that the types of medication used to treat asthma, as well as the symptoms of asthma itself, may cause or trigger the expression of increased symptoms of ADHD; however, research is mixed regarding etiology [16–23]. Specifically, questions have been raised regarding the impact of chronic hypoxia on children's neurocognitive and behavioral functioning [22]. Medications such as corticosteroids and beta agonists have also been examined as potential mediators of the relation between asthma and ADHD [24, 25]. In addition to this, the age-linked

diagnostic criteria of ADHD make it difficult to identify directionality and causality between these disorders.

Children with either condition display higher rates of problem behaviors (e.g., defiance, aggression, noncompliance) and worse performance on measures of executive functioning than children without either condition [26–30]. Behavior problems in children with ADHD are generally explained through models of correlated risk or developmental precursors, essentially attributing the development of behavior disorders to either shared risk factors (e.g., genetics) or disrupted family functioning, respectively [31, 32]. Children with asthma are thought to exhibit higher rates of behavioral and psychological distress due to the demands of managing a chronic health condition, increased burden on the family, or side effects from medications [33, 34]. Pediatric asthma alone is shown to significantly influence the child's overall and health-related quality of life, with asthma symptom severity, sleep quality, and mental health identified as predictors of quality of life in this population [35–37]. Children with asthma and an additional comorbid condition, such as ADHD, demonstrate even worse emotional and behavioral functioning than children with asthma alone [26]. These difficulties are shown to persist into adulthood, and adults with both asthma and ADHD have higher rates of mental illness, legal involvement, unemployment, and medical problems than adults without those diagnoses [38–40].

No studies to date have examined whether a comorbid diagnosis of asthma significantly influences the severity or expression of ADHD symptoms. It is also unclear how a comorbid diagnosis of asthma is related to the expression of behavior, attention, and executive functioning in children with ADHD. Beyond expanding this novel area of research, findings have implications for treatment of children with ADHD and asthma. Given established relations between asthma, ADHD, and poor outcomes across the life span, identification of areas for intervention is key. The current study examines the association between asthma and ADHD symptoms in a clinical sample. We hypothesized that children with asthma and ADHD would have greater difficulties with behavior, attention, and executive functioning compared to children with ADHD alone. We also sought to better characterize gender differences in children with ADHD and asthma compared to children with ADHD alone.

Methods

Procedures

Institutional review board approval was obtained through the Johns Hopkins University School of Medicine. 1230 children, adolescents, and young adults with ADHD

referred for neuropsychological evaluation at the Kennedy Krieger Institute between 2009 and 2014 were considered for inclusion in the present study. Participants were generally referred for neuropsychological evaluation to characterize cognitive functioning and guide treatment planning. If more than one parent or caregiver attended the neuropsychology appointment, they were invited to complete questionnaires together if desired; otherwise, the primary caregiver completed measures independently. Self-report measures of behavior were not systematically collected from all participants due to the clinical nature of these appointments, and thus were not examined in this study.

The inclusion criteria for the present study were 6–18 years of age at the time of neuropsychological evaluation, English identified as primary spoken language, diagnosis of ADHD, sufficient information available in hospital electronic medical records to extract key variables, and completion of parent-report measures of emotional-behavioral and/or executive functioning as part of the evaluation. Exclusion criteria included: diagnosis of an autism spectrum disorder, intellectual disability, or fetal alcohol syndrome disorder, prior cancer treatment, prior cardiac surgery, prenatal exposure to nonprescribed drugs, premature birth (<35 weeks gestation), identified or suspected child maltreatment or prolonged foster care placement, history of psychotic features, prior traumatic brain injury (excluding concussions), and formally diagnosed hearing or visual impairment.

Questionnaires

Demographics

Participant demographic information was obtained from questionnaires completed by the parent or caregiver at their neuropsychological evaluation and included age, gender, ethnicity, and prescribed medications. Demographic, psychiatric, neuropsychological, and medical variables were also taken directly from each participant's electronic medical record. Co-occurring diagnoses, including asthma, were also extracted from the medical records. Authors identified 71 youth comorbid asthma and matched youth with ADHD only based on gender, age, and general comorbid diagnoses.

Executive functioning

Parents or caregivers of participants completed the age-appropriate parent-report version of the Behavioral Rating Inventory of Executive Function, Second Edition (BRIEF) as part of the neuropsychological evaluation. The BRIEF is a standardized questionnaire designed to assess domains and subdomains of executive functioning via parent ratings of observable everyday behaviors

[41]. Composite indices include the Behavioral Regulation Index (BRI) and Metacognition Index, as well as an overall Global Executive Composite score. BRI consists of the Inhibition, Shifting, and Emotional Control subscales, while the MRI includes Working Memory, Initiation, Plan/Organize, Organization of Materials, and Monitoring subscales. *T*-scores ≥ 65 are considered clinically significant. The BRIEF demonstrates excellent psychometric properties ($\alpha = .80-.98$).

Behavioral, emotional, and social functioning

Parents or caregivers of participants completed the age-appropriate parent-report version of the Behavior Assessment System for Children-Second Edition (BASC-2) as part of the neuropsychological evaluation [42]. The BASC-2 is a standardized questionnaire designed to assess multiple aspects of behavioral, emotional, and social functioning. Overall domains include externalizing problems, internalizing problems, behavioral skills, and adaptive skills. Subscales include symptoms of hyperactivity, aggression, conduct problems, anxiety, depression, somatization, attention problems, atypicality, withdrawal, adaptability, social skills, leadership, activities of daily living, and functional communication. *T*-scores between 60 and 69 are considered in the “at risk” range, while *T*-scores ≥ 70 are considered clinically significant. The BASC-2 has demonstrated acceptable psychometric properties ($\alpha = .80-.90$). The adaptive skills composite and its associated subscales were not examined for the present study.

ADHD symptomatology

Parents or caregivers of participants completed the parent-report version of the Conners 3rd Edition-Parent (Conners 3-P) as part of the neuropsychological evaluation [43]. The Conners-3 is a standardized questionnaire based on diagnostic criteria designed to assess multiple aspects of behavioral, emotional, and social functioning. Subscales include General Psychopathology, Inattention, Hyperactivity/Impulsivity, Learning Problems, Executive Functioning, Defiance/Aggression, Peer Relations, Family Relations, ADHD Inattentive, ADHD Hyperactive-Impulsive, ADHD Combined, Oppositional Defiant Disorder, and Conduct Disorder. *T*-scores between 60 and 64 are considered in the “high average” range, while *T*-scores ≥ 65 are considered clinically significant. The Conners 3-P shows adequate psychometric properties ($\alpha = .77-.97$).

Statistical analyses

We first provided descriptive data on our overall sample’s demographic characteristics, cognitive functioning, comorbid diagnoses, psychosocial variables, and medication status. Main scales and subsequent subscales

of both the BASC-2 and BRIEF were examined. This information is also provided for each diagnostic group (i.e., ADHD only, asthma and ADHD). Pearson’s chi-square test was used to explore relations between child’s asthma status and medication regimen. *T*-tests and logistic regressions were conducted to determine group differences in executive functioning and social and emotional functioning based on the participant’s asthma status. Gender differences were also examined using *t*-tests and logistic regressions. Analyses of variance (ANOVAs) and post hoc tests were also used to examine group differences. SPSS version 22 was used for all statistical analyses [44]. *p*-Values < 0.05 were considered statistically significant.

Results

The final sample included seventy-one participants with diagnoses of ADHD and asthma matched by age and gender to a group of seventy-one participants with ADHD only. The sample had a mean age of 10.4 and comprised mostly boys. Almost 80% of the sample was Caucasian or African-American. All participants were administered standard tests of intelligence, and the mean intelligence quotient (IQ) was 94.5. Chi-square analyses indicated comparable ADHD medication use between groups, with no significant difference found based on asthma diagnosis ($\chi^2(3) = 2.09, p = .55$). Chi-square analyses also indicated comparable comorbid diagnoses between groups, with no significant difference found based on asthma diagnosis ($\chi^2(5) = 4.34, p = .50$). Sample demographics are detailed in Table 1.

Data from parent-report measures were first analyzed dichotomously, using the clinical significance cutoff *T*-score as the grouping variable. Sixty-two percent of children with asthma and ADHD displayed clinically elevated levels of hyperactivity per the BASC-2, while only 44% of children with ADHD alone had clinically elevated scores ($\chi^2(1) = 4.35, p < .05$). Fifty percent of children with asthma and ADHD displayed clinically elevated levels of externalizing behaviors on the BASC-2, while only 30% of children with ADHD alone had clinically elevated scores ($\chi^2(1) = 5.22, p < .05$). Almost forty percent of children with asthma and ADHD displayed clinically elevated levels of anxiety on the BASC-2, while only 23% of children with ADHD alone had clinically elevated scores ($\chi^2(1) = 3.97, p < .05$). Eighty-eight percent of children with asthma and ADHD displayed clinically elevated levels of hyperactive/impulsive behaviors on the Conners 3-P, while only 53% of children with ADHD alone had clinically elevated scores ($\chi^2(1) = 13.24, p < .001$). Mean results for the sample are displayed in Figure 1. No other group differences on any of the measures were found using cutoff score dichotomization.

Table 1. Sample demographic characteristics.

	ADHD only	Asthma and ADHD	Total sample
Gender, <i>n</i> (%)			
Male	49 (69%)	49 (69%)	98 (69%)
Female	22 (31%)	22 (31%)	44 (31%)
Age, mean (SD)	10.4 (2.8)	10.4 (2.8)	10.4 (2.8)
IQ, mean (SD)	95.6 (11.8)	93.4 (14.1)	94.5 (12.9)
Ethnicity, <i>n</i> (%)			
Caucasian	35 (49.3%)	34 (47.9%)	69 (48.6%)
African-American	33 (31.0%)	23 (32.4%)	45 (31.7%)
Latino	1 (1.4%)	3 (4.2%)	4 (2.8%)
Mixed	3 (4.2%)	1 (1.4%)	4 (2.8%)
Asian	1 (1.4%)	0 (0%)	1 (0.7%)
Unknown	9 (12.7%)	10 (14.1%)	19 (13.4%)
ADHD medications, <i>n</i> (%)			
Stimulant	21 (29.6%)	23 (32.4%)	44 (31.0%)
Nonstimulant	1 (1.4%)	1 (1.4%)	2 (1.4%)
Both	2 (2.8%)	0 (0.0%)	2 (1.4%)
None	47 (66.2%)	47 (66.2%)	94 (66.2%)
Asthma medications, <i>n</i> (%)			
Controller only	—	18 (25.4%)	—
Rescue inhaler only	—	12 (16.9%)	—
Both	—	15 (21.1%)	—
None	—	26 (36.6%)	—
Comorbid diagnoses, <i>n</i> (%)			
Learning disability	12 (16.9%)	14 (19.7%)	26 (18.3%)
Other medical	1 (1.4%)	4 (5.6%)	5 (3.5%)
Allergies	1 (1.4%)	9 (12.7%)	10 (7.0%)
Mood disorder	13 (18.3%)	10 (14.1%)	23 (16.2%)
Speech/language disorder	6 (8.4%)	5 (7.0%)	11 (7.7%)
Developmental delay	1 (1.4%)	2 (2.8%)	3 (2.1%)
Sleep disorder	1 (1.4%)	1 (1.4%)	2 (1.4%)
Multiple	9 (12.7%)	12 (16.9%)	21 (14.8%)
None	45 (63.4%)	41 (57.7%)	86 (60.6%)

Data were then analyzed using raw, continuous data. Scores on the BASC-2 Hyperactivity subscale differed significantly by group ($t(1,128) = 1.98, p = .05$), with higher scores seen in children with asthma and ADHD. Participants with asthma and ADHD also had higher scores on the Anxiety, Somatization, and Internalizing subscales of the BASC-2 ($t(1,125) = 2.25, p < .05$; $t(1,126) = 3.29, p < .01$; $t(1,125) = 3.15, p < .01$; respectively). Scores on the Conners 3-P Hyperactivity/Impulsivity subscale

were higher for children with asthma and ADHD ($t(1,84) = 2.66, p < .01$). All t -test findings remained significant in linear regression analyses after controlling for ADHD medication status. Scores on the BRIEF did not differ significantly based on group.

Given documented gender differences in ADHD presentation, post hoc analyses were performed to further explore group differences in boys and girls. Boys with asthma and ADHD had higher scores than boys with only ADHD on the BASC-2 Somatization and Internalizing subscales ($t(1, 84) = 2.84, p < .01$; $t(1, 83) = 2.32, p < .05$; respectively). Girls with asthma and ADHD had higher scores on the BASC-2 Hyperactivity and Conduct subscales ($t(1,40.6) = 2.17, p < .05$; $t(1,40) = 2.02, p = .05$; respectively), as well as on the BASC-2 Anxiety and Internalizing subscales ($t(1,40) = 2.55, p < .05$; $t(1,40) = 2.16, p < .05$; respectively) compared to girls with only ADHD. Girls with asthma and ADHD had higher scores on the Conners 3-P Hyperactivity/Impulsivity subscale compared to girls with only ADHD ($t(1,26) = 2.47, p < .05$). All t -test findings remained significant in linear regression analyses after controlling for ADHD medication status.

A one-way ANOVA was done to examine differences among all four categorizations of diagnosis and gender. Statistically significant differences between groups were indicated on the BASC-2 Somatization ($F(2,27) = 4.467, p = .021$) and Internalizing ($F(2,27) = 4.467, p = .021$) subscales, as well as the Conners 3-P Hyperactive/Impulsive subscale ($F(2,27) = 4.467, p = .021$). The results are displayed in Table 2.

Discussion

No differences between children with asthma and ADHD and children with ADHD alone were found between

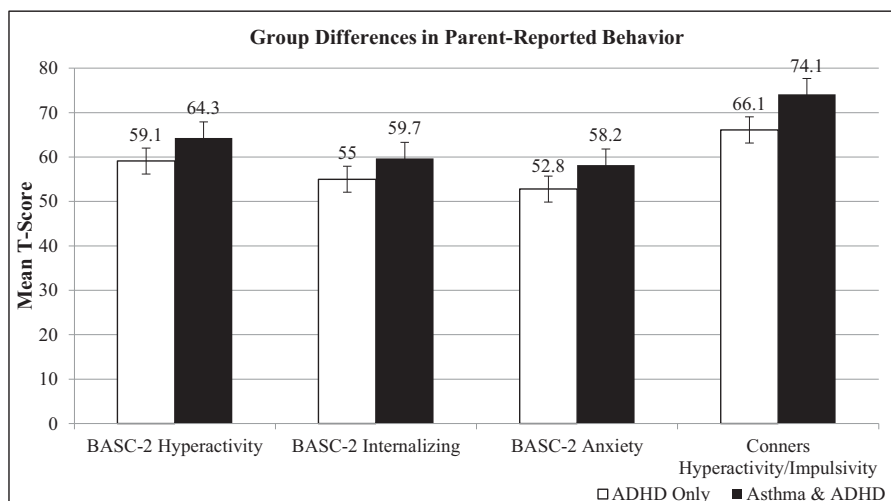
**Figure 1.** Group differences in parent-reported child behavior.

Table 2. One-way analysis of variance of behavioral variables by diagnosis and gender.

Variable	Group 1 M(SD)	Group 2 M(SD)	Group 3 M(SD)	Group 4 M(SD)	F	p	Tukey HSD
Somatization	47.8 (11.5)	43.8(9.5)	56.8(16.9)	51.3(17.7)	4.68	.004**	1, 2 < 3
Internalizing	52 (13.0)	49.2(10.1)	59.4(16.0)	58.5(16.7)	3.45	.019*	2 < 3
Hyperactivity	61.2 (15.6)	54.9(15.5)	63.9(13.7)	64.9(14.7)	2.19	.026*	—
Conduct	54.8 (16.0)	50.9(11.3)	55.9(12.3)	59.8(16.5)	1.42	.240	—
Anxiety	54.5 (12.7)	49.3(10.0)	57.8(15.2)	59.1(14.1)	2.39	.072	—
Hyp/Imp	68.5 (14.1)	61.1(15.5)	73.7(12.8)	74.8(13.8)	3.24	.091	2 < 3

Note. Group 1 = Male w/ADHD; Group 2 = Female w/ADHD; Group 3 = Male w/asthma and ADHD; Group 4 = Female w/asthma and ADHD.

groups in any aspect of executive functioning on the BRIEF. In contrast, analyses revealed higher parent report of hyperactivity, anxiety, and internalizing symptoms on the BASC-2 and Conners 3-P in children with both asthma and ADHD compared to those with ADHD alone. Further analyses revealed gender differences between groups. Boys with asthma and ADHD displayed higher levels of somatization and internalizing symptoms than boys with only ADHD. Girls with asthma and ADHD displayed higher levels of hyperactivity/impulsivity, conduct problems, anxiety, and internalizing behaviors compared to girls with ADHD alone.

Results suggest that in children with ADHD, comorbid asthma is associated with increased behavioral and internalizing symptoms. Increased behavioral and internalizing symptoms seen in children with both asthma and ADHD may be due to their medical condition. For example, these children may have greater anxiety due to their asthma regimen or recurrent asthma attacks. No difference was found on cognitive variables (i.e., BRIEF or IQ), suggesting that chronic hypoxia may be less influential in explaining these differences.

Gender differences found in this sample are broadly consistent with existing asthma and ADHD literature. A study of adults with asthma found that men and women with asthma reported higher levels of psychological distress than healthy adults [45]. Girls with ADHD are generally reported to have more symptoms of anxiety than boys with ADHD or healthy controls [46, 47]. Within-gender comparisons indicated that girls and boys with diagnoses of asthma and ADHD demonstrated greater behavior problems and anxiety symptoms than their peers with only ADHD. When all four gender and diagnostic groups were examined, however, the only remaining differences were somatization and internalizing symptoms in boys with asthma and ADHD compared to ADHD controls. These findings suggest that children with comorbid diagnoses of asthma and ADHD demonstrate greater psychological and behavioral distress than their same-gender peers with ADHD alone, with boys with asthma and ADHD appearing to exhibit the most significant deficits. Of note, these findings were not influenced by medication status.

If a child with asthma and ADHD has significant behavior or emotional concerns, it may influence their ability to be adherent to their medical regimen, whether it is for asthma or ADHD medications. This can have wide-ranging repercussions for their health, functioning at school, and relationships at home. This finding is supported by previous research suggesting that children with asthma who are more anxious or depressed generally have poorer health [48].

In the context of these findings, recommendations may be made to medical providers regarding screening and care for children with asthma and ADHD. Professionals should explore the topic of behavior with their patients' parents; if concerns are raised, the family may be referred for medication management or behavioral psychology services (e.g., behavioral parent training, cognitive-behavior therapy), the two evidence-based treatments for ADHD and mood disorders in children and adolescents [49, 50]. Additionally, medical team members should assess whether behavioral or emotional concerns are interfering with the child's health, either through nonadherence or more frequent asthma exacerbations due to anxiety.

With regard to gender differences found in this sample, clinical implications are more nuanced. Boys with asthma and ADHD emerged as the most impaired group in this sample, while girls with asthma and ADHD were reported to display a wider range of deficits. Providers should consider including social skills training to augment treatment for girls with comorbid asthma and ADHD to address the peer difficulties (e.g., conduct problems) often seen in girls with ADHD [51]. Providers should make a point to screen for symptoms of anxiety or depression in boys with asthma and ADHD, as behavior problems may distract from the presence of clinically significant internalizing symptoms. As always, early intervention is key and children should undergo a comprehensive evaluation to clarify diagnostic impressions and guide treatment.

This study has several limitations. First, the data are cross-sectional, which disallows causal interpretation. While an attempt was made to obtain teacher ratings of behavior for all participants, only a small number of teachers responded, and thus, these data are not included

in this manuscript. Future research on this topic should employ a longitudinal design with multiple sources of data in order to strengthen confidence in findings. Further, the sample was comprised of children with ADHD referred for neuropsychological evaluations, which confers a referral bias and may render this a more severe group than the general population of children with asthma and ADHD. Additionally, no medical information was gathered regarding participants' asthma (e.g., severity or duration), which would better characterize the asthma and ADHD sample and promote further interpretation of the findings. Participants' caregivers did report on asthma medication, which may serve as a proxy indicator of asthma severity. Common method variance must also be considered as a limitation of all clinical research using questionnaires. Finally, sample sizes for gender comparisons were reduced in some analyses, which increases the probability of statistical error, specifically Type 1.

Conclusion

It appears that children with asthma and ADHD exhibit greater behavioral difficulties than children with ADHD alone. Gender may play a role, with boys with asthma and ADHD demonstrating greater behavioral problems and internalizing symptoms than peers with ADHD alone. Comparisons are limited given the cross-sectional nature of the data. Providers should assess for behavioral and emotional distress in their patients with asthma and ADHD. Future research should incorporate medical variables, asthma-specific questionnaires, and a larger sample size to determine the specific mechanisms of these differences.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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