

Attention deficit hyperactivity disorder, tic disorder, and allergy: Is there a link? A nationwide population-based study

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Background: Attention deficit hyperactivity disorder (ADHD) and tic disorder usually co-occur in the same individuals, but the underlying mechanisms remain unclear. Previous evidence has shown that a frequent coexistence of allergic diseases was noted in patients with ADHD or tic disorder. We attempted to investigate the possible link among ADHD, tic disorder, and various allergic diseases. **Methods:** Utilizing the Taiwan National Health Insurance Research Database from 1996 to 2010, 5,811 patients with ADHD alone, 1,816 patients with tic disorder alone, and 349 patients with dual diagnoses of ADHD and tic disorder were identified and compared with age-/gender-matched controls (1:4) in an investigation of the association among ADHD, tic disorder, and allergic diseases. **Results:** Patients with dual diagnoses of ADHD and tic disorder had a significantly higher prevalence of allergic diseases and psychiatric comorbidities, including allergic rhinitis (43% vs. 28.4% vs. 33.6% vs. 19.7%, $p < 0.001$), asthma (27.5% vs. 17.2% vs. 18.2% vs. 11.9%, $p < 0.001$), atopic dermatitis (10.6% vs. 8.4% vs. 7.0% vs. 5.9%, $p < 0.001$), allergic conjunctivitis (55.6% vs. 34.7% vs. 43.5% vs. 26.3%, $p < 0.001$), obsessive compulsive disorder (4.0% vs. 1.3% vs. 2.0% vs. 0.1%, $p < 0.001$), and anxiety disorder (22.1% vs. 18.0% vs. 6.0% vs. 0.5%, $p < 0.001$) than the ADHD alone group, the tic alone group, and the control group. Furthermore, ADHD patients with more allergic diseases (≥ 3 comorbidities: OR: 3.73, 95% CI: 2.65~5.25; 2 comorbidities: OR: 2.52, 95% CI: 1.82~3.47; 1 comorbidity: OR: 1.87, 95% CI: 1.41~2.49) exhibited an increased risk of tic disorder compared with ADHD patients without allergic disease. **Conclusion:** A significant association among ADHD, tic disorder, and allergic diseases was noted in our study. The results may inspire further studies to clarify the underlying mechanisms and help us understand more about the complex etiology of ADHD, tic disorder, and their co-occurrence. **Keywords:** Attention deficit hyperactivity disorder, tic disorder, allergy.

Attention deficit hyperactivity disorder (ADHD) and tic disorder are neurodevelopmental disorders that begin in childhood, and they frequently co-occur in the same individuals, although they have very diverse clinical symptoms: ADHD exhibits the inability to marshal and sustain attention and modulate the activity level, and tic disorder manifests bouts of sudden, rapid, and involuntary motor or phonic movements (Leckman, 2002; Rapaport, 2005; Rothenberger, Roessner, Banaschewski, & Leckman, 2007). This coexistent effect is of clinical and scientific value, because the coexistence of tic disorder has an adverse impact on patients with ADHD (Greimel et al., 2011; Lin, Lai, & Gau, 2012). Furthermore, the co-occurrence of ADHD and tic disorder plays an important role in medication choice, because neurostimulants may exacerbate the symptoms of tic disorder in about 5–10% of ADHD patients (Roessner, Robatzek, Knapp, Banaschewski, & Rothenberger, 2006). However, the coexistent prevalence of ADHD and tic disorder ranged from

15% to 34% in previous studies due to the different methodologies and subject populations (Schlender, Schwarz, Rothenberger, & Roessner, 2011; Spencer et al., 1999). The co-occurrence of ADHD and tic disorder implies that these two distinct diseases may share some common disease mechanisms (Steeves & Fox, 2008), despite the fact that the pathophysiology of both diseases remains unclear.

There has been growing interest in the roles of atopy and allergic immunity in ADHD in the last decade. Evidence of a high prevalence of allergic comorbidities (i.e., asthma and atopic dermatitis) in ADHD patients has been reported (Fasmer, Halmoy, Eagan, Oedegaard, & Haavik, 2011; Schmitt, Romanos, Schmitt, Meurer, & Kirch, 2009). Schmitt et al. found that 1436 patients with ADHD were significantly associated with atopic dermatitis compared with the controls [odds ratio (OR): 1.54; 95% confidence interval (CI): 1.06–2.22] (Schmitt et al., 2009). Fasmer et al. reported that the risk of asthma was significantly elevated in the ADHD patient group ($n = 594$) compared with the controls ($n = 719$) (OR: 2.54, 95% CI: 1.89–3.44) (Fasmer et al., 2011). Immunological dysregulation, including hypersecretion of Ig-E, increased eosinophilic activity, and

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a predominantly T helper type 2 (Th₂) cytokine over-secretion, accounted for the hypothesized pathophysiology of the comorbid association between ADHD and allergic diseases (Agrawal & Bharadwaj, 2005; Bieber, 2008; Kira, 2002; Schmitt, Buske-Kirschbaum, & Roessner, 2010; Yarlagaadda, Alfson, & Clayton, 2009).

The relationship of tic disorder with allergy was seldom investigated. Ho et al. found higher rates (56.9% vs. 44.3%) of allergic diseases in those with tic disorder than the control group (Ho, Shen, Shyur, & Chiu, 1999). A recent study demonstrated that patients with tic disorder had increased comorbidities of asthma (OR: 1.82, 95% CI 1.47~2.24), atopic dermatitis (OR: 1.61, 95% CI 1.32~1.95), and allergic conjunctivitis (OR: 1.33, 95% CI 1.13~1.57) (Chang et al., 2011). Some immunological and genetic studies have supported the comorbidity. Hartmann et al. reported an increased histamine concentration in patients with Tourette's syndrome (Hartmann, Worbe, & Arnulf, 2012). Ercan-Sencicek et al., using the analysis of linkage in a two-generation pedigree of Tourette's syndrome, found a functional mutation in the *HDC* gene encoding L-histidine decarboxylase (the rate-limiting enzyme in histamine biosynthesis) and suggested that histaminergic neurotransmission ought to play an important role in the mechanism and modulation of Tourette's syndrome and tic disorder (Ercan-Sencicek et al., 2010). Fernandez et al. analyzed rare copy number variations in Tourette's syndrome and showed enrichment of genes within histamine receptor (subtypes 1 and 2) signaling pathways, as well as axon guidance, cell adhesion, nervous system development, and synaptic structure and function processes (Fernandez et al., 2012).

Based on the aforementioned evidence regarding the co-occurrence of ADHD, tic disorder, and allergic diseases with each other, and the lack of a related study in the literature, we proposed a possible biological link among these three disorders. We used a nationwide population-based case-control study design to investigate this comorbid association and hypothesized that an increased prevalence of allergic diseases would be noted among patients with dual diagnoses of ADHD and tic disorder when compared with patients who had ADHD or tic disorder only.

Methods

Data source

This study was based on data from the National Health Insurance Research Database (NHIRD) audited and released by the National Health Research Institute. The National Health Insurance (NHI) program was implemented in 1995, and covers up to 99% of all 23,000,000 residents of Taiwan now (<http://www.nhi.gov.tw/>). Comprehensive information on insured subjects is included in the database, including demographic data, dates of clinical visits, and details of prescriptions.

The diagnostic codes used were based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).

Inclusion criteria for the ADHD alone group, tic disorder alone group, ADHD + tic group, and control group

In this study, 1,000,000 subjects, approximately 4.3% of the population of Taiwan, were randomly selected from the NHIRD. Those identified as having 'attention deficit hyperactivity disorder' (ICD-9-CM code: 314) by psychiatrists and those identified as having 'tic disorder' (ICD-9-CM code: 307.2) by pediatricians, psychiatrists, and neurologists were included as the study group. The study group was divided into three subgroups: ADHD alone, tic disorder alone, and ADHD + tic disorder. The age- and gender-matched control group (4 for every patient in the study cohort) was randomly identified from the subjects after eliminating patients who had been given a diagnosis of ADHD or tic disorder. Comorbidities of asthma (ICD-9-CM codes: 493, 493.0, 493.1, or 493.9), allergic rhinitis (ICD-9-CM code: 477), atopic dermatitis (ICD-9-CM codes: 691 or 691.8), and allergic conjunctivitis (ICD-9-CM codes: 372.05 and 372.14) were identified by internists/pulmonologists/rheumatologists/pediatricians, internists/family physicians/pediatricians, dermatologists/pediatricians, and ophthalmologists. Besides, obsessive-compulsive disorder (ICD-9-CM code: 300.3) and anxiety disorder (ICD-9-CM codes: 300.X except 300.3 and 300.4) were assessed as the confounding factors because they commonly co-occur in the clinical practice (Mathews & Grados, 2011; O'Rourke et al., 2011; Pollak et al., 2009; Yoshimasu et al., 2012). All diagnoses were given at least twice by corresponding physicians for diagnostic validity.

Statistical analysis

In comparing the differences between the four groups (ADHD alone, tic disorder alone, ADHD + tic, and control group), analysis of variance (ANOVA) was used for continuous variables and Pearson's Chi-square test was applied for nominal variables. Post hoc analysis and 2 × 2 factor analysis were performed to clarify which factor (tic disorder or ADHD) plays the most important role or interacts together to the allergic vulnerability. When investigating the risk of allergic comorbidities in ADHD+tic disorder, ADHD alone, tic disorder alone, and control group, multiple logistic regressions were performed to calculate the OR with 95% CI after adjusting for age, gender, residence location, and comorbid psychiatric disorders.

Furthermore, we used multiple logistic regression analysis to evaluate the risk of tic disorder in ADHD patients with allergic comorbidities, and the risk of allergic comorbidities in patients with ADHD or tic disorder, and the risk of ADHD in patients with tic disorder with allergic diseases. A two-tailed *p*-value of less than 0.05 was considered statistically significant. All data processing and statistical analyses were performed with Statistical Package for Social Science (SPSS) version 17 software (SPSS Inc) and Statistical Analysis Software (SAS) version 9.1 (SAS Institute, Cary, NC).

Results

In all, 6,160 patients were identified as having ADHD and 2,165 patients as having tic disorder. Among them, 349 patients had dual diagnoses of ADHD and tic disorder, with males predominant. The patients with ADHD + tic disorder had a significantly higher prevalence of allergic diseases and psychiatric comorbidities, including allergic rhinitis (43% vs. 28.4% vs. 33.6% vs. 19.7%, $p < 0.001$), asthma (27.5% vs. 17.2% vs. 18.2% vs. 11.9%, $p < 0.001$), atopic dermatitis (10.6% vs. 8.4% vs. 7.0% vs. 5.9%, $p < 0.001$), allergic conjunctivitis (55.6% vs. 34.7% vs. 43.5% vs. 26.3%, $p < 0.001$), obsessive-compulsive disorder (4.0% vs. 1.3% vs. 2.0% vs. 0.1%, $p < 0.001$), and anxiety disorder (22.1% vs. 18.0% vs. 6.0% vs. 0.5%, $p < 0.001$) (Table 1) than the other three groups. In addition, more comorbidities of allergic diagnoses were found in patients with ADHD + tic disorder than in patients with ADHD alone, tic disorder alone, and the controls (Table 1). The 2×2 factor analysis found independent/additive effects of ADHD ($p < 0.001$) and tic disorder ($p < 0.001$) on the vulnerability to allergic comorbidities in the whole study sample. However, the interactive effect of ADHD and tic disorder on the allergic comorbidities was not significant in our study ($p = 0.194$).

The logistical regression analysis demonstrated that ADHD+tic group (OR: 3.73, 95% CI: 2.92~4.76), tic disorder alone group (OR: 2.88, 95% CI: 2.60~3.20), and ADHD alone group (OR: 1.64, 95% CI: 1.54~1.75) had the elevated risk of having allergic comorbidities compared with control group after adjusting for age, gender, residence location, and comorbid psychiatric disorders (Table 2). Furthermore, if only considering the risk of allergic comorbidities in patients with ADHD or tic disorder,

Table 2 Odds ratio of allergic diseases in patients with ADHD alone, tic disorder alone, ADHD + tic disorder, and control group

	Crude OR (95% CI)	mOR (95% CI) ^a
Control group	1	1
ADHD alone	1.75 (1.65~1.85)	1.64 (1.54~1.75)
Tic disorder alone	2.22 (2.02~2.45)	2.88 (2.60~3.20)
ADHD + Tic disorder	4.13 (3.24~5.25)	3.73 (2.92~4.76)

^aAdjusted by age, gender, residence location, and psychiatric comorbidities.

patients with dual diagnoses (OR: 1.76, 95% CI: 1.57~1.99) and patients with tic disorder alone (OR: 2.30, 95% CI: 1.80~2.95) were more likely to have allergic diseases than patient with ADHD alone.

When compared with ADHD patients without allergic comorbidity, ADHD patients with ≥ 3 allergic diseases (OR: 3.73, 95% CI: 2.65~5.25), 2 allergic diseases (OR: 2.52, 95% CI: 1.82~3.47), or 1 allergic disease (OR: 1.87, 95% CI: 1.41~2.49) had increased ORs of tic disorder after controlling age, gender, residence location, and psychiatric comorbidities (Table 3). Furthermore, if considering the risk of ADHD in patients with tic disorder with allergic

Table 3 Odds ratio of tic disorder in ADHD with allergic diseases

Number of allergic diseases	Crude OR (95% CI)	mOR (95% CI) ^a
0	1	1
1	1.88 (1.42~2.49)	1.87 (1.41~2.49)
2	2.51 (1.83~3.44)	2.52 (1.82~3.47)
≥ 3	3.87 (2.78~5.39)	3.73 (2.65~5.25)

ADHD, attention deficit hyperactivity disorder.

^aAdjusted by age, gender, residence location, and psychiatric comorbidities.

Table 1 Characteristics of patients with ADHD alone, ADHD + Tic, and Tic alone, and control

	Tic alone (a) (n = 1,816)	ADHD (n = 6,160)		Control (d) (n = 31,904)	p-value	Post-hoc analysis
		ADHD alone (b) (n = 5,811)	ADHD + Tic (c) (n = 349)			
Age (years, SD)	21.85 (16.71)	15.81 (7.33)	15.22 (4.14)	17.17 (10.49)	<0.001	a > d > b ≈ c
Gender (M, %)	1,245 (68.6)	4,449 (76.6)	316 (90.5)	19,060 (77.4)	<0.001	c > b ≈ d > a
Allergic diseases (n, %)						
Allergic rhinitis	611 (33.6)	1,649 (28.4)	150 (43.0)	4,866 (19.7)	<0.001	c > a > b > d
Asthma	330 (18.2)	1,001 (17.2)	96 (27.5)	2,939 (11.9)	<0.001	c > a ≈ b > d
Atopic dermatitis	127 (7.0)	490 (8.4)	37 (10.6)	1,444 (5.9)	<0.001	c > a ≈ b > d
Allergic conjunctivitis	790 (43.5)	2,015 (34.7)	194 (55.6)	6,484 (26.3)	<0.001	c > a > b > d
Average number of allergic comorbidities (n, SD)	1.01 (1.01)	0.87 (0.96)	1.34 (1.06)	0.61 (0.85)	<0.001	c > a > b > d
Allergic comorbidities (n, %)					<0.001	
0	712 (39.2)	2,621 (45.1)	90 (25.8)	14,172 (57.5)		
1	584 (32.3)	1,812 (31.2)	117 (33.5)	6,636 (26.9)		
2	311 (17.1)	881 (15.2)	76 (21.8)	2,599 (10.5)		
≥ 3	206 (11.3)	497 (8.6)	66 (18.9)	1,233 (5.0)		
Psychiatric comorbidities (n, %)						
Obsessive-compulsive disorder	36 (2.0)	73 (1.3)	14 (4.0)	25 (0.1)	<0.001	c > a > b > d
Anxiety disorder	109 (6.0)	1,047 (18.0)	77 (22.1)	164 (0.5)	<0.001	c > b > a > d

ADHD, attention deficit hyperactivity disorder.

diseases, tic patients with more allergic comorbidities (≥ 3 comorbidities: OR: 1.63, 95% CI: 1.11~2.41; 2 comorbidities: OR: 1.38, 95% CI: 0.96~1.99; 1 comorbidity: OR: 1.29, 95% CI: 0.93~1.78) were prone to have the vulnerability to ADHD than those without allergic diseases.

Discussion

Our results supported the study hypotheses that there is a coexistent link among allergy, tic disorder, and ADHD. The ADHD + tic group had a significantly higher prevalence of allergic diseases, including asthma, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis, than the other three groups. Our results also suggested the independent/additive effects, but not interactive effect, of ADHD and tic disorder on the vulnerability to allergic comorbidities (Rothenberger et al., 2007). Furthermore, ADHD patients with more allergic comorbidities exhibited an increased risk of tic disorder when compared with those without allergic diseases.

Research data concerning the causal association between ADHD and allergies were conflicting (Pelsers, Buitelaar, & Savelkoul, 2009). In late 1980, Marshall et al. hypothesized that allergic reactions engendering cholinergic/adrenergic activity imbalances in the central nervous system led to ADHD symptoms in some children (Marshall, 1989). However, in the 1990s, several small sample-sized studies failed to support this allergic hypothesis (Biederman, Milberger, Faraone, Guite, & Warburton, 1994; Gaitens, Kaplan, & Freigang, 1998). In the 2000s, some studies with a larger sample size revalidated the significant association between allergic diseases and ADHD (Fasmer et al., 2011; Schmitt et al., 2009, 2010). ADHD patients, similar to allergic/atopic patients, exhibited significant relationships with HLA-DRB1 and HLA-DR4 (Aureli et al., 2008; Odell, Warren, Warren, Burger, & Maciulis, 1997) and had elevated proinflammatory cytokine concentrations [i.e., interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)- α] (Mittleman et al., 1997; Oades, Dauvermann, Schimmelmann, Schwarz, & Myint, 2010). Oades et al. investigated the different cytokine concentrations, including IL-2, IL-6, IFN- γ , IL-16, IL-10, and IL-13, and found a marginal increase in the ADHD group compared with healthy controls (Oades et al., 2010). Assessing the cerebrospinal fluid cytokine levels of patients with ADHD, Mittleman et al. suggested that ADHD had both cell-mediated and humoral immunity dysfunction (Mittleman et al., 1997).

Previous studies on the association between tic disorder and major histocompatibility complex (MHC) genes are limited and with inconsistent results. Min et al., typing HLA-A, B, C, and DR in 73 patients with Tourette's disorder and 291 normal subjects, showed that patients with Tourette's disorder had higher frequencies of HLA-A11 and A26

(Min, Lee, Park, Park, & Namkoong, 1991). Caine et al. found no evidence for a linkage between a gene locus determining susceptibility to tic disorder and the HLA loci (Caine et al., 1985). However, in clinical practice, the comorbidity of allergy and tic disorder is usually noted (Chang et al., 2011; Finegold, 1985; Kim, Moote, & Mazza, 1997). Some evidence has supported the cytokines hypothesis regarding tic disorder (Bos-Veneman et al., 2010; Leckman et al., 2005; Martino, Dale, Gilbert, Giovannoni, & Leckman, 2009; Morer et al., 2010). When investigating the role of cytokine profiles in tic disorder, Bos-Veneman et al. demonstrated that the IL-2 concentration was positively associated with tic severity (Bos-Veneman et al., 2010). Leckman et al. found increased serum TNF- α and IL-12 at baseline and during symptom exacerbation in children with Tourette's disorder (Leckman et al., 2005). Morer et al. focused on the genetic expressions of various cytokines in basal ganglion extracted from patients with Tourette's disorder and showed that patients with Tourette's disorder had an increased expression of monocyte chemotactic factor (MCF)-1 and IL-2 when compared with healthy controls (Morier et al., 2010). In addition, decreased numbers of regulatory CD4(+) and CD8(+) T cells, serum immunoglobulin-G3, immunoglobulin-A, and immunoglobulin-M were found in the patients with Tourette's syndrome compared with the healthy controls (Kawikova et al., 2007, 2010). Those evidences indicated that Tourette's syndrome exhibited a disturbance and alteration of both T cell and B cell immune systems, and a dysregulation of proinflammatory cytokine production and secretion. Further studies are needed to investigate the possible comorbid or casual association.

Regarding treatment options in ADHD and tic disorder, new clinical evidence has shown a potential effect of histamine H₃ receptor antagonist in ADHD treatment, by improving patients' inattention and impulsivity symptoms (Brioni, Esbenshade, Garrison, Bitner, & Cowart, 2011; Schwartz, 2011; Tiligada, Kyriakidis, Chazot, & Passani, 2011). However, in a recent randomized, double-blind case-control study, Weisler et al. showed that JNJ-31001074, a highly selective H₃ receptor antagonist, did not display significant clinical effectiveness in the treatment of adult ADHD patients (Weisler, Pandina, Daly, Cooper, & Gassmann-Mayer, 2012). Several clinical trials regarding the effect of other H₃ receptor antagonists in ADHD treatment are still ongoing (Brioni et al., 2011; Esbenshade et al., 2008; Lazewska & Kiec-Kononowicz, 2010; Tiligada et al., 2011). In contrast to the newly discovered potential therapeutic effect of antihistamine in ADHD treatment, studies related to antihistamine and tic disorder are very limited. Wadenberg et al. suggested that spiradoline, a kappa-opioid receptor agonist with antihistamine properties, decreased tic severity in patients with Tourette's disorder (Wadenberg,

2003). Wand et al.'s study, using self-reported data from 200 patients with Tourette's disorder, showed that 30% of patients had used antihistamine and 40% reported being satisfied with the medical care they were receiving (Wand, Fulton, Shady, Champion, & Hubka, 1988). The potential therapeutic role of antihistamine in ADHD and tic disorder may offer a future alternative treatment choice for patients with dual diagnoses, but verification of the definite treatment efficacy requires further study.

Finally, some current evidences delineated the hypothesis of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) on the development or relationship of tic disorder, obsessive compulsive disorder, and ADHD (Murphy, Kurlan, & Leckman, 2010; Sanchez-Carpintero, Albesa, Crespo, Villoslada, & Narbona, 2009; Snider & Swedo, 2004; Swedo et al., 1998). The etiology of obsessive-compulsive disorder, ADHD, and tic disorder in the PANDAS is still unknown, but is theorized to occur as a result of poststreptococcal autoimmunity and a production of antibodies to group A streptococcus that cross-react with the cellular components of the basal ganglia, particularly in the caudate nucleus and putamen (Mittleman, 1997; Murphy et al., 2010; Snider & Swedo, 2004). Assessing 46 patients with Tourette's syndrome and/or early-onset obsessive-compulsive disorder and PANDAS, Leckman et al. showed that patients with PANDAS, similar to those with obsessive-compulsive disorder and Tourette's syndrome, exhibited dysregulated cytokine profiles (i.e., IL-12, TNF- α) compared with non-PANDAS patients, and the increase in these cytokine profiles was noted in the clinical exacerbation (Leckman et al., 2005). The results suggested that children with PANDAS and related conditions (i.e., obsessive-compulsive disorder and Tourette's syndrome) might have an inflammatory process involving the brain (Leckman et al., 2005; da Rocha, Correa, & Teixeira, 2008). However, Singer et al. failed to find the immune markers to correlate with clinical exacerbations in children with PANDAS (Snider & Swedo, 2004). In our study, after adjusting for obsessive compulsive disorder and anxiety disorder, we still found that patients with ADHD + tic disorder, ADHD alone, and tic disorder alone were more likely to have allergic

diseases than control group. We hypothesized that the altered immune reaction and dysregulated cytokine secretion may be the common pathway among those distinct diseases. However, further studies would be required to investigate this association and underlying pathophysiology among them.

Some study limitations should be addressed here. First, the diagnoses of ADHD, tic disorder, and allergic diseases may be underestimated because only those who sought medical help were included in our study. However, their diagnoses were more validated than self-reported diagnoses, because only those patients with at least two consistent diagnoses given by board-certificated physicians were included in our study. Second, some information was not supplied by the NIHRD, such as personal lifestyle, stressful life events, environmental factors, and family history. We cannot evaluate the impact of those factors in our study.

Conclusion

This is the first report to investigate the possible association among ADHD, tic disorder, and allergic diseases. ADHD patients with tic disorder had a greater propensity toward allergic diseases, and those with ADHD and allergic diseases had a higher risk of tic disorder. Our results may inspire the further studies to clarify the underlying mechanisms and help us understand more about the complex etiology of ADHD and tic disorder.

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Key points

- The additive model of ADHD + tic disorder could be confirmed.
- ADHD and tic disorder frequently co-occur in the same individuals, and the allergic diseases commonly coexist with ADHD or tic disorder in the clinical practice.
- The role of allergy/atopy on ADHD gradually gains the clinical and scientific concerns in the last decade, but that on the tic disorder is still unknown.
- It is the first study to propose the association among ADHD, tic disorder, and allergic diseases.
- ADHD patients with tic disorder have a greater propensity toward allergic diseases, and those with ADHD and allergic diseases have a higher risk of tic disorder.

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