



Original Article

Association between allergic diseases, allergic sensitization and attention-deficit/hyperactivity disorder in children: A large-scale, population-based study

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Abstract

Background: Increasing prevalence of allergic diseases has been matched by parallel trends in attention-deficit/hyperactivity disorder (ADHD). However, previous studies concerning the association between ADHD and allergic diseases have been inconsistent. Moreover, it is not clear whether this association is modified by allergic sensitization status. Therefore, we evaluated the association between allergic diseases, allergic sensitization, and ADHD in children.

Methods: We conducted a large-scale cross-sectional, population-based survey to investigate the relationship between allergic diseases, allergic sensitization, and ADHD. Children aged between 3 and 6 years were selected from kindergartens, and received skin prick tests (SPTs) for mite, cockroach, dog, milk, egg, and crab allergens. Information about allergic diseases, environmental exposures, and physician-diagnosed ADHD were collected. Multiple logistic regressions were performed to estimate the association between allergic diseases and ADHD, with adjustments made for potential confounders.

Result: A total of 2772 children were found to be eligible for analysis; of these 411 (14.8%) had atopic dermatitis (AD), 954 (34.4%) had allergic rhinitis (AR), 451 (16.3%) had asthma, and 28 (1.01%) had ADHD. Children who had AD and asthma with allergic sensitization were found to be at increased risk for ADHD, with adjusted ORs (95% CI) of 4.50 (1.28–15.86) and 3.65 (1.07–12.49). Children who had AR, allergic conjunctivitis, or food allergies were also related to ADHD, though failed to reach statistical significance.

Conclusion: Our results suggest that AD and asthma with allergic sensitization are associated with ADHD in children. As allergic sensitization is an increased factor of developing allergic diseases, early control of environmental and allergens exposure could help to modify the burden of ADHD.

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Keywords: ADHD; Asthma; Atopic disorders

List of abbreviations: ADHD, Attention-Deficit/Hyperactivity Disorder.

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is the most common behavioral disorder in children.¹ The prevalence of ADHD is increasing in many countries, including Taiwan.² The cumulative prevalence of ADHD diagnosis

increased from 0.06 to 1.64% from 1996 to 2005 in Taiwan, but the reasons for the rise are still undetermined.² Prevalence of ADHD was reported from 1.0% to 7% in school-aged children all over the world, and was three times more likely to occur in boys compared to girls.^{2,3} Recognizable symptoms of ADHD include difficulties with attention, impulsivity, and hyperactivity.^{4,5} ADHD is a genetically complex and highly heritable brain disorder; however, it is still unclear how specific genes interact with adverse environmental factors and lead to the various brain abnormalities observed in ADHD.^{3,6,7}

In 2004, the Global Initiative of Asthma estimated that more than 300 million people worldwide and 7–15% of children are affected by asthma, making it the leading cause of childhood chronic medical illness.⁸ However, the prevalence of other allergic diseases, including atopic dermatitis (AD) and allergic rhinitis (AR), is also increasing,⁸ with the global prevalence of childhood AR reported to be as high as 39.7%.^{5,7,8} Children with allergic diseases have greater difficulty in school.^{9,10} Their often-described hyperactive and impulsive behaviors have been thought to be secondary to these chronic illnesses or their treatment.¹¹ However, research regarding the association between ADHD and allergic diseases is often conflicting.^{5,12–15}

Allergic sensitization is an important risk factor for the development and severity of allergic diseases.^{3–6} The association between ADHD and allergic sensitization was sourced in comorbidity or causality has been discussed in some studies,^{2–6} but the exact relationship between allergens exposure and ADHD is unclear. Both ADHD and allergic sensitization depend on a complex interaction between genetic and environmental factors. If allergic sensitization is associated with ADHD, prevention of allergic sensitization might play a role in decreasing the burden of ADHD.^{2–6} Although some studies have presented the association between ADHD and allergic diseases or allergic sensitization, the data of the most published studies were small-scale, meta-analysis or analyzing health insurance database.^{3–6} This is the first large-scale, population-based study for better understanding the association between ADHD, allergic diseases and allergic sensitization. We conducted a cross-sectional survey on 2772 children to investigate the relationship between allergic diseases, allergic sensitization (positive SPTs), and ADHD.

2. Methods

2.1. Study population

We conducted a population-based, cross-sectional survey on kindergarten children (aged 3–6 years) residing in 11 communities in Taiwan in 2010.¹⁶ A total of 3264 school children (i.e. the Childhood Environment and Allergic diseases Study CEAS cohort) were recruited. After excluding subjects without skin prick test (SPT) results ($N = 435$), with multiple gestations ($N = 27$), and inability to answer questions in Chinese ($N = 30$), 2772 participants were found to be eligible for this study. The informed consents of providing the questionnaire and SPT were obtained from the parents or

guardians. The study protocol was approved by the Institutional Review Board of Taipei Hospital (IRB No.: TH-IRB-09-04) and complied with the principles outlined in the Helsinki Declaration.

2.2. Case definitions

Parents or guardians were asked to complete the standardized questionnaire. Cases of AD were defined by positive responses to the questions: “Has your child ever had AD diagnosed by a physician?” and “Has your child ever had recurrent itchy rash for at least 6 consecutive half-month periods over elbows, knees, face, wrists, neck, periauricular and eyebrow areas?” Cases of asthma were defined as a positive response to “physician-diagnosed asthma”, together with a positive response to nocturnal cough or exercise-induced wheeze over the past 12 months. Cases of AR were defined by positive responses to the questions “Has your child ever been diagnosed as having AR by a physician?” and “Has your child ever had a problem with sneezing, or a runny or blocked nose, when your child did not have a cold or the flu?”

Cases of allergic conjunctivitis were defined by positive responses to the questions “Has your child ever been diagnosed as having allergic conjunctivitis by a physician?” and “Has your child ever had a problem with recurrent itching, redness, burning or tearing of the conjunctivas?” Cases of food allergy were defined by positive responses to the questions “Has your child ever been diagnosed as having food allergy by a physician?” and “Has your child ever had a problem with itching in the mouth, eczema, swelling of the lips, face, tongue and throat or other parts of the body, wheezing, nasal congestion, or trouble breathing due to particular foods?” Children with ADHD show a persistent pattern of inattention and hyperactivity-impulsivity behaviors were defined according to the criteria of the American Psychiatric Association's Diagnostic and Statistical Manual, Forth edition (DSM-4).^{1,2,4,5} The conditions of disease in children were confirmed by board-certified child psychiatrists or pediatric neurologists, according to the clinical evaluation.^{1,2,4,5}

2.3. Exposure measurements

The standard ISAAC-Chinese version questionnaire with additional questions concerning environmental allergen exposures was answered by the parents. The questionnaire also contained questions on basic demography, residential environmental factors (such as environmental tobacco smoking, pets and cockroaches at home, dampness of the house, fungus on the house wall, and carpets at home), and family history of atopic diseases.

2.4. Laboratory methods

Allergic sensitizations were defined by SPTs on 6 common allergens, including house dust mites (HDMs mix, including Der p, Der f, Der m, and Blot allergens), cockroaches, dog dander, milk, egg, and crab allergens (ALK-Abello, Round

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