



# Relation Between Attention-Deficit Hyperactivity Disorder and IgE-Dependent Allergy in Pediatric Patients

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## Abstract

Food allergy is a common condition in children and adolescent, remitting with time. Few clinical studies have emphasized the link between food allergies and psychosocial conditions, suggesting a profound impact of atopic diseases on the development of attention-deficit hyperactivity disorder (ADHD) in children. The objective of this study was to compile and assess available studies on the comorbidity or causality between ADHD and atopic food allergy in children. We discuss epidemiology, interrelated mechanisms, and potential dietary interventions in the management of children with ADHD.

## Keywords

ADHD · Allergy · Atopy · Children · IgE · Food · Psychosocial status

manifestations occur in childhood (Bierderman and Faraone 2005). The main symptoms are hyperactivity, impulsivity, and attention deficit, which are inappropriate for the child's age and are present across a range of settings causing impairment in functioning. The prevalence of ADHD is about 5% in children and adolescents and 3% in adults (Polanczyk et al. 2007; Swanson et al. 1998). ADHD is believed to equally affect children of all social classes. However, strong evidence supports the notion that ADHD is more common among the poor (Russell 2016).

There are three main types of the disease according to the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association 2013): having the predominance of hyperactivity and impulsivity, or attention deficit, or a mixture of both. ADHD is highly heritable. A study performed in twins reports the mean heritability of ADHD to be around 76%. On the other hand, biopsychosocial models of ADHD include both genetic and environmental, including epigenetic, inflammatory, toxic, social, and other interactions leading to increased risk of ADHD. Clearly, there is no simple causal explanation (Kollins et al. 2008; Vaidya and Stollstorff 2008; Kim et al. 2006). Whether ADHD and

## 1 Attention-Deficit Hyperactivity Disorder (ADHD)

Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder in which first

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allergy are interrelated is still an open and highly disputable question. Reports concerning allergies in children with ADHD, suggesting a possible causal background, have created a growing concern among patients and families (Lin et al. 2016).

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## 2 Allergy

Food allergy is a process that occurs reproducibly after intake of certain foods. The process includes an immunologic response with IgE production or it may be non-IgE-mediated. It can also be of non-immunologic background, assuming the form of intolerance, the exemplary of which may be lactose intolerance. The IgE-mediated food allergy can be confirmed by allergen-specific IgE testing and by specific clinical symptoms occurring after exposure to allergens (Rona et al. 2007).

Clinical symptoms of IgE-dependent allergy include urticarial problems, angioedema, cough, runny nose, vomiting, headache, severe cardiac complications, and anaphylaxis (Schnyder and Pichler 2009). This type of reactions, characterized by the production of specific IgE antibodies, is the most common. Symptoms occur shortly after contact with allergen. Allergens enter the body from the air or ingested food (Sampson 1999). In industrialized countries, more than 15% of people suffer for direct allergy, resulting in rhinitis, asthma, conjunctivitis, or atopic dermatitis. Food allergies, which involve the formation of IgE antibodies, give rise to symptoms hours after food digestion. The symptoms include burning, itching, nausea and vomiting, abdominal pain in extreme cases, asthma, confusion, and even anaphylaxis. These symptoms often appear after ingestion of peanuts and fish (Ghunaim et al. 2005).

Pediatrics patients with food allergy are 2–4 times more likely to have related conditions, such as atopic dermatitis, asthma, or allergic rhinitis, compared to children without food allergy (Branum and Lukacs 2009). A risk for developing food allergy associates with preexisting allergic disease or family history of food allergy (Rona

et al. 2007). There are currently no recommendations on the medications for preventing IgE- or non-IgE-mediated food-induced allergy reactions (Boyce et al. 2010). The most certain method to avoid allergic reactions is having a diet free of specific allergens. Children with food allergy and their caregivers should be instructed in the interpretation of food labels. Another possibility is to retest the food suspected of causing an allergic response, at a time interval that depends on the child's age and medical history (Sampson 1999).

The presence of IgE is usually confirmed using an in vivo prick skin test or in vitro tests assessing the level of IgE in the serum (Burks et al. 2011). Skin testing have some limitations, e.g., depending on the skin condition, which underscores the role IgE testing in the serum (Sicherer et al. 2012). Currently, single allergen testing, using a fluoroluminescence method, has been accepted as a reference method for specific IgE diagnostics. A disadvantage of the method is the possibility of only a single allergen detection, which may impede a complete assessment of a disease and increase the cost of further diagnostic efforts. Multiple allergen simultaneous testing (MAST) is more profitable to this end (Shin et al. 2010).

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## 3 Allergy in Patients with Attention-Deficit Hyperactivity Disorder

Feingold (1975) has proposed a hypothesis that different types of food that could act as allergens in atopic diseases may also lead to the development of hyperactivity. Coexistence of allergy in patients with ADHD has been studied since the early 1980s. The studies have clearly noted an increase in the prevalence of allergic disease accompanying ADHD. However, majority of data are anecdotal and of low quality (Miyazaki et al. 2017; Belfer 2008). The relationship between allergy and ADHD may be divided into two subgroups: one focusing on behavioral symptoms, including symptoms of ADHD in children with allergic diseases, and the other that

is more epidemiologically oriented and focuses on comorbidities. Patients with allergic disease such as eczema, asthma, or allergic rhinitis may also exhibit hyperactive and impulsive behavior. These patients may need an integrated combination of diagnostics, prevention, and treatment strategies (Boris and Mandel 1994). For instance, scores on the hyperactivity/impulsivity and inattention subscales are significantly higher in children with allergic rhinitis than in control subjects, although such children may have not necessarily been diagnosed with ADHD (Feng et al. 2017).

Schmitt et al. (2009) have studied a group of 1436 patients with atopic dermatitis and found direct relationship to the co-occurrence of ADHD. Fasmer et al. (2011) have reported an increased prevalence of asthma in ADHD patients, and those who have more symptoms of ADHD have a still higher rate of asthma. Similar conclusions have been drawn by Mogensen et al. (2011) in a study involving 1480 pairs of twins. Chen et al. (2013) have gathered information the allergic diseases coexisting with ADHD and found that 25.2% of ADHD patients have asthma, 40.6% have allergic rhinitis, and 17.9% have atopic dermatitis. Chou et al. (2013) have found that ADHD patients have a significantly higher prevalence of allergic rhinitis (28.4%) compared with the general population (15.2%). The prevalence of allergic disease in ADHD patients is independent of environmental and lifestyle factors such as parental smoking, breast feeding, or the beginning of day care at an early age (Schmitt et al. 2010).

Food hypersensitivity, including true allergy, and ADHD may share etiologic pathways, as a behavioral response to food often occurs in ADHD. There are studies that evaluate the effect of dietary restrictions and point to significant benefits gained from the elimination diet in some patients suffering from attention hyperactivity disorders (Verlaet et al. 2014). Chou et al. (2013) have reported that ADHD patients have a higher prevalence of allergy and asthma, but not atopic dermatitis, than the general population has. In addition, ADHD is more prevalent in boys than girls and often is diagnosed when children are at school. The prevalence of ADHD also is greater

in the urban areas. In the US study conducted in children and adolescents, which encompassed 354,416 subjects, Strom et al. (2016) have reported that the severity of atopic dermatitis is associated with that of ADHD. The prevalence of ADHD also was overall greater in children with the accompanying allergic diseases, and it was estimated at 7.3% in eczema, 10.9% in asthma, 8.9% in hay fever, 11.9% in eczema and asthma, 9.8% in eczema and hay fever, 12.9% in asthma and hay fever, and 14.5% in eczema and asthma and hay fever. ADHD is definitely a frequent comorbidity of atopic dermatitis, particularly the genetically underlain form of atopic dermatitis linked to the filaggrin gene mutations (Chiesa Fuxench 2017). Likewise, a systematic review and meta-analysis published in 2017 has revealed that children with ADHD are more likely to have asthma, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis than the healthy peers (Miyazaki et al. 2017), but no such relationship was substantiated in case of food allergy. Similar results have been published by Chen et al. (2017) concerning asthma, atopic eczema, and allergic rhinitis. Moreover, the authors demonstrate that individuals with allergic diseases have about 50% greater chance of developing ADHD compared to healthy subjects. A biological plausibility exists that ADHD and allergic disorders share a common background at the translational level involving gene interactions, although the exact mechanisms of this association are unclear as it lacks causality. Nonetheless, molecular biology has provided some possible cues on the association between allergic disorders and ADHD. One is that patients with atopic diseases are exposed to higher levels of pro-inflammatory cytokines which permeate through the blood-brain barrier and activate neuro-immune mechanisms involving emotional and behavioral symptoms related to ADHD (Schmitt et al. 2010). Another possibility is that allergy could impair the mechanisms of synaptic plasticity in the prefrontal cortex, causing cognitive brain dysfunction characteristic of ADHD (Goto et al. 2010). In support of that notion, Trikojat et al. (2015) have found that patients with seasonal allergic rhinitis have a slowdown in information processing speed,

which causes changes in attentional control, both in and off symptomatic season, and which associates with IgE levels. Ishiujii et al. (2009) and Sun et al. (2012) have investigated cortical cingulate activity involved with affect and emotion, in atopic dermatitis patients and healthy controls during histamine-induced itch, using functional magnetic resonance imaging. The authors demonstrate changes in cortical activity in atopic dermatitis, compared with the healthy condition, which associate with the measures of disease intensity, including impulsivity and inattention.

#### 4 Summary and Conclusions

Epidemiological population studies show an association between allergic disorders and attention-deficit hyperactivity disorder. A variety of allergies associates with different subtypes of ADHD. It has been noticed that the highest incidence of atopic dermatitis occurs in patients with allergic rhinitis and in ADHD patients in whom attention deficit is a predominant symptom. Genetic problems linked to immunity, dysfunction of cortical plasticity, and the influence of environmental factors are the presumed pathological underpinnings of allergies and ADHD, but the exact mechanisms underlying the co-occurrence of both pathologies remain unclear.

The association of allergy and ADHD is of raising clinical interest as both pathologies are sharply on the rise globally and notably involve childhood and adolescent periods of life. The most common diseases that associate with ADHD are atopic dermatitis, allergic rhinitis, and asthma. We believe this brief review will serve to raise awareness of the issue and to indicate the need for meticulous workup to identify the agents one is allergic and to assess cognitive functions.

**Conflicts of Interest** The authors declare no conflicts of interest in relation to this paper.

#### References

- American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders, 5th edn. American Psychiatric Publishing, Arlington. ISBN 978-0-89042-555-8
- Belfer ML (2008) Child and adolescent mental disorders: the magnitude of the problem across the globe. *J Child Psychol Psychiatry Allied Disc* 49(3):226–236
- Bierderman J, Faraone SV (2005) Attention-deficit hyperactivity disorder. *Lancet* 366:237–248
- Boris M, Mandel FS (1994) Food and additives are common causes of the attention deficit hyperactive disorder in children. *Ann Allergy* 72(5):462–468
- Boyce JA, Assa'ad A, Burks AW et al (2010) Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol* 126(6):1105–1118
- Branum AM, Lukacs SL (2009) Food allergy among children in the United States. *Pediatrics* 124(6):1549–1555
- Burks AW, Jones SM, Boyce JA et al (2011) NIAID-sponsored 2010 guidelines for management of food allergy: applications in the pediatric population. *Pediatrics* 128:955–965
- Chen MH, Su TP, Chen YS, Hsu JW, Huang KL, Chang WH, Bai YM (2013) Allergic rhinitis in adolescence increases the risk of depression in later life: a nationwide population-based prospective cohort study. *J Affect Disord* 145(1):49–53
- Chen MH, Su TP, Chen YS, Hsu JW, Huang KL, Chang WH, Chen TJ, Bai YM (2017) Comorbidity of allergic and autoimmune diseases among patients with ADHD. *J Atten Disord* 21(3):219–227
- Chiesa Fuxench ZC (2017) Atopic dermatitis: disease background and risk factors. *Adv Exp Med Biol* 1 (027):11–19
- Chou PH, Lin CC, Lin CH, Loh e-W, Chan CH, Lan TH (2013) Prevalence of allergic rhinitis in patients with attention-deficit/hyperactivity disorder: a population-based study. *Eur Child Adolesc Psychiatry* 22:301–307
- Fasmer OB, Halmøy A, Eagan TM, Oedegaard KJ, Haavik J (2011) Adult attention deficit hyperactivity disorder is associated with asthma. *BMC Psychiatry* 11:128
- Feingold BF (1975) Hyperkinesis and learning disabilities linked to artificial food flavors and colors. *Am J Nurs* 75:797–803
- Feng B, Jin H, Xiang H, Li B, Zheng X, Chen R, Shi Y, Chen S, Chen B (2017) Association of pediatric allergic rhinitis with the ratings of attention-deficit/hyperactivity disorder. *Am J Rhinol Allergy* 31 (3):161–167
- Ghunaim N, Grönlund H, Kronqvist M, Grönneberg R, Söderström L, Ahlstedt S, van Hage-Hamsten M (2005) Antibody profiles and self-reported symptoms to pollen-related food allergens in grass pollen-allergic patients from northern Europe. *Allergy* 60(2):185–191

- Goto Y, Yang CR, Otani S (2010) Functional and dysfunction synaptic plasticity in prefrontal cortex: roles in psychiatric disorders. *Biol Psychiatry* 67 (3):199–207
- Ishijima Y, Coghill RC, Patel TS, Oshiro Y, Kraft RA, Yosipovitch G (2009) Distinct patterns of brain activity evoked by histamine-induced itch reveal an association with itch intensity and disease severity in atopic dermatitis. *Br J Dermatol* 161(5):1072–1080
- Kim JW, Kim BN, Cho SC (2006) The dopamine transporter gene and the impulsivity phenotype in attention deficit hyperactivity disorder: a case-control association study in a Korean sample. *J Psychiatr Res* 40 (8):730–737
- Kollins SH, Anastopoulos AD, Lachiewicz AM, FitzGerald D, Morrissey-Kane E, Garrett ME, Keatts SL, Ashley-Koch AE (2008) SNPs in dopamine D2 receptor gene (DRD2) and norepinephrine transporter gene (NET) are associated with continuous performance task (CPT) phenotypes in ADHD children and their families. *Am J Med Genet B Neuropsychiatr Genet* 147B(8):1580–1588
- Lin YT, Chen YC, Gau SS, Yeh TH, Fan HY, Hwang YY, Lee YL (2016) Associations between allergic diseases and attention deficit hyperactivity/oppositional defiant disorders in children. *Pediatr Res* 80(4):480–485
- Miyazaki C, Koyama M, Ota E, Swa T, Mlunde LB, Amiya RM, Tachibana Y, Yamamoto-Hanada K, Mori R (2017) Allergic diseases in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis. *BMC Psychiatry* 17:120
- Mogensen N, Larsson H, Lundholm C, Almqvist C (2011) Association between childhood asthma and ADHD symptoms in adolescence: a prospective population-based twin study. *Allergy* 1:224–1230
- Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA (2007) The worldwide prevalence of ADHD: a systematic review and meta-regression analysis. *Am J Psychiatry* 164(6):942–948
- Rona RJ, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E, Sigurdardottir ST, Lindner T, Goldhahn K, Dahlstrom J, McBride D, Madsen C (2007) The prevalence of food allergy: a meta-analysis. *J Allergy Clin Immunol* 120(3):638–646
- Russell AE (2016) The association between socioeconomic disadvantage and attention deficit/hyperactivity disorder (ADHD): a systematic review. *Child Psychiatry Hum Dev* 47:440–458
- Sampson HA (1999) Food allergy. Part 1: immunopathogenesis and clinical disorders. *J Allergy Clin Immunol* 103(5 pt 1):717–728
- Schmitt J, Romanos M, Schmitt NM, Meurer M, Kirch W (2009) Atopic eczema and attention-deficit/hyperactivity disorder in a population-based sample of children and adolescents. *JAMA* 7:724–726
- Schmitt J, Buske-Kirschbaum A, Roessner V (2010) Is atopic disease a risk factor for attention-deficit/hyperactivity disorder? A systematic review. *Allergy* 65(12):1506–1524
- Schnyder B, Pichler WJ (2009) Mechanisms of drug-induced allergy. *Mayo Clin Proc* 84(3):268–272
- Shin JW, Jin S, Lee JH, Cho S (2010) Analysis of MAST-CLA results as a diagnostic tool in allergic skin diseases. *Ann Dermatol* 22:35–40
- Sicherer SH, Wood RA, American Academy of Pediatrics Section on Allergy and Immunology (2012) Allergy testing in childhood: using allergen-specific IgE tests. *Pediatrics* 129(1):193–197
- Strom MA, Fishbein AB, Paller AS, Silverberg JI (2016) Association between atopic dermatitis and attention deficit hyperactivity disorder in U.S. children and adults. *Br J Dermatol* 175(5):920–929
- Sun L, Cao Q, Long X, Sui M, Cao X, Zhu C, Zuo X, An L, Song Y, Zang Y, Wang Y (2012) Abnormal functional connectivity between the anterior cingulate and the default mode network in drug-naive boys with attention deficit hyperactivity disorder. *Psychiatry Res* 201(2):120–127
- Swanson J, Castellanos FX, Murias M, LaHoste G, Kennedy J (1998) Cognitive neuroscience of attention deficit hyperactivity. *Curr Opin Neurobiol* 8 (2):263–271
- Trikojat K, Buske-Kirschbaum A, Schmitt J, Plessow F (2015) Altered performance in attention tasks in patients with seasonal allergic rhinitis: seasonal dependency and association with disease characteristics. *Psychol Med* 45(6):1289–1299
- Vaidya CJ, Stollstorff M (2008) Cognitive neuroscience of attention deficit hyperactivity disorder: current status and working hypotheses. *Dev Disabil Res Rev* 117 (18):2407–2423
- Verlaet AA, Noriega DB, Hermans N, Savelkoul HF (2014) Nutrition, immunological mechanisms and dietary. *Eur Child Adolesc Psychiatry* 23(7):519–529