

## Childhood Neurological Health and Immune Reactivity: Are ADHD and Autism Allergic Diseases?

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Attention Deficit Hyperactivity Disorder (ADHD) is a common psychiatric disorder in children, and its prevalence is on the rise in many countries.<sup>1</sup> Hallmarks of the disorder include cognitive difficulties such as low attention span and behavioral problems such as hyperactivity and impulsiveness. Autism spectrum disorders (ASDs) are also common behavioral conditions that affect one in 59 children.<sup>2</sup> ASDs encompass a number of neurodevelopmental disorders characterized by language deficits, weakened executive function, impaired social skills, lower mentalizing properties, and repetitive behaviors. These symptoms most commonly emerge around two to three years of age. The clinical presentation of the disorder varies widely and distinct subgroups of the disease exist including classic autism, Asperger syndrome, and several other forms.

Symptom aggravation in ADHD and autism can occur for seemingly unknown reasons. In this article, I propose that food and environmental allergies and sensitivities may offer a possible explanation for both the pathogenesis of these disorders and their exacerbations. Testing for allergies and food sensitivities— and treatment of the patient if warranted—can therefore be extremely effective in this group of patients.

### Allergies, Intolerances, and ADHD

Children with ADHD are more likely to suffer from allergic diseases. In one study of 100 children with ADHD compared with 60 healthy controls, 35% of the ADHD children

had allergies. Most of the allergies were a combination of allergic rhinitis and bronchial asthma, and the most common allergens were hay dust (43%) and pollens (37.5%).<sup>3</sup> Children with allergies were more likely to have a more severe form of ADHD.<sup>3</sup>

Asthma, allergic rhinitis, and food allergies have been implicated in not only the worsening of symptoms in ADHD but also its development.<sup>4</sup> Jiang and colleagues found that a single food allergy, food allergy combined with allergic rhinitis or asthma, and food allergy combined with both allergic rhinitis and asthma were independently linked to an elevated risk of ADHD.<sup>5</sup>

Further evidence supporting the association between allergies and ADHD is that in both disorders there are imbalances in neurotransmitters such as dopamine, norepinephrine, and 5-hydroxytryptamine.<sup>5</sup> Furthermore, immunity-related genes may be involved in ADHD,<sup>6</sup> and clinical studies have demonstrated that allergic diseases and neurological disorders often exist simultaneously in the same patient.<sup>5</sup> This could be due to genetic factors, neurotransmitter imbalances, neuroimmunity, and problems in the brain-gut axis.<sup>5</sup> These factors have led one group of researchers to propose that ADHD may itself be an allergic disease.<sup>6</sup>

Food intolerance has been known to cause ADHD symptoms since at least the 1970s when Feingold observed hyperactivity and learning disabilities in children who ate artificial food flavors and colors.<sup>7</sup> In 1992,



Egger and colleagues published a study where 116 children with ADHD were found to develop hyperactivity after eating certain foods.<sup>8</sup> The researchers demonstrated that desensitizing 20 ADHD children to foods that triggered their hyperactivity allowed 16 of them to eat the offending foods without the emergence of ADHD symptoms. In the control group of ADHD children who were not desensitized, only 4 of 20 became tolerant to the offending foods. More recent studies have indicated that an elimination diet featuring the avoidance of foods that produce reactions may yield benefits in children with ADHD.<sup>9,10</sup>

The connection between ADHD and celiac disease adds to the evidence that food sensitivities may play a role in ADHD symptoms or may contribute to the etiology of the disorder. Niederhofer and

Pittschieler observed a higher prevalence of ADHD symptoms in untreated celiac disease patients compared to the general population.<sup>11</sup> Consuming a gluten-free diet for 6 months reduced ADHD symptoms. The majority of patients (74%) preferred to remain on the gluten-free diet due to a pronounced reduction of symptoms.

## Autism and Immune Reactivity

As with ADHD, there is a relationship between autism spectrum disorders (ASDs) and gluten intolerance. Researchers have observed a greater risk of ASDs in children whose mothers have celiac disease.<sup>12</sup> Furthermore, compared to controls, individuals with ASDs and their relatives have a greater prevalence of impaired intestinal permeability.<sup>13</sup> Patients with ASDs on a gluten- and casein-free diet have a healthier gut barrier compared to patients not on the diet.<sup>13</sup> Other studies of gluten- and casein-free diets in ASD patients yielded similar results.<sup>14,15</sup> A subgroup of autistic patients are also known to produce antibodies against gliadin peptides.<sup>16</sup> It is thought that the sensitivity to gluten in this population may be linked to the development and/or worsening of ASD symptoms.<sup>17</sup> Consequently, I order a celiac antibody panel for all of my ADHD and ASD patients.

Beyond gluten sensitivity, ASDs are associated with other food allergies and intolerances.<sup>18</sup> Both ASDs and allergic responses to food have a similar mechanism of action. Mast cells, innate lymphoid cells, and Th2 cells are activated during allergic responses.<sup>19</sup> These cells synthesize type-2 cytokines (IL-4 and IL-13), which trigger the microglia and macrophages to use a phenotype known as M2A.<sup>19</sup> M2A-polarized macrophages and microglia are important in tissue repair through the release of growth factors such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1.<sup>19</sup> Likewise, in ASD, there occurs increased type-2 cytokines, microglia

activation, M2A polarization, and a rise in growth factor levels.<sup>19</sup> In neurons, these growth factors lead to activation of the enzyme mammalian Target of Rapamycin (mTOR), which blocks autophagy and prevents the removal of redundant synapses in the central nervous system.<sup>19</sup> According to one group of researchers, "It is therefore conceivable that allergy contributes to the prevalence and severity of ASD via an increased release of growth factors in the brain."

In mice with cow's milk allergy, diets that reduce mTOR activity in the prefrontal cortex and amygdala improve behavioral problems similar to those seen in autistic children.<sup>20</sup> This suggests mTOR may be a mechanism of action by which allergies can lead to autistic symptoms.

The sensitization to dietary proteins (especially to wheat, cow's milk, and soy) that occurs in children with ASDs may be due to an abnormal innate immune response that leads to GI inflammation and exacerbation of behavioral symptoms.<sup>21</sup> Gastrointestinal and behavioral symptoms experienced by children with ASDs often resolve when an elimination diet is implemented.<sup>21</sup>



## Cross-Reactivity in ADHD and Autism

Cross-reactivity refers to the fact that people sensitized to inhaled allergens also react to specific types of fruits, vegetables, and even in some cases animal protein.<sup>22</sup> It is estimated that 80% of all cases of food allergy in adults are preceded by a clinical or subclinical sensitization to inhaled allergens.<sup>23</sup> A substantial percentage of ADHD patients are sensitized to Bermuda grass.<sup>24</sup> Many people who are allergic to Bermuda grass also react to cantaloupes and tomatoes.<sup>25</sup> There is also a high prevalence of dust mite sensitization in children with ADHD.<sup>24</sup> Dust mites cross-react with shrimp and mollusks.<sup>25</sup>

Therefore it is important for clinicians to be aware that children with ADHD or ASDs who react to airborne allergens may also exhibit behavioral and other symptoms after ingesting cross-reacting foods. Antibody assessment panels measuring IgE, IgA, and IgG can help determine which foods may pose a problem.

## Conclusion

A strong link exists between childhood neurological disorders and inhaled allergens and food allergies/intolerances. Prevalence of allergic disorders is high in children with ADHD or autism. In these children, cross-reactivity between inhaled allergens such as pollens and various foods can occur. This leads to a possible exacerbation of ADHD or ASD symptoms in children sensitized to inhaled allergens who consume the corresponding food or foods. Furthermore, there is a high prevalence of celiac disease in this group of patients and gluten-free diets often resolve symptoms. As always, I prefer to test rather than guess. Thus, I recommend all patients with ADHD and ASDs undergo U.S. BioTek's celiac antibody panel and to test for food allergies and intolerances using the antibody assessment panels.

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