

Food Allergy and Psychiatric Disorders

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FOOD ALLERGY

Food allergy is the hypersensitivity reactions of the body to foods through the immune system. Food allergy is different from food intolerance where no allergens or reactions are observed. The immune system has no role in food intolerance. These are disorders related to enzymatic functions in the digestive system.^[1]

In the first encounter with the allergen, T cells secrete the cytokine group called interleukin. The increased number of T cells stimulates B cells, the task of which is to produce antibodies, through interleukin-4 (IL-4) and a high amount of immunoglobulin E (IgE) is released into the blood. Immunoglobulin E in the blood binds to the appropriate surface receptors of mast and basophil cells involved in the acute inflammatory response. After this step, IgE coated cells are susceptible to allergen.^[2,3]

If the same allergen is encountered again, the allergen binds to the IgE molecules on the surface of the mast and basophil cells. When mast and basophil cells are activated, they degranulate and release inflammatory mediators such as histamine to surrounding tissues. These mediators cause many systemic effects such as smooth muscle contraction,

ABSTRACT

Food allergies are the hypersensitivity reactions of our body against food by means of immune system. They should not be confused with reactions known as "food intolerance" where an allergen and hypersensitivity reaction are not involved. Food allergy can affect many organs and systems in the body. Itching, burning, redness, urticaria (hives), nasal obstruction, sneezing, watery eyes and anaphylaxis are the symptoms of general reaction. Contrary to popular belief, food allergy is a problem not only for children and adolescents but also for adults. The question of whether these reactions affecting many organs and systems is a direct cause or predisposition factor for psychiatric disorders has been the subject of many studies for many years. Major depressive disorder, bipolar personality disorder, panic attack, anxiety and social phobia are just a few of these diseases. Food allergy reduces the quality of life of the individual. Therefore the nutrients and allergic reactions they cause during the diagnosis and treatment of these diseases are of great importance.

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nerve stimulation, vasodilatation, mucosal secretion. These results in runny nose, itching, shortness of breath and anaphylaxis.^[2,3]

PSYCHOSOCIAL EFFECT OF FOOD ALLERGY AND QUALITY OF LIFE (QoL)

There is strong evidence that food allergy affects the QoL of children and adolescents as well as their families. In a study conducted by Avery et al.^[4] To directly ask children to report their QoL. Used the food allergy-specific QoL scale and found that children with peanut allergy reported lower QoL scores than children with insulin-dependent diabetes mellitus (IDDM). Another study using approved general QoL scales reported that children with peanut allergy reported significantly worse QoL than healthy siblings.^[5] In the same study, those with high levels

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of food-specific IgE antibodies were also found to be poor in mental health and general health. Obviously further studies are needed in this area using QoL scales specific to the approved food allergy currently available.^[6]

Food allergy may also have an effect on anxiety. Lyons and Forde^[7] found that food allergy was associated with increased anxiety levels in adolescents and Avery et al.^[4] reported that children with peanut allergy are more concerned about eating and have higher levels of anxiety and fear than children with IDDM (Insulin Dependent Diabetes Mellitus) who manage allergies. In contrast, King et al.^[5] asked children with peanut allergy and their siblings to complete an approved child anxiety scale and found out that the results of the scale were significantly lower than the approved healthy norms. This was probably due to norms from different children in different countries. In addition, the scale used in this study was developed to assess clinical anxiety levels and may not be sensitive enough for food-related anxiety.^[6]

In another study, Herbert and Dahlquist^[8] found that people aged 18 to 22 were more concerned about food allergies than people who reported only a history of anaphylaxis. There was no significant difference in anxiety or depression between patients with and without food allergies. However, in this study, online personal reporting methods were used instead of clinical interviews, and the majority of the participants were university students who could cause deviations in reported anxiety levels.^[6]

PSYCHIATRIC DISORDERS AND FOOD ALLERGY

According to the theory of macrophage depression proposed in 1991, the mechanisms involved in the pathogenesis of depression are macrophage activation and overexpression of proinflammatory cytokines. Proinflammatory cytokines, due to their ability to penetrate into the blood-brain barrier (BBB), can affect the metabolism and secretion of neurotransmitters in the central nervous system (CNS), leading to irregular homeostasis.^[9]

There is much evidence to support this theory: the imbalance of proinflammatory and antiinflammatory mediators is observed before the onset of the disease;^[10] significantly higher pro-inflammatory cytokine levels are observed in the acute phase of depression;^[11] higher markers of inflammation are associated with the risk of recurrence of the

next depressive episode;^[12] concentrations of high markers of inflammation are associated with disease progression.^[13] Many anti-inflammatory drugs have been shown to be successful in patients with major depressive disorder.^[14]

Several studies have demonstrated a relationship between intestinal permeability and inflammation: Celiac disease,^[15] autoimmune hepatitis,^[16] and Parkinson's disease.^[17] According to a study conducted in 2017, IgG food hypersensitivity may lead to systemic inflammation and may be a triggering factor for the development of MDD.^[18]

The undigested food compounds, which will normally be broken down in the intestine, and enters the bloodstream and the epitopes merge with food IgG antibodies to form immune complexes. This triggers the immune inflammatory cascade. Uncontrolled release of proinflammatory mediators may contribute to low-grade systemic inflammation and low-grade neuroinflammation; this can occur as a result of pathological processes in the CNS (central nervous system); so changes in neurotransmitter metabolism, neurogenesis, glutamate excitotoxicity, and then sustain and prolong depression.^[19]

DEPRESSION

Studies have shown that the frequency of allergy is higher in patients with depression.^[20] Preliminary data suggest that patients with a history of allergy may have an increased suicide rate.^[21] According to a study in Brown-Norway rats, exposure to susceptible allergens and aeroallergens causes allergy-related T-cell type 2 (Th2) cytokine gene expression in the prefrontal cortex, as well as anxiety-like and aggressive behavior. Therefore susceptibility and exposure to aeroallergens peaking in the spring may cause seasonal exacerbation of suicide risk factors such as anxiety, depression, hostility/aggression and sleep disturbance.^[21]

Another study conducted in 1993 shows that food allergy causes depression symptomatology. According to this study, cholinergic system activity and sensitivity play a major role in the production of endogenous depression symptomatology. As a result of allergen-induced overactivation, the cholinergic system becomes prominent in the adrenergic-cholinergic system. This causes a wide variety of severe depressive symptoms. Each symptom occurs severely and permanently. Dysphoria, crying, guilt and helplessness and suicidal ideation are common. Memory problems are important, diffuse fatigue is

chronic, concentration and attention are significantly reduced, motivation to participate in enjoyable activities is dramatically reduced and sleep is deeply disrupted. These symptoms can be experienced even if external psychological stressors are not important. As cholinergic activity becomes more dominant, the number and severity of depression symptoms increase. In fact, a certain threshold of cholinergic-adrenergic activity imbalance must be crossed before depression symptomatology is demonstrated or experienced. A higher threshold should be exceeded before the person who meets the criteria for clinical depression experiences symptomatology. The interaction between allergies, other disturbing medical disorders and psychological stress can quickly lead to a vicious cycle. Physical discomfort, loss of productivity, and impairment of personal relationships caused by these physical diseases create psychological stress that further exacerbates the imbalance of cholinergic-adrenergic activity, exacerbating physical and psychological problems. Undoubtedly this interaction with stress has led to a widespread belief that depression in allergy sufferers is a purely psychological and reactive depression. It is not surprising to conclude that, in many people, the imbalance is likely to be caused by the factor that balances cholinergic adrenergic activity beyond the threshold at which significant symptoms of depression occur, possibly caused by psychological stress. While the obvious correlation between presenting depression symptoms and increased psychological stress reports revealed that stress was the cause, the important role of predisposing factors remained hidden. Conventional allergy treatments (eg, avoidance of allergens, desensitization therapy) may be useful for those in whom allergy plays an important role in the formation of depressive symptomatology. Failure to treat an allergy disorder may limit the degree of recovery from depression, even when appropriate psychotherapy and psychotropic drugs are used.^[22]

It is not certain that allergic problem causes behavior disorder. However, increased psychological or neurophysiological factors due to allergic condition are thought to cause behavioral dysfunction. For example, Kittler and Baldwin^[23] reported that food allergy can aggravate children's minimal brain dysfunction and behavioral dysfunction. Millman et al.^[24] reported that a combination of psychotherapy and allergy therapy improves school performance and behavior of children with learning disabilities, analyzed by a range of neuropsychological assessment scales.

Some articles show that there is a relationship between food sensitivity and attention deficit disorder. A particularly interesting report has shown that transcallosal evoked potential delays are reduced in a very short time, possibly after the administration of a hypoallergenic diet in children with learning difficulties and food sensitivity. This report shows that interhemispheric communication is dramatically slowed down in some food-sensitive, learning-impaired children. The double-blind placebo-controlled experimental method did not reveal possible effects of allergen foods.^[25]

In a study published by Patten and Williams^[26] 36,984 people were asked some questions via web-based forms. The aim of the study was to determine whether there was any relationship between food allergy and axis 1 disorders (major depression, bipolar disorder, panic disorder/agoraphobia and social phobia). Accordingly major depressive disorder correlates significantly with food allergy. Although there is a significant difference in the prevalence of bipolar disorder and food allergy, the relationship between agoraphobia and sociophobia, although weak, is also statistically significant.^[26]

In another web-based study conducted in Japan in 2018, the results suggest that there is a relationship between food allergy and psychiatric disorders.^[27] However the number of allergens was also taken into consideration in this study by Hidese and his team.^[27] According to this study, food allergy was more common in individuals with a history of clinical depression than in the control group, which was dependent on the number of allergens. In addition, food allergy turned out to be a precursor to depression. Among the food allergens, allergy rates to shrimp, egg, mackerel, crab, kiwi, milk, banana, squid and other allergens were higher in the depression group than in the control group. The proportion of individuals with severe psychological discomfort was higher in the food allergy group than in the non-food allergy group and increased with the number of allergens. These results indicate that food allergy is associated with depression and psychological stress. Food allergy was more common in the depression group than in the control group. These results also agree with the findings of a Canadian-based cross-sectional study reported by Patten and Williams^[26]

However, another study by Patten et al.,^[28] published in 2009, found no statistical association between food allergy and psychosocial disorders. According to this study conducted on 15,254 people, it was observed that major depression

increased the risk of developing non-food allergy. Some evidence of an increased incidence of major depression associated with non-food allergies found uncorrected analysis, but the relationship did not persist after multivariate adjustments. Therefore the results of this study primarily support the idea that major depression is associated with an increased risk of allergies.^[28] This result, which falsifies many studies supporting this relationship, may have been due to the epigenetic factors of the subjects, the technique of the study, childhood stressors, and most importantly, genetic factors. However, the results of this study do not support the hypothesis that the psychosocial effect of allergies increases the risk of major depression.

As can be seen, the relationship between food allergy and psychiatric disorders is still unclear. Many studies are needed in this field. The effects of side factors such as epigenetics and genetics should be taken into consideration by means of multidisciplinary researches along with genetic research techniques developed in recent years.

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