

Food-specific IgG guided elimination diet; a role in mental health?

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INTRODUCTION

It is well known that diet and gut health affect mental health symptoms such as stress-related disorders, depression and anxiety¹. Bi-directional signalling between the gut and the brain includes communication via the immune system, central nervous system and the endocrine (hormonal) system which in turn impacts mood and behaviour. This “communication” is under the influence of the gut microbiota; the gut is home to hundreds of trillions of microorganisms which form part of the gut-microbiome-brain axis. The complex interactions involved are influential in a number of disorders in which inflammation has been implicated including depression, schizophrenia, autism-spectrum disorders (ASDs) and attention-deficit hypersensitivity disorder (ADHD)². Mood states have even been linked with the composition of the microbiome in mentally and physically healthy adults³.

Increased gut permeability appears to be the cornerstone of gut-microbiome-brain interaction. This can lead to translocation of gut microbiota and their products, and incompletely digested nutrients such as food proteins, into the blood stream⁴⁻⁵. Structural similarities exist between the intestinal and blood brain barriers⁶, and studies have shown that the blood brain barrier may also be vulnerable to changes in the gut microbiota⁷. The immune system, and immune inflammatory process provide key communication pathways between the gut and brain. Diet, the composition of the gut microbiota, and health are intrinsically linked⁸.

GUT MICROBIOME

The biggest changes in the composition of the gut microbiome and neuronal development occur in childhood and adolescence⁹. Psychiatric, and other, illnesses such as schizophrenia, substance abuse, irritable bowel and mood disorders frequently first manifest themselves during the teenage years and there is a call to better understand the way that gut microbiota can be manipulated to contribute

to treatment of mental illnesses in the developing teen¹⁰. Early life stress can also have a significant impact on the microbiological content of the intestine and immune functioning; that early life stress can also impact adult psychopathology has also long been appreciated in psychiatry¹¹.

There is also increasing evidence that brain inflammation is involved in the pathogenesis of neuropsychiatric diseases. For example, mast

cells are present in the brain where they regulate blood brain permeability and brain function, and it is proposed that they may be involved in the pathogenesis of “brain fog”, headaches and ASDs, which worsen with stress¹². Mast cells, and other immune cells, can be activated through IgG-dependent mechanisms^{1,11,15}, and IgG antibodies to foods are associated with inflammation¹⁶. This is significant in relation to the inflammatory component of many disorders.

It is known that diet strongly influences the composition of the microbiome. Gut microbiota are known to be influential in the susceptibility to food sensitivities¹⁷, and there is a strong statistical correlation between risk for ASD and atopic diseases, such as asthma, eczema, food allergies and food intolerance¹⁸. Food provocation in food intolerant patients is characterised by a general and systemic immune activation¹⁹.

DEPRESSION

Depression is not only linked to changes in neurotransmission in the central nervous system but also changes via hormonal, inflammatory and immune mechanisms, and many studies have shown elevated levels of pro-inflammatory cytokines in those with depression. Serotonin is a critical signalling molecule in the brain-gut-microbiota axis, approximately 95% of serotonin in the body is compartmentalised in the gut, and there is emerging evidence that the serotonergic system may be under the influence of the gut microbiota; references in Kelly *et al* (2015)⁷. A role for IgG hyper-sensitivity in the pathogenesis and therapy of depressive disorders has been reported⁵. Indeed, in the largest study of its kind, Allergy UK commissioned a retrospective postal survey of those who had elevated food-specific IgG levels and had

purchased a YorkTest food-specific IgG-guided diet programme. Of the 708 subjects reporting psychological conditions, including depression, anxiety, behavioural problems, hyperactivity, mental fog, ASD and panic attacks, 81% reported an improvement in their condition following a food-specific IgG-guided elimination diet²⁰.

The association between the gluten-mediated immune response and neurological and psychiatric manifestations is also well established²¹. Non-coeliac gluten sensitivity (NCGS), identified by measuring gliadin-specific IgG antibodies²², represents a unique condition with different manifestations than coeliac disease²³. Gluten ataxia has customarily been considered to be the main neurological manifestation of coeliac disease, however, recent findings have shown that gluten ataxia patients are better classified within the NCGS group, than within the coeliac disease group²⁴. Interestingly NCGS can also predict vulnerability to dementia²⁵.

SCHIZOPHRENIA

Studies have shown that the gut microbiota play a key role in the immunopathogenesis of schizophrenia. There has been a call for strategies that focus on microbiota targeted therapies to improve symptoms and to decrease the immune dysregulation seen in patients with schizophrenia^{26,27}. People with schizophrenia have raised anti-gliadin IgG antibodies compared to normal controls²⁸; similarly reported raised anti-milk casein and anti-yeast IgG antibodies, and potentially other food-specific IgG antibodies^{29,30}. Studies have indicated the selective diffusion of anti-milk casein and anti-wheat IgG antibodies between the blood and the cerebral spinal fluid in those with schizophrenia. In several reports a cross-reactivity between anti-gliadin antibodies and brain proteins has

been described; referenced in Severance *et al* (2015)³⁰. It is postulated that food-specific IgG antibodies pass through a permeable blood brain barrier and are directly pathological to the brain, perhaps binding to important brain proteins. This is consistent with other findings of immune sensitivities to foods in a variety of other brain diseases and conditions including bipolar disorder, ataxia, epilepsy and autism³¹. Therapies which aim to remove the antigenic (food) source and normalise gut and brain barrier functions in schizophrenia have been proposed³².

ASD

Many children with ASDs present with gut symptoms, altered gut microbiota and intestinal permeability. Increasing evidence indicates that ASD pathogenesis also involves brain inflammation² and a permissive blood brain barrier³³. There is an increase in intestinal permeability in those with ASD compared to healthy children; this correlates with the production of higher levels of anti-gliadin and anti-casein specific IgG antibodies concluding that IgG-guided elimination diet could be considered as a medical nutrition therapy in ASD³⁴. In addition, there are increased plasma concentrations of IgG-specific antibodies to milk proteins and gliadin in those with autism compared with their siblings³⁵. Children with ASDs have higher levels of immunoglobulins against cow's milk-derived allergens, and milk intake by these patients has been shown to significantly worsen some of their behavioural symptoms³⁶. These data were backed up by a small pilot study in ASD showing an overall improvement in behavioural symptoms after IgG-guided elimination diet³⁷. The behavioural improvement in ADHD that accompanied an improved IgG score has also been documented³⁸.

CONCLUSION

The food choices that are made by every individual, both because of survival needs and taste preference, cause a substantial and significant variability in gut microbiota. Alterations in the gut, including gut permeability and the composition of the gut microbiome are now considered to be important for treatment across an array of medical conditions. This emphasises the importance of targeting regulators of the immune system in a wide range of medical conditions, particularly psychiatric disorders⁸. Manipulating the microbiota, either by dietary changes, prebiotics, probiotics or even fecal microbial transplantation, seem rational strategies for the prevention and treatment of diseases³⁹.

There is an increasing body of literature that links diet and the composition of the gut microbiome to mental health disorders, but, so far, very little about what specific targeted dietary changes are needed to help⁴⁰. Whether food-specific IgG-guided elimination dietary changes could fulfil such a role has yet to be evidenced fully, however, the new paradigm linking leaky gut, food-specific IgG, inflammation and mental health is both interesting and encouraging in helping our understanding⁵. Much of the focus on a role for food-specific IgG antibodies in mental health disorders has been on gliadin, wheat, yeast and milk, particularly in ASD and schizophrenia. This approach has now been broadened out to include testing for IgG reactions to a wide range of food proteins that are reflective of a typical diet. The important point here is that dietary intervention, on this basis, is personalised; dependent on specific tailored food-IgG test results, providing a unique targeted approach, and this makes sense immunologically. What is clear is that restoration and maintenance of healthy intestinal, and blood brain, barriers is key to improved health, and dietary changes based on IgG-guided elimination diet show promise as a viable intervention strategy.

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