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Review

Food-Specific IgG Guided Elimination Diet; A Role in Mental Health?

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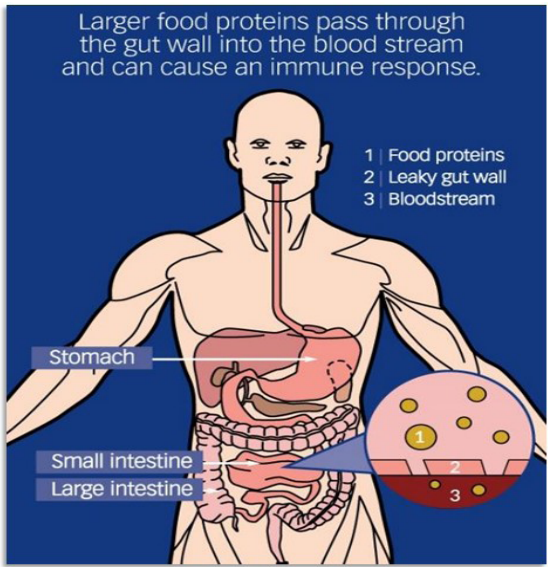
Introduction

It is well known that diet and gut health affect mental health symptoms such as stress-related disorders, depression and anxiety [1]. 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 adults [3].

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 stream [4,5] Structural similarities exist between the intestinal and blood brain barriers [6], and studies have shown that the blood brain barrier may also be vulnerable to changes in the gut microbiota [7]. Blood brain barrier breakdown is complex and due to disruption of the tight junctions, altered transport of molecules and inflammatory responses which appear to initiate and/or contribute to disorders such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, ASD and others [8,9]. 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 linked [10].

Measurement of food-specific IgG antibodies is used as a strategy for identifying foods to which a subject may be sensitive. This type of testing is now considered "mainstream" as many choose to use this approach as a starting point for an elimination diet. The test is not diagnostic of any condition, but is used as an aid to management of dietary intake, a "starting point" for an elimination diet. Increased intestinal permeability can allow larger food proteins to pass through into the blood stream where they may, or may not, trigger an IgG immune response (see Figure 1). There is evidence across a growing number of trials that diet adjusted to food-specific IgG levels to foods can lead to symptom improvement [11].These include those in IBS [12-18], inflammatory bowel disease (IBD) [19,20], migraine[17,21], weight gain [22], rheumatoid arthritis [23] and looking at overall quality of life measures [22].

Key Words: Food Intolerance; Food IgG; Mental Health; Gut Microbiota; Microbiome; Brain; Depression; Autism; ADHD; Schizophrenia, Intestinal Permeability; Blood Brain Barrier; Dietary Change Elimination Diet



Gut Microbiome

The biggest changes in the composition of the gut microbiome and

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neuronal development occur in childhood and adolescence [24] 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 teen [25]. 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 psychiatry [26].There is also increasing evidence that brain inflammation 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 stress [27]. Mast cells, and other immune cells, can be activated through IgG-dependent mechanisms [28-30], and IgG antibodies to foods are associated with inflammation [31].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 sensitivities [32], and there is a strong statistical correlation between risk for ASD and atopic diseases, such as asthma, eczema, food allergies and food intolerance [33]. Food provocation in food intolerant patients is characterised by a general and systemic immune activation [34].

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 reported [5]. 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 food-specific IgG-guided elimination diet [11].

The association between the gluten-mediated immune response and neurological and psychiatric manifestations is also well established [35]. Non-coeliac gluten sensitivity (NCGS), identified by measuring gliadin-specific IgG antibodies [36], represents a unique condition with different manifestations than coeliac disease [37]. 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 group [38]. Interestingly NCGS can also predict vulnerability to dementia [39].

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 [40,41]. People with schizophrenia have raised anti-gliadin IgG antibodies compared to normal controls [42] similarly reported raised anti-milk casein and anti-yeast IgG antibodies, and potentially other food-specific IgG antibodies [43,44].

Severance et al (2015) [45], showed data supporting the concept that cerebral spinal fluid (CSF)-related barrier and flow abnormalities may be present in those with schizophrenia and this may affect the way that food-specific IgG antibodies are distributed between the CSF and serum. The study postulated that food-specific IgG antibodies might pass through a transiently permeable blood CSF, or blood brain, barrier and be directly pathological to the brain, perhaps binding to important brain proteins. Immune sensitivities to foods have been found in a variety of other brain diseases and conditions including bipolar disorder, ataxia, epilepsy and autism [46]. Therapies which aim to remove the antigenic (food) source and normalise gut and brain barrier functions in schizophrenia have been proposed [45].

ASD

Many children with ASDs present with gut symptoms, altered gut microbiota and intestinal permeability. Increasing evidence indicates that ASD pathogenesis also involves brain inflammation (2) and a permissive blood brain barrier [47]. 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 ASD [48]. In addition, there are increased plasma concentrations of IgG-specific antibodies to milk proteins and gliadin in those with autism compared with their siblings [49]. 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 symptoms [50]. These data were backed up by a small pilot study in ASD showing an overall improvement in behavioural

symptoms after IgG-guided elimination diet [51]. The behavioural improvement in ADHD that accompanied an improved IgG score has also been documented [52].

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 disorders [10]. Manipulating the microbiota, either by dietary changes, prebiotics, probiotics or even fecal microbial transplantation, seem rational strategies for the prevention and treatment of diseases [53].

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 help [54]. Whether food-specific IgG-guided elimination dietary changes could fulfil such a role, directly or indirectly, 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 understanding [5]. 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, and the composition of the gut microbiota, are key to improved health, and dietary changes based on IgG-guided elimination diet show promise as a viable intervention strategy.

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