

## Gluten Intolerance, Celiac Disease, and Neuropsychiatric Disorders: A Translational Perspective

**Authors :** Jessica A. Hellings, Piyushkumar Jani

**Abstract :** Background: Systemic autoimmune disorders are increasingly implicated in neuropsychiatric illness, especially in the setting of treatment resistance in individuals of all ages. Gluten allergy in fullest extent results in celiac disease, affecting multiple organs including central nervous system (CNS). Clinicians often lack awareness of the association between neuropsychiatric illness and gluten allergy, partly since many such research studies are published in immunology and gastroenterology journals. Methods: Following a Pubmed literature search and online searches on celiac disease websites, 40 articles are critically reviewed in detail. This work reviews celiac disease, gluten intolerance and current evidence of their relationship to neuropsychiatric and systemic illnesses. The review also covers current work-up and diagnosis, as well as dietary interventions, gluten restriction outcomes, and future research directions. Results: Gluten allergy in susceptible individuals damages the small intestine, producing a leaky gut and malabsorption state, as well as allowing antibodies into the bloodstream, which attack major organs. Lack of amino acid precursors for neurotransmitter synthesis together with antibody-associated brain changes and hypoperfusion may result in neuropsychiatric illness. This is well documented; however, studies in neuropsychiatry are often small. In the large CATIE trial, subjects with schizophrenia had significantly increased antibodies to tissue transglutaminase (TTG), and antigliadin antibodies, both significantly greater gluten antibodies than in control subjects. On later follow up, TTG-6 antibodies were identified in these subjects' brains but not in their intestines. Significant evidence mostly from small studies also exists for gluten allergy and celiac-related depression, anxiety disorders, attention-deficit/hyperactivity disorder, autism spectrum disorders, ataxia, and epilepsy. Dietary restriction of gluten resulted in remission in several published cases, including for treatment-resistant schizophrenia. Conclusions: Ongoing and larger studies are needed of the diagnosis and treatment efficacy of the gluten-free diet in neuropsychiatric illness. Clinicians should ask about the patient history of anemia, hypothyroidism, irritable bowel syndrome and family history of benefit from the gluten-free diet, not limited to but especially in cases of treatment resistance. Obtaining gluten antibodies by a simple blood test, and referral for gastrointestinal work-up in positive cases should be considered.

**Keywords :** celiac, gluten, neuropsychiatric, translational

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