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IS GLUTEN KILLING YOUR BRAIN?

In the past decade, awareness of the potential harmful effects of gluten has risen exponentially within the medical community and general public. An increasing number of healthcare practitioners are recognizing that celiac disease is just one extreme manifestation of gluten sensitivity and that many other patients may unknowingly be suffering from non-celiac gluten sensitivity (NCGS). While non-celiac gluten sensitivity is most often associated with digestive system symptoms, it turns out that this disorder may have equally detrimental effects on the brain. Read on to learn about the relationship between non-celiac gluten sensitivity and the brain and how treatment of this condition may successfully reverse mental health disorders and neurodegenerative disease.

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What is non-celiac gluten sensitivity?

Non-celiac gluten sensitivity (NCGS) is a chronic gastrointestinal disorder distinct from celiac disease, in which individuals experience a wide array of symptoms upon eating gluten. (1, 2) While celiac disease was long considered to be the only legitimate manifestation of gluten sensitivity, research indicates that the spectrum of gluten sensitivity is much broader than originally suspected. (3, 4, 5, 6) The term NCGS is used to designate other forms of gluten sensitivity along this spectrum. As in celiac disease, NCGS stimulates the immune system; however, NCGS has been found to stimulate innate immune activity, whereas celiac disease activates both the innate and adaptive immune systems. (7) In addition, NCGS increases CD-associated antibodies but does not cause atrophy of the intestinal villi. (8) Symptoms of NCGS improve or disappear when gluten is removed from the diet and recur if gluten is reintroduced. The diagnostic criteria for NCGS are as follows:

- Ingestion of gluten elicits rapid occurrence of intestinal and extraintestinal symptoms
- Symptoms disappear when gluten is removed from the diet and recur if gluten is reintroduced
- Wheat allergy has been ruled out
- Specific markers of celiac disease have been ruled out
- Intestinal mucosa is normal (no villous atrophy)
- Antigliadin antibodies (primarily IgG) may be positive (50 percent of NCGS patients are positive)
- HLA-DQ2 and/or HLA-DQ8 may be positive (40 percent of NCGS patients are positive)

Research estimates that approximately 18 million Americans have gluten sensitivity, a figure that is six times greater than the number of Americans who have celiac disease. (9) Despite the wealth of scientific evidence on this topic, and the astonishing numbers of people who may be affected by NCGS, there is a general lack of physician awareness of symptoms, related disorders, and testing for NCGS, and this condition remains largely undiagnosed and untreated.

While gluten sensitivity is perhaps the most frequently cited non-celiac, non-allergic reaction to wheat, it is also possible for people to demonstrate sensitivity to other peptides in wheat such as



wheat lectin agglutinin (WGA), alpha-amylase trypsin inhibitors, and gluten exorphins, which are byproducts of gluten digestion that act as opioids. (10, 11, 12) Sensitivity to these peptides can cause symptoms similar to gluten sensitivity. The term used to describe this reactivity is non-celiac wheat sensitivity (NCWS).

Finally, although NCGS and NCWS are more common than is typically acknowledged, there is no evidence to support the claim that gluten causes neurological disease in people who aren't gluten intolerant. Gluten does not affect all people in the same way. However, in those who are sensitive and susceptible, gluten can have significant effects on neurological health.

Non-celiac gluten sensitivity affects the gut-brain axis

Symptoms of NCGS may be limited to GI distress, including diarrhea, constipation, and bloating; however, a growing body of research indicates that, in certain susceptible individuals, NCGS can have a significant impact on the brain. This is cause for concern, given the estimated number of people who may have undiagnosed NCGS and the dramatically rising numbers of people experiencing mental health disorders and neurodegenerative disease.

The link between gluten and mental health

NCGS appears to affect the brain by altering activity along the gut-brain axis, which is the bidirectional communication system between the enteric nervous system in the gut and the central nervous system in the brain and spinal cord. The gut-brain axis links gut function with emotional and cognitive centers in the brain. (13) Inputs that affect gut health, such as diet and the composition of the microbiome, ultimately affect brain function. Non-celiac gluten sensitivity incites inflammation in the gut and, through the gut-brain axis, can cause inflammation and dysfunction in the brain.

NCGS can trigger neuroinflammation

In NCGS, gluten-triggered inflammation in the gut can instigate inflammation in the brain, referred to as neuroinflammation. Neuroinflammation has been found to play a central, triggering role in brain-related disease. In NCGS, there is a series of steps in the process that ultimately culminates in neuroinflammation and brain changes.

1. Consumption of gluten triggers dysbiosis and gut inflammation and increases the permeability of the intestinal barrier.
2. Increased intestinal permeability allows lipopolysaccharides (LPSs) produced by gut bacteria to leak out of the intestine and into the systemic circulation. Leaked LPSs trigger the immune system to release pro-inflammatory cytokines.
3. LPSs and pro-inflammatory cytokines in the circulation cause toxins to accumulate in the blood stream, inciting systemic inflammation.
4. When systemic inflammation reaches the brain, it creates neuroinflammation.
5. Neuroinflammation leads to brain dysfunction, cognitive impairment, and an increased vulnerability to neurodegenerative disease.

Neuroinflammation has been associated with depression and anxiety, (14) bipolar disorder, (15, 16) schizophrenia, (17) ADHD, (18) and an increased vulnerability to neurodegenerative diseases (19). Therefore, NCGS may be an underlying cause of neuroinflammation, gradually altering the normal, healthy functioning of the brain and leading to manifestations of mental health problems and neurological disease. (20)



Gluten, depression, and anxiety

Non-celiac gluten sensitivity has been linked to both depression and anxiety. In NCGS, gluten may lead to depressive symptoms by inducing abnormalities in serotonin production and causing changes in the gut microbiota. ([21](#), [22](#), [23](#))

While there is limited research about the effects of a gluten-free diet on anxiety and depression in patients with NCGS, a longitudinal study of celiac disease patients found that a one-year-long trial of a gluten-free diet significantly improved anxiety symptoms. ([24](#)) In a small case study of patients diagnosed with celiac disease in adulthood who had previously been unsuccessful with antidepressant therapies, a gluten-free diet was found to quickly improve depressive symptoms. ([25](#))

Gluten and bipolar disorder

Bipolar disorder, a mental health disorder characterized by periods of alternating elation and depression, as well as fluctuations in energy, is notorious for being resistant to conventional pharmaceutical treatment. Research has demonstrated that neuroinflammation is a common denominator in patients with bipolar disorder. ([26](#)) A growing body of evidence indicates that gluten sensitivity may be a key instigator of neuroinflammation in bipolar individuals. Several studies have found that individuals with bipolar disorder demonstrate significantly increased levels of IgG antibodies to gliadin in their blood, but not other markers of celiac disease, suggesting the presence of non-celiac gluten sensitivity. ([27](#), [28](#))

Gluten and schizophrenia

In the medical community, the prevailing belief regarding schizophrenia is that it is a chronic, incurable disorder that can only be managed with a cocktail of pharmaceutical drugs. However, under-the-radar scientific evidence has been around for years indicating that gluten sensitivity may play a major role in the pathogenesis of schizophrenia. As early as the 1950s, researchers were examining the link between gluten sensitivity and schizophrenia; several studies found that schizophrenics experienced significant symptomatic improvement upon commencement of a gluten-free diet. ([29](#), [30](#), [31](#), [32](#)) More recently, a number of studies have demonstrated that individuals with recent-onset psychosis and multi-episode schizophrenia have increased IgG and IgA antibodies to gliadin, suggesting the presence of non-celiac gluten sensitivity. ([33](#), [34](#)) The mechanism by which gluten sensitivity induces symptoms of schizophrenia is through induction of inflammation in both the gut and brain, via the gut-brain axis.

Gluten and autism

Autism may be part of the gluten-sensitivity spectrum. While research does not implicate gluten as the sole cause of autism, non-celiac gluten sensitivity appears to play a role in the gut-brain axis dysfunction characteristic of autism. ([35](#)) It is hypothesized that the opioid-like peptides formed from the incomplete breakdown of gluten leak out of the intestine, enter the systemic circulation, and cross the blood-brain barrier, detrimentally affecting neurotransmission and causing alterations in behavior. ([36](#)) Children with autism have been found to have significantly increased levels of IgG antibodies to gliadin, ([37](#)) and a gluten-free diet may produce a positive change in autistic behaviors. ([38](#))



Gluten and ADHD

Non-celiac gluten sensitivity may also contribute to behavioral changes characteristic of attention-deficit/hyperactivity disorder. (39) A six-month gluten-free diet has been reported to improve symptoms in patients with ADHD. (40)

Gluten and neurodegenerative disease

Through its effects on the gut-brain axis, ingestion of gluten may also predispose NCGS individuals to cognitive decline and an increased vulnerability to neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. (41) The systemic inflammation characteristic of non-celiac gluten sensitivity may promote the deposition of amyloid plaques and neurofibrillary tangles, phenomena characteristic of Alzheimer's disease. (42) In addition, a recent study has concluded that intestinal dysfunction represents one of the earliest manifestations of Parkinson's disease pathology; thus, the disease originates in the intestine and appears to spread to the brain via the gut-brain axis. (43)

Repairing the gut-brain axis

To alter the progression of mental health disorders and neurodegenerative disease precipitated by non-celiac gluten sensitivity, the health of the gut-brain axis must be restored. This can be accomplished by eating a gluten-free diet, restoring the health of the microbiome, reducing systemic inflammation, and rehabilitating the gut-brain axis through vagus nerve stimulation.

Eliminate gluten from the diet

The fundamental basis of treatment for non-celiac gluten sensitivity is removal of gluten from the diet. Research indicates that when gluten is removed from the diets of individuals with NCGS, this can result in a complete resolution of symptoms. (44) A nutrient-dense diet that contains plentiful vegetables; some fruit; high-quality sources of animal protein; a healthy balance of fats, nuts, and seeds; and perhaps some gluten-free grains is a great framework for a balanced gluten-free diet.

Restore the microbiome

Restoration of the microbiome is crucial in the treatment of NCGS, as long-term ingestion of gluten in individuals with NCGS can result in significant dysbiosis. Research indicates that probiotics such as *Bifidobacteria* and *Lactobacilli*, combined with prebiotics such as FOS and inulin, may help reduce neuroinflammation in NCGS by restoring a normal microbial balance. (45, 46)

Reduce inflammation

Another aspect of NCGS that must be addressed is oxidative damage and antioxidant depletion. Eating an anti-inflammatory gluten-free diet is key for reducing gut and brain inflammation. However, repletion of antioxidants is also crucial. This can be done by consuming antioxidant-rich foods, which come with a "full package" of beneficial compounds that benefit our health, as well as by supplementing with certain targeted nutrients such as ubiquinone and acetyl-L-carnitine, which have been found to protect the brain against oxidative damage. (47)



Try vagus nerve stimulation

The vagus nerve is a cranial nerve that links the brain to the intestine, as well as to several other key visceral organs, and is a critical component of the gut–brain axis. Two types of signals travel along the vagus nerve: afferent signals, which convey information from the gut to the brain, and efferent signals, which transport information from the brain to the gut. The vagus nerve mediates activity of the parasympathetic nervous system, the division of the nervous system responsible for “rest and digest” functions. Stimulation of the vagus nerve has been shown to reduce the body’s response to stress, decrease heart rate and blood pressure, stimulate digestion, reduce inflammation, and change the function of certain parts of the brain. [\(48\)](#)

Vagus nerve stimulation sends a mild pulse of electrical energy through the vagus nerve, thus activating the parasympathetic nervous system. In conventional vagus nerve stimulation, a device is surgically implanted under the skin and connected to the left branch of the vagus nerve using a wire. When activated, the device sends electrical signals along the vagus nerve. Fortunately, this invasive form of vagus nerve stimulation is no longer a necessity, as there are now a handful of noninvasive vagus nerve stimulation devices available. While not yet mainstream in the United States, these noninvasive devices have been approved in Europe for treating epilepsy, depression, and pain.

Vagus nerve stimulation may be useful for healing the gut–brain axis in non-celiac gluten sensitivity, due to its ability to downregulate stress and the inflammatory response and upregulate healing processes. Vagus nerve stimulation attenuates injury to the gut induced by lipopolysaccharides and repairs tight junctions between intestinal epithelial cells. [\(49\)](#) By reversing dysbiosis and sealing up the gut, systemic inflammation is reduced, and this in turn reduces neuroinflammation induced by gluten sensitivity. Vagus nerve stimulation has also been found to be effective in the treatment of depression and bipolar disorder, and emerging research suggests it may also benefit individuals with schizophrenia, autism, and Alzheimer’s disease [\(50, 51, 52, 53, 54\)](#); this evidence further confirms the potential of vagus nerve stimulation to repair both ends of the gut–brain axis—the intestine and the brain.