Gluten Ataxia and IMT

Meg Blanchet, M.A., L.M.T., C.H.P.

June 5, 2012

Abstract

This article focuses on the neurological condition gluten ataxia. Current research into gluten sensitivity and ataxia will be reviewed. The perspective that Integrative Manual Therapy brings to the body reveals additional causative factors to Ataxia and gluten sensitivity. The implications could open new areas of focus for research and the recognition of more effective treatment approaches.

Introduction

Gluten ataxia (i.e. GA, previously considered one type of idiopathic sporadic ataxia) is most often classified as an autoimmune disorder characterized by damage to the Purkinje fibers of the cerebellum, caused by the ingestion of gluten proteins.[1] "Typical symptoms include difficulty walking or walking with a wide gait, frequent falls, difficulty judging distances or position, visual disturbances and tremor."[2] It can also affect swallowing, speech and the coordination of the arms as well.

Although it has been postulated by a number of authors[3] that gluten may be responsible for quite a wide range of diseases, gluten ataxia is actually one of a small number of auto-immune disorders agreed upon by the majority of researchers to be the clear product of gluten consumption.[4, 5]

Given that GA is a condition that often occurs without an overt digestive component, it provides an interesting lens through which to consider the perspective offered by the application of IMT. This paper's conclusion will discuss how the positive treatment results achieved using IMT with a client suffering from gluten ataxia reflect the potential for a new understanding of gluten sensitivity in general.

Background on Gluten

Gluten is the main structural protein (gliadins) complex in wheat —including semolina, durum and spelt— with an equivalent (glutenins) in kamut, triticale, barley, rye,[6] and oats (the last included not because of its inherent gluten content, but due to the contamination which occurs as it is grown in the same fields and processed with the same machines as wheat).[7]

The awareness that gluten can have a deleterious impact on some individuals initially occurred because of Celiac Disease.[8] Although this "mal-absorption syndrome" was first identified by Dr. Samuel Gee in 1888, his analysis —which described an inability to absorb dietary fat— was accurate but incomplete. The link between diet and the accompanying symptoms was not made until the 1930's when Dr. Dicke discovered that a wheat-free diet yielded a complete remission of Celiac symptoms; [9] and in 1944, a Dutch physician noticed that the children under his care before the Nazi invasion, who had been suffering from bloating, diarrhea, stomach cramping and fatigue, improved when bread became unavailable.[10]

It was not until the 1960s, when an implement was created to take biopsies from the small intestine, that Celiac was redefined as a condition that "required intestinal damage, verified by a biopsy, which improves after excluding gluten."[11]

In 1994, it was projected that 1 in 10,000 people would be diagnosed with Celiac disease.[12] In 2007, Dr. Alessio Fasano, a gastroenterologist, researcher and pediatrician from the University of Maryland, commented on the current rate of Celiac in the United States:

> "The incidence of celiac disease is rising sharply— and not just due to greater awareness. Tests comparing old blood samples to recent ones show the rate has increased four-fold in the last 50 years, to at least 1 in 133 Americans."[13]

And in The Gluten Connection, Shari Lieberman, PhD says that:

> "The gluten problem touches far more of the US population than the 1 out of 133 who have celiac disease. Some researchers now speculate that as many as 29%, almost 3 out of 10 people, are gluten sensitive (GS). And approximately 81 % have a genetic predisposition toward gluten sensitivity."[14]

Regarding how and why people react to gluten, there are differing discussions in the literature. Although the words allergy and sensitivity/intolerance are often used interchangeably, there is a large difference between the two. Lieberman clarifies the difference between food allergies and food sensitivities:

In an allergic reaction, the body produces a food-specific antibody called immunoglobulin E (IgE) that attaches to the food in an attempt to destroy it, while the other side of the antibody attaches to a (immune system) mast cell, thereby producing an acute histamine reaction. [15] Allergic responses are generally strong and short lived, depending on their severity.

> "Aside from anaphylaxis, which is violent and must be counteracted quickly to avoid death, the effects of an allergic reaction are not long-term."[16]

With allergies, the only way to avoid a reaction is to avoid the substance, but the reaction, if caught in time, can generally be treated.[17]

Because food intolerances, or food immune reactivity (FIR) stimulate symptoms that can be delayed by hours to days, the cause(s) can be difficult to identify. The antibodies[18] produced by FIR do not produce a histamine response, and depending on the individual, symptoms can take any number of forms.[19]

> "According to Mäki, gluten intolerance may often be symptom-free, and people may be unaware that they have the condition if their symptoms are mild or atypical. Three out of four people with gluten intolerance have not been diagnosed, which also means that they are as yet going without treatment.
>
> "Mäki's research team has concluded that the criteria for diagnosing gluten intolerance must be rewritten, since early stages of the condition do not meet the criteria, yet is important to treat. The current criteria for diagnosis focus on damage to the intestinal villi and the small intestine, established in a tissue sample

> from the small intestine. However, early stages of gluten intolerance are not identifiable from tissue samples." [20]
>
> "The broadened definition that many of these scientists are now advocating also includes routinely testing all patients for certain 'genetic markers,' such as human leukocyte antigen (HLA) markers; these are proteins found on the surface of our white blood cells that help identify susceptibility to dietary gluten."[21]
>
> "HLA are associated with the progression of infectious diseases and the susceptibility to an incredibly wide range of chronic, noninfectious diseases, including celiac disease."[22]

Lieberman postulates that Celiac Disease is not a separate condition from gluten intolerance, but that the flattening of the villi in the small intestine is actually the end result of gluten intolerance that has gone unattended. Due to the insidious nature of this kind of sensitivity, Lieberman says the source of symptoms can go undetected for years, causing chronic inflammation which can lead to severe tissue damage, permanent organ damage and/or a hyper-activated immune system. Unlike the case with food allergies:

> "In gluten sensitivity, no medications alleviate symptoms. The only treatment is to eliminate all gluten from your diet— for life."[23]

Joseph A Murray, a gastroenterologist at the Mayo Clinic in Rochester, MN, points out that the source of reactivity to gluten is not just a genetic predisposition but that the dramatic rise in gluten-related conditions may be a phenomenon being caused by actual changes in our food.

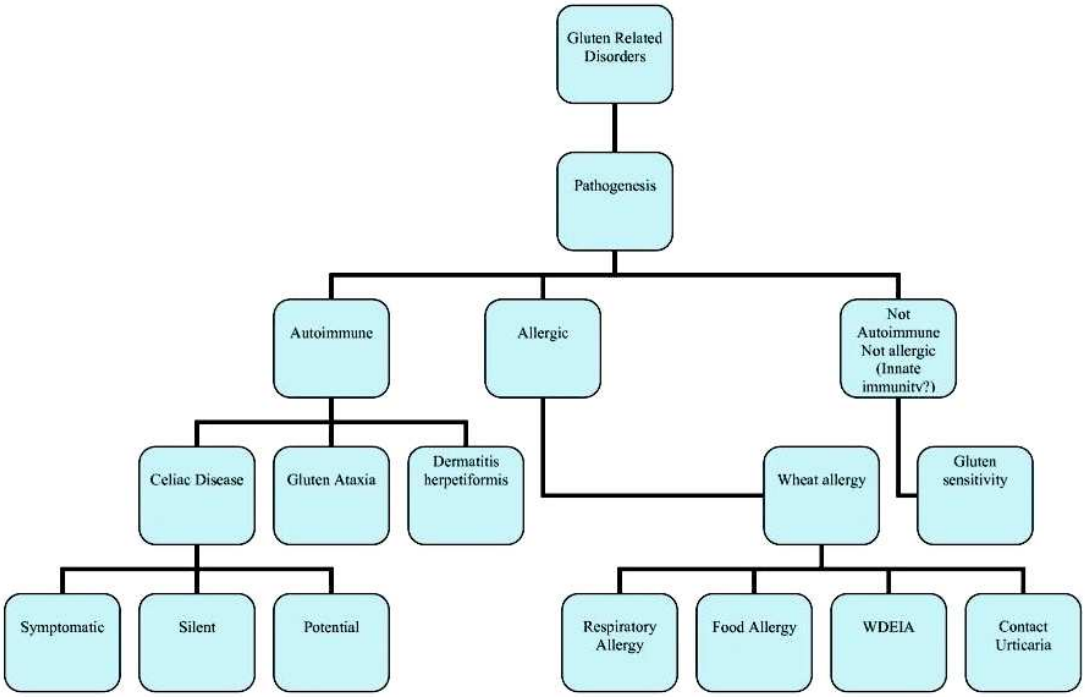
> "People aren't born with this. Something triggers it and with this dramatic rise in all ages, it must be something pervasive in the environment. One possible culprit: agricultural changes to wheat that have boosted its protein content. ...It's also being diagnosed in people as old as 70 who've eaten gluten safely all their lives."[24]

I would submit that the hybridization of gluten grains on the basis of commercial characteristics as opposed to nutrition could very well be an important factor in what is becoming a common and insidious contribution to the rise in gluten-related conditions around the world.

Gluten Ataxia

In the BioMed paper, Spectrum of Gluten-related Disorders: Consensus on New Nomenclature and Classification, a panel of 15 experts reached the consensus that the impact of gluten involves three categories: autoimmune, [25] allergic and "gluten sensitivity."

Spectrum: Figure 1. [26]



Classifying Ataxia as an autoimmune disease, they state:

> "There is evidence to suggest that there is antibody cross-reactivity between antigenic epitopes on Purkinje cells and gluten proteins." [27]

The identification of the specific neurological structures involved, and the term "gluten ataxia," were derived from the results of a 1998 research study by Dr. M. Hadjivassiliou involving 28 subjects with GA. Upon the death of two of the subjects, autopsies performed yielded specific anatomical information.

> "Gluten sensitivity is an important cause of apparently idiopathic ataxia, and may be progressive. The ataxia is a result of immunological damage to the cerebellum, to the posterior columns of the spinal cord, and to peripheral nerves. We propose the term Gluten Ataxia to describe this disorder." [28]

Referring to GA as a dysfunction of a hyper-activated immune system, Lieberman offers an alternative possibility:

> "Gluten may also cause the production of antibodies that affect the balance of inhibitory and excitatory neurotransmitters in the central nervous system, resulting in symptoms of ataxia and neuropathy."[29]

Although there are differing viewpoints as to the exact mechanism of the ataxia disease process, the majority of the researchers agree that gluten is a causative factor in at least 41% of the cases of idiopathic sporadic ataxia.[30] Furthermore, it is thought that the damage can be irreversible, and that prevention thru a gluten-free diet (GFD) is the key:

> "The response to treatment with a GFD depends on the duration of the ataxia prior to the diagnosis of GS. Loss of Purkinje cells in the cerebellum, the end result of prolonged gluten exposure in patients with GA, is irreversible and prompt treatment is more likely to result in improvement or stabilization of the ataxia."[31]

In the April 2012 International Journal of Neuroscience, Ghazal speaks definitively about the importance of gluten and a GFD as the mechanism for creating improvement:

> "Gluten Ataxia is a known cause of sporadic ataxia… Gluten Ataxia should be considered in all patients with sporadic ataxia with or without abdominal symptoms, as early diagnosis and treatment may result in neurological improvement."[32]

At present the majority of researchers agree that gluten is the cause of GA, and a contributor to multiple other conditions (although the medical community seems to be much slower at making use of these findings... but that is a discussion unto itself.) The mechanism for how gluten can be causing disease processes in independent areas as diverse as the skin, digestive system and nervous system is a thought provoking question.

Implications of Integrative Manual Therapy

The improvements that occurred with a client with gait dysfunction offer food for thought in terms of further investigation into how gluten contributes to GA and to disease processes in general.

My client's presenting problems were a restricted gait pattern with balance issues, incontinence, and discomfort in the prostate area. The most significant pretreatment measurements were:

1) His left leg measured minus 10 degrees dorsiflexion, causing his left knee to be pushed posterior and restricting his ability to take a full stride. Although both strides were restricted, the left was much more so.

2) The range of motion of his right hip was quite restricted, with flexion measuring 45 degrees.

Using Integrative Manual Therapy diagnostic tools to "map" the energetics on the three anatomical planes, the cecum area was identified as the highest priority area for treatment. Using energetic IMT techniques, the cecum and the exudate that was flowing from it were treated.[33]

No bio-mechanical work was done to treat the client's range of motion, yet, post-treatment assessment reflected noticeably improved dorsiflexion, and right hip flexion had improved by 30 degrees. The client commented that walking was easier and his balance was improved and, due to improvement of his dorsiflexion, he had a longer, more even stride.

Conclusion

In the ataxia research, references were generally limited to biochemistry and the impact on the brain.[34] At times there was mention as to whether there were Celiac symptoms.

The implications of being successful at improving gait and balance by working with exudate and the cecum creates a new context for thinking about GS and ataxia, especially given IMT's understanding that the cecum is the primary site compromised by gluten. If, in fact, gluten is causing the cecum to lose integrity and to leak exudate into the pelvic bowl, this could help to explain why so many conditions are purported to be sensitive to the ingestion of gluten.[35]

How could there be full function of the contents of the pelvic bowl if the organs, nerves and blood vessels residing there are being exposed to toxic exudate? (It is of note that this is also congruent in the case of my client whose other symptoms included incontinence and issues with his prostate.) Imagine the implications if exudate travels more widely around the body and exposes diverse structures! This is one way of conceiving how gluten could be having such a profound effect on so many different systems of the body.

My intention here is to suggest the potential benefit of widening the lens of research in regard to the mechanism of gluten's impact. Further study into the role of the cecum in conditions involving gluten has the potential to yield dramatic results. A case study using IMT to assess and treat a larger pool of GA patients could demonstrate that a GFD is not the only means of improvement. (Given Lieberman's theory about the role of neurotransmitters and ataxia, the inclusion of IMT's work with neurotransmitters might be productive in lessening other symptoms as well.) Although a GFD is clearly important with ataxia, Integrative Manual Therapy has the potential to offer breakthroughs in the treatment of in those suffering with gluten ataxia.

Footnotes

1 American Academy Of Neurology. Sensitivity To Gluten May Result In Neurological Dysfunction; Independent Of Symptoms. Science Daily. http://www.sciencedaily.com/releases/2002/04/020424073708.htm.

"Study results show that patients with gluten ataxia have antibodies against Purkinje cells. Antibodies against gluten (antigliadin antibodies) have also been found to cross-react with Purkinje cells." (Hadjivassiliou M.)

2 Boyd, C. Gluten Attack: Ataxia, A Controversial Call. Living Without. http://www.livingwithout.com/issues/4_12/ataxia-2366-1.html?pg=2. Published February/March, 2011.

3 Braly J, Hoggan R. *Dangerous Grains: Why Gluten Cereal Grains May Be Hazardous To Your Health.*

Lieberman, S. *The Gluten Connection: How Gluten Sensitivity May Be Sabotaging Your Health– and What You Can Do to Take Control Now.*

Hernandez-Lahoz C, Mauri-Capdevila G, Vega-Villar H, et al. Neurological Disorders Associated with Gluten Sensitivity. http://www.ncbi.nlm.nih.gov/pubmed/21796607. *Revista de Neurologia*. Published Sept. 1, 2011.

4 Sapone A, Bai JC, Ciacci C, et al. Spectrum of gluten-related disorders: consensus on new nomenclature and classification. *BMC Medicine.* 2012; 10:13.

Celiac Disease (digestive) and Dermatitis Herpetiformis (skin) are identified as the other two gluten-caused autoimmune disorders.

5. Gluten Ataxia. http://lifeischange.wordpress.com/2011/04/12/gluten-ataxia. Life is Change blog. Published April 12, 2011.

"Different organs can be affected by different types of gluten sensitivity. In celiac disease, sometimes called gluten-sensitive enteropathy, the small bowel is affected. In dermatitis herpetiformis, the skin is targeted, resulting in an itchy rash. With gluten ataxia, damage takes place in the cerebellum, the balance center of the brain that controls coordination and complex movements like walking, speaking and swallowing."

6 Sapone A, Bai JC, Ciacci C, et al.

7 Lieberman, S., p. xviii.

8 Wikipedia. Coeliac disease. http://en.wikipedia.org/wiki/Coeliac_disease.

Explanation of Celiac: "Upon exposure to gliadin, and specifically to three peptides found in prolamins, the enzyme tissue transglutaminase modifies the protein, and the immune system cross-reacts with the small-bowel tissue, causing an inflammatory reaction. That leads to a

truncating of the villi lining the small intestine (called villous atrophy). This interferes with the absorption of nutrients, because the intestinal villi are responsible for absorption. The only known effective treatment is a lifelong gluten-free diet."

9 Braly J, Hoggan R., p. 11.

10 Lieberman, S., p. x.

11 Braly J, Hoggan R., p. 12.

Dr. Braly believes that this focus on mal-absorption and the necessity of intestinal damage is overly narrow, and means that those who are looking fairly healthy who also have celiac or GS get overlooked.

12 Lapid, Nancy. The Celiac Disease Diagnosis Rate. About.com
http://celiacdisease.about.com/od/diagnosingceliacdisease/a/DiagnosisRate.htm
Updated April 1, 2009.

13 Beck, M. Clues to Gluten Sensitivity. Wall Street Journal: Health Journal.
http://online.wsj.com/article/SB10001424052748704893604576200393522456636.html
Published March 15, 2011.

14 Lieberman, S., p. 6.

15 Sapone A, Bai JC, Ciacci C, et al.

Using wheat allergy as an example: "WA is defined as an adverse immunologic reaction to wheat proteins. Depending on the route of allergen exposure and the underlying immunologic mechanisms, WA is classified as a classic food allergy affecting the skin, gastrointestinal tract or respiratory tract; wheat-dependent, exercise-induced anaphylaxis (WDEIA); occupational asthma (baker's asthma) And rhinitis; and contact urticaria. IgE antibodies play a central role in the pathogenesis of these diseases."

16 Ibid, p. 19

17 Ibid, p. 17.

18 Ibid, p. 19

19 Lieberman, S., p.19.

20 Suomen Akatemia (Academy of Finland). Gluten intolerance in Finland has doubled, experts say. http://www.sciencedaily.com/releases/2010/03/100305083306.htm.
Published March 5, 2010. Accessed May 24, 2012.

21 Braly J, Hoggan R., p. 14.

22 Ibid, p. 28.

23 Lieberman, S., p. 20.

24 Beck, M.

25 Hudnell, J. Gluten Ataxia: Sporadic Ataxia With Gluten Sensitivity. Yahoo Voices. http://voices.yahoo.com/gluten-ataxia-sporadic-ataxia-gluten-sensitivity-4123473.html?cat=5. Published Aug 28, 2009.

Congruent with the auto-immune viewpoint, Stephen Gislason, MD states that: "People with Gluten Ataxia often have anti-gliadin antibodies present that attack certain cells in the brain."

26 Ibid.

27 Ibid.

28 Hadjivassiliou M, Grünewald RA, Chattopadhyay AK, et al. Clinical, radiological, neurophysiological, and neuropathological characteristics of gluten ataxia. *Lancet*. Published November 14, 1998. http://www.ncbi.nlm.nih.gov/pubmed/9843103.

29 Lieberman, S., p.20.

30 Ibid, p. 32.

31 Sapone A, Bai JC, Ciacci C, et al.

32 Ghazal FA, Singh S, Yaghi S, et al. Gluten Ataxia: An Important Treatable Etiology of Sporadic Ataxia. International Journal of Neuroscience. Published May 18, 2012. http://www.ncbi.nlm.nih.gov/pubmed?term=Gluten Ataxia%3A An Important Treatable Etiology of Sporadic Ataxia

33 Definition of Exudate. MedicineNet. http://www.medterms.com/script/main/art.asp?articlekey=9900

Exudate: A fluid rich in protein and cellular elements that oozes out of blood vessels due to inflammation and is deposited in nearby tissues. The altered permeability of blood vessels permits the passage of large molecules and solid matter through their walls. The vessels seem to weep, to sweat, in keeping with the Latin "exsudare," to sweat out, from which exudate is derived.

34 Sapone A, Bai JC, Ciacci C, et al.

"There is antibody cross-reactivity between antigenic epitopes on Purkinje cells and gluten proteins. Widespread deposition of transglutaminase antibodies has been found around brain vessels in patients with GA… Antibodies against tTG6, a primarily brain-expressed transglutaminase, have been found in patients with GA."

35 Braly J, Hoggan R., p. 6.

"In fact, well over 150 medical conditions have now been reported as over-represented among gluten-sensitive individuals."

References

American Academy Of Neurology. Sensitivity To Gluten May Result In Neurological Dysfunction; Independent Of Symptoms. Science Daily. http://www.sciencedaily.com/releases/2002/04/020424073708.htm. April 24, 2002. Accessed May 7, 2012.

Beck, M. Clues to Gluten Sensitivity. Wall Street Journal: Health Journal. http://online.wsj.com/article/SB10001424052748704893604576200393522456636.html Published March 15, 2011.

Boyd, C. Gluten Attack: Ataxia, A Controversial Call. Living Without. http://www.livingwithout.com/issues/4_12/ataxia-2366-1.html?pg=2. Published February/March, 2011. Accessed May 17, 2012.

Braly J, Hoggan R. *Dangerous Grains: Why Gluten Cereal Grains May Be Hazardous To Your Health*. Penguin Putnam: New York, NY; 2002

Bürk K, Bösch S, Müller CA, et al. Sporadic cerebellar ataxia associated with gluten sensitivity. http://www.ncbi.nlm.nih.gov/pubmed/11335703. Brain. 2001 May;124(Pt 5):1013-9. PMID: 11335703 [PubMed - indexed for MEDLINE].

Caputo I,Lepretti M, Martucciello S, et al. Enzymatic Strategies to Detoxify Gluten: Implications for Celiac Disease. Enzyme Research. 2010; 2010: 174354. doi: 10.4061/2010/174354 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2963796/?tool=pmcentrez&report=abstract. PMCID: PMC2963796. Published online October 7, 2010.

Definition of Exudate. MedicineNet. http://www.medterms.com/script/main/art.asp?articlekey=9900. Accessed May 20, 2012.

Ford, RP. The gluten syndrome: a neurological disease. http://www.ncbi.nlm.nih.gov/pubmed/19406584. Medical Hypotheses. 2009 Sep;73(3):438-40. Epub 2009 Apr 29. PMID: 19406584 [PubMed - indexed for MEDLINE]

Ghazal FA, Singh S, Yaghi S, et al. Gluten Ataxia: An Important Treatable Etiology of Sporadic Ataxia. International Journal of Neuroscience. http://www.ncbi.nlm.nih.gov/pubmed?term=Gluten Ataxia%3A An Important Treatable Etiology of Sporadic Ataxia. [PubMed. PMID: 22512541. Published May 18, 2012, ahead of print.]

Gluten Ataxia. http://lifeischange.wordpress.com/2011/04/12/gluten-ataxia. Life is Change blog. Published April 12, 2011.

Griffith, J. How Gluten can affect the Brain: From Seizures and Headaches to Anxiety and Inattention. http://www.mybrainhealth.org. Presentation made to the Gluten Intolerance Group (Corte Madera), February 8, 2011.

Habek M, Hojsak I, Barun B, et al. Downbeat nystagmus, ataxia and spastic tetraparesis due to coeliac disease. http://www.ncbi.nlm.nih.gov/pubmed/21390533. Neurological Sciences. 2011 Oct;32(5):911-4. Epub 2011 Mar 10. PMID: 21390533. [PubMed - indexed for MEDLINE]

Hadjivassiliou M, Davies-Jones G, Sanders D, et al. Dietary treatment of gluten ataxia. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1738682/?tool=pmcentrez. Journal of Neurology, Neurosurgery, and Psychiatry. 2003 September; 74(9): 1221–1224. doi: 10.1136/jnnp.74.9.1221. PMCID: PMC1738682.

Hadjivassiliou M, Grünewald RA, Chattopadhyay AK, et al. Clinical, radiological, neurophysiological, and neuropathological characteristics of gluten ataxia. http://www.ncbi.nlm.nih.gov/pubmed/9843103. Lancet. 1998 Nov 14;352(9140):1582-5. PMID: 9843103. [PubMed - indexed for MEDLINE]

Hamed N, Perlman S. *Nutrition and the Patient with Progressive Central Nervous System Disease— A Manual for Patients and Their Familie*s. Self-published January, 1990. First edition revised May 7, 2009.

Hernandez-Lahoz C, Mauri-Capdevila G, Vega-Villar H, et al. Neurological Disorders Associated with Gluten Sensitivity. http://www.ncbi.nlm.nih.gov/pubmed/21796607. Revista de Neurologia. 2011 Sep 1;53(5):287-300. PMID: 21796607 [PubMed - indexed for MEDLINE; article in Spanish.]

Hudnell, J. Gluten Ataxia: Sporadic Ataxia With Gluten Sensitivity. Yahoo Voices. http://voices.yahoo.com/gluten-ataxia-sporadic-ataxia-gluten-sensitivity-4123473.html?cat=5. Published Aug 28, 2009. Accessed May 7, 2012.

Kheder A, Currie S, Romanowski C, Hadjivassiliou M. Progressive ataxia with palatal tremor due to gluten sensitivity. http://www.ncbi.nlm.nih.gov/pubmed/22252893. Movement Disorders. 2012 Jan;27(1):62-3. doi: 10.1002/mds.23987. PMID: 22252893 [PubMed- indexed for MEDLINE].

Lapid, Nancy. The Celiac Disease Diagnosis Rate. About.com. http://celiacdisease.about.com/od/diagnosingceliacdisease/a/DiagnosisRate.htm Updated April 1, 2009.

Lieberman, S. *The Gluten Connection: How Gluten Sensitivity May Be Sabotaging Your Health– And What You Can Do to Take Control Now*. Rodale Books: New York, NY; 2007

Nanri K, Shibuya M, Taguchi T, et al. Selective loss of Purkinje cells in a patient with anti-gliadin-antibody-positive autoimmune cerebellar ataxia.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3042899/?tool=pmcentrez. Diagnostic Pathology. 2011; 6: 14. PMCID: PMC3042899. doi: 10.1186/1746-1596-6-14. Published online February 4, 2011.

National Ataxia Foundation. http://www.ataxia.org.

Sapone A, Bai JC, Ciacci C, et al. Spectrum of gluten-related disorders: consensus on new nomenclature and classification. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3292448/?tool=pmcentrez. BMC Medicine. 2012; 10:13. PMCID: PMC3292448. doi: 10.1186/1741-7015-10-13. Published online February 7, 2012.

Suomen Akatemia (Academy of Finland). Gluten intolerance in Finland has doubled, experts say. ScienceDaily. http://www.sciencedaily.com/releases/2010/03/100305083306.htm. Published March 5, 2010. Accessed May 24, 2012.

Wikipedia. Coeliac disease. http://en.wikipedia.org/wiki/Coeliac_disease. Updated June 4, 2012.

Wikipedia. Gluten-sensitive Idiopathic Neuropathies. http://en.wikipedia.org/wiki/Gluten-sensitive_idiopathic_neuropathies. Updated March 28, 2012.

Wikipedia. Human Leukocyte Antigen. http://en.wikipedia.org/wiki/Human_leukocyte_antigen. Updated May 20, 2012.