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Efficacy of a Gluten Free Diet to Help Relieve Migraines in Chronic Migraine Patients

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Efficacy of a gluten free diet to help relieve migraines in chronic migraine patients: A case series

By

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When examining the world population, approximately 11% of people experience migraines. A chronic migraine is classified as a headache that occurs on a frequent basis in which the pain is quick to occur unilaterally, and is a throb that is considered a moderate to intense level of pain. It is believed that a migraine brain is intensely sensitive to deviations from homeostasis. This case series research investigated the effect of a gluten-free diet on individuals with chronic migraines. Participants completed a five-month study consisting of dietary and physical measurements, recording migraines, and a gluten-free diet with a re-introduction period. In conclusion, the results were difficult to determine due to various limitations. This study appeared to have the most effect on one participant by reducing his migraines from 10 to 3 per month. More research is necessary to determine the efficacy of a gluten-free diet to help alleviate migraines.

Keywords: migraines, gluten-free diet

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CHAPTER I

INTRODUCTION

Migraines

When examining the world population, it has been discovered that approximately 11% of people experience migraines. In the United States, this consists of approximately 17.6% of females and 5.6% of males. A migraine is classified as a headache that occurs on a frequent basis in which the pain is quick to occur, is unilateral, and includes a throb that is considered to be a moderate to intense level of pain (Rockett et al., 2012b). Studies conducted in the United States have estimated the cost of diagnosing and treating migraines to be 1 billion dollars per year. Indirectly, when considering employers and businesses, it can cost 13 billion dollars per year collectively due to missed work time and lost productivity because of migraines (Semenov, 2015). Migraines are considered to be the seventh highest disabler because of the impact on a person's quality of life (Charles, 2017; Semenov, 2015). The International Headache Society (2018) reports that migraines are ranked as the third most prevalent disorder in the world (Headache Classification Committee of IHS, 2018).

There are many symptoms that migraines produce, and the duration of the migraines can occur anywhere between 4-72 hours (Rockett et al., 2012b). People suffering from migraines can exhibit symptoms such as photophobia, sonophobia, osmophobia, allodynia, nausea, and vomiting (Burstein, Noseda & Boorsook, 2015;

Charles, 2017). Researchers have concluded that a brain suffering from migraines is different from a normal, non-migraine afflicted brain. It is believed that a migraine afflicted brain is intensely sensitive when it deviates from homeostasis. The hypothalamus regulates the various systems within the body to keep levels at homeostasis. When homeostasis is disturbed, it is believed that the hypothalamic neurons are where the migraine may originate (Burstein et al., 2015).

The exact etiology of migraines is still under investigation (Martin & Seaman, 2015). Sometimes migraines can occur instantaneously, while at other times they can be preceded by prodromes. Auras can occur prior to the prodromes and the migraine attack. There are two proposals as to how prodromes and migraines develop which will be discussed later.

Gluten

Gluten is the protein that is the remaining sticky mass that occurs after washing wheat flour with water. This protein gives excellent baking properties that creates fluffy breads and cakes that will adhere together and not crumble upon touching (Ford, 2009). This capability is due to its ability to be heat stable, and not only does it create the elasticity, but also helps products retain moisture and flavor (Biesiekierski, 2017). Gluten can be broken down into hundreds of parts, but the main focus is on these two proteins: gliadin and glutenin. Gliadin is the protein within the gluten that creates the autoimmune response in a susceptible individual. There are four major groups that make up the single chain polypeptide, gliadin: α-gliadin, β-gliadin, γ-gliadin, and ω-gliadin. It is not unusual to see both, α-gliadin and β-gliadin, referred to as α-gliadin because they are similar. Gliadin is the protein that allows the gluten to adhere to other items in the products and

provides the capability for the product to elongate and not immediately break off. The glutenin gives the elastic nature to products as well as the strength within the flexibility (Balakireva & Zamyatnin Jr., 2016).

Gluten can appear in a variety of food items, it is not exclusive to baked goods. It is most well-known to be found in wheat, barley and rye. However, it can also be found in derivatives of wheat like wheatberries, semolina, farina, and farro. Common whole food items that contain gluten would include pastas, breads, cereals, breakfast items like pancakes, sauces and gravies, and beer. An individual in need of eating gluten-free must also be aware of items that are seemingly gluten-free until one discovers the process by which the food item is prepared. Using French fries as an example, potatoes are gluten free; however, it is common for fries to be coated with a type of wheat flour before frying. In addition, the fries could come into cross-contamination via the oil used in the fryers that were also used for breaded, gluten-containing products ("Sources of Gluten").

Gluten Related Disorders

When gluten creates a response from the body, it can manifest itself via three major types of gluten related disorders (GRD): celiac disease (CD), non-celiac gluten sensitivity (NCGS), and wheat allergy (Balakireva & Zamyatnin Jr., 2016; Biesiekierski, 2017).

Celiac Disease

CD is genetic and an autoimmune disorder that is characterized by small bowel enteropathy when exposed to gluten (Leccioli, Oliveri, Romeo, Berretta, & Rossi, 2017; Zi, Julian & Hadjivassilious, 2018). Currently, it is known to affect 1% of the Western

world (Balakireva & Zamyatnin Jr., 2016; Biesiekierski, 2017). This disorder is clinically recognized by malabsorption, which can be shown by chronic diarrhea, abdominal pain, bloating, flatulence, and distension, iron-deficiency anemia, osteoporosis, and fatigue (Biesiekierski & Iven, 2015). Those with CD not only have GI symptoms, but often exhibit extraintestinal symptoms such as dermatitis herpetiformis or gluten ataxia (Balakireva & Zamyatnin Jr., 2016). This reaction occurs in the gastrointestinal tract by creating inflammation of the lining, atrophy of the villi, and increases the individual's gut permeability. Those that have active, latent, or dormant CD will carry the HLA-DQ2 or DQ8 genetic codes (Balakireva & Zamyatnin Jr., 2016; Biesiekierski, 2017). A gluten-free diet (GFD) is currently the only treatment.

Wheat Allergy

Wheat allergy is an immune response not only to wheat but also can react to other proteins within wheat. The immune response is due to the IgE mediated response against the different components within wheat, especially the gliadin protein. These individuals can have skin reactions, rashes or swelling, or anaphylaxis within minutes or hours of ingestion (Biesiekierski, 2017; Nijeboer et al., 2013).

Non-Celiac Gluten Sensitivity

The first documented cases of NCGS were written by Ellis and Linaker in 1978. In 1980, Cooper and colleagues documented on cases where the patients responded to a gluten free diet, but did not have CD (Leccioli et al., 2017). The first name for this category was "gluten sensitivity" which was given in 2011 (Czaja-Bulsa, 2015).

However, when the International Expert Meeting on GRD commenced in 2012, the name was finalized as “non-celiac gluten sensitivity” (Czaja-Bulsa, 2015; Leccioli et al., 2017).

NCGS is often confused with irritable bowel syndrome because of the similarity of symptoms such as abdominal pain, bloating, flatulence, and bowel habit abnormalities (Balakireva & Zamyatnin Jr., 2016; Nijeboer et al., 2013). Individuals can also display extra-intestinal symptoms, such as, “brain fog”, fatigue, tingling and/or numbness in hands and feet, musculoskeletal pain, and headache. It is possible for those with NCGS to have neurological involvement as well as psychiatric issues (Ford, 2009; Hadjvassiliou at al., 2006; Nijebeor, Bontkes, Mulder, & Bouna, 2013; Losurdo et al., 2018). Headaches in individuals with NCGS is a common finding, however, there is little research investigating the association (Losurdo et al., 2018). Leccioli et al. (2017) defined NCGS as, “a condition in which symptoms are triggered by gluten ingestion, in the absence of celiac-specific antibodies and of classical celiac villous atrophy, with variable Human Leukocyte Antigen (HLA) status and variable presence of first generation anti-gliadin antibodies (AGA)” (Leccioli et al., 2017). The HLA-DQ2/DQ8 isoforms can be found in approximately 50% of the NCGS population, approximately 30% of the general population also has the DQ2/DQ8 status (Balakireva & Zamyatnin Jr., 2016; Leccioli et al., 2017). However, it is difficult to diagnose NCGS since there are no biomarkers for this condition. It is recommended that a diagnosis can be made after evaluating symptoms, excluding CD and WA, and conducting a double-blind placebo-controlled gluten challenge. If there is improvement during the elimination of gluten from the diet, then a diagnosis could be made. Some studies (Leccioli et al., 2017) observed that when an individual goes through a gluten re-challenge as a NCGS candidate, they are then re-

classified as a CD patient. Since there are no biomarkers and flux of self-diagnosis, it is difficult to assess the prevalence. It appears that NCGS is more common in females and young to middle age adults, and may range between 0.6-6.0% (Leccioli et al., 2017).

Pathogenic mechanisms are unknown for this disease. In result, there are some hypotheses as to the potential triggers of this disease. There is some early evidence concerning wheat lectin agglutinin and the potential effect it could have on intestinal permeability and activation of the immune system (Biesiekierski & Iven, 2015). Fermentable olio-, di, monosaccharides and polyols (FODMAPs) are also being investigated as a potential trigger by some researchers and others think that these compounds could be elements to exacerbate issues in the gut that have been created by another factor. Wheat α-amylase trypsin inhibitors (ATIs) are another component of the wheat protein that is being discussed. ATIs are part of the water soluble albumins, and when combined with globulins, they make up 10-20% of total wheat proteins. ATIs have capabilities to stimulate the immune system, specifically dendritic cells, macrophages, and monocytes. Through activation pathways, they can create a release of proinflammatory cytokines. There have been studies, in vivo, in vitro and ex vivo, conducted to determine if the ATIs or other components of the gluten causes innate inflammation. While ex vitro studies have suggested the opposite, in mice studies the pure dietary wheat gluten, without the ATIs, had no immune response (Leccioli et al., 2017).

An additional hypothesis regarding the pathways of NCGS investigate human microbiota, specifically the *Firmicutes* and *Bacteriodetes* phyla, and their influence on the integrity of the GI barrier via the manufacturing of short chain fatty acids (SCFAs).

Of the SCFAs, butyrate is a primary source for energy. The role of butyrate is to promote epithelial cell differentiation, help stimulate the mucin secretion and epithelial antimicrobial peptides, and prevent microbial translocation. When there is a low amount or absence of butyrate, the GI tissue is going to experience mucosal atrophy and coloncyte apoptosis. The thinning of the mucosal layer can increase gut permeability and give the increased possibility of microbial translocation. If gluten and ATIs were ingested, they would be able to bind to toll-like receptors (TLRs), which are important in the innate immune system, and create that inflammatory response in parts of the body, other than the gut. This could explain the extra-intestinal manifestations, like headaches, that are exhibited by NCGS individuals (Leccioli et al., 2017).

This case series research study is focused specifically on individuals that could fall into this population.

Migraine caused from gluten

The autonomic nervous system (ANS) regulates the sympathetic and parasympathetic nervous systems. Their pathways are driven by neurotransmitters. The regulation of the gut is driven by the ANS, as well as the cardiovascular system, uterus, bladder, and glands. Thus, if gluten is ingested by an individual sensitive to it, it creates damage to the nerve endings, which in turn, damages the balance between the parasympathetic system and the sympathetic system. It generates a gluten sensitivity not focused on gut damage, but neurological dysfunction instead (Ford, 2009).

The explanation of why there are extra-intestinal manifestations are unclear and in need of more research. Theories are debating if these extra-intestinal manifestations are occurring due to a leak in the blood brain barrier, and antibodies are able to cross over

and react with brain antigens (Hadjivassiliou et al., 2010). If the hypothesis regarding the thinning of the mucosal lay of the GI tract, which allows permeability and inflammatory molecules to escape the digestive system and go into the bloodstream. These circulating antigens are able to bind to TLRs that will initiate the immune response outside of the intestinal tract. It could give an argument as to why the reaction to gluten is not solely GI, but also extra-intestinal. (Leccioli et al., 2017).

Zioudrou, Streaty, and Klee (1979) evaluated peptides in the body and the potential role of the alternative source from gluten and its part in extra-intestinal symptoms. Dietary protein is an alternate source of peptides, and wheat gluten is made up of dietary proteins. The dietary proteins this paper is examining are gliadin and glutenin. Zioudrou et al. (1979) compare peptide activity in the brain similar to opioids and being able to connect with opioid receptors in the brain. The peptides are broken into two parts, the endorphins and enkephalins. If the peptide source is provided by gluten, then they are called exorphins since they are of exogenous origin. They concluded, "In order for exorphins to function as opioid peptides in the central nervous system in vivo they must: (a) be produced in the gastrointestinal tract, (b) survive degradation by intestinal proteases, (c) be absorbed, without degradation, into the blood stream, (d) cross the blood-brain barrier and thereby reach central opiate receptors, (e) interact as opiates with these receptors" (Zioudrou, Streaty & Klee, 1979). More recently, Liu & Udenigwe (2019) discussed the opioid-like activities of gluten exorphins and the influence opioid peptides can have on regulatory functions within the central nervous system and the gastrointestinal system. They link the potential for the gluten exorphins to have an affect, in genetically susceptible individuals, on gut permeability (Liu & Udenigwe, 2019),

which gluten's potential role in gut permeability has been discussed in detail previously. Research in this area is lacking a full explanation as how exactly gluten is causing extra-intestinal symptoms, which include headaches.

In this case series research study, individuals with chronic migraines were asked to participant in a gluten-free diet to determine if it could help reduce or completely relieve their migraines. The main purpose of this case series study was to determine the efficacy of a GFD on each individual. The secondary aim was to evaluate if consuming a GFD had a positive impact on body composition, blood pressure and glucose levels in each individual. The last aim was to determine if there was a level of gluten that an individual could tolerate before inducing a migraine.

CHAPTER II

LITERATURE REVIEW

Migraines

According to Bunner, Agarwal, Gonzales, Valente, and Barnard (2014), in America, migraines can affect all ages collectively affecting more than 28 million individuals (Bunner, Agarwal, Gonzales, Valente, & Barnard, 2014). Headaches and migraines can be classified in multiple categories, and a migraineur's headaches can often fall into more than one category. For the purposes of this study, the intent was to look for individuals with chronic migraines. The definition of a chronic migraine consists of an individual that has had headaches lasting at least 15 days of the month, and eight of those headaches must qualify as migraines. Within the chronic migraine umbrella, there can be migraines with and without auras. Auras are a transient focal neurological symptom that can occur prior to a migraine or can occur periodically during a migraine. The symptoms can consist of fully reversible visual, sensory, speech and/or language, motor, brainstem, and retinal symptoms. Visual auras are the most common, occurring in 90% of individuals and the second most common involve the sensory issues. Auras will be described in further detail later (Headache Classification Committee of HIS, 2018).

Migraines can also occur without auras, which is the most common type of migraine. Menstrual migraines fall under this category. Prodromes are not unusual to occur a few hours to a day before the migraine attacks, and individuals may experience

postdromal effects once the migraine is gone. As previously mentioned, migraines without auras can exhibit symptoms involving fatigue, neck stiffness, sensitivity to light and/or sound, nausea, difficulty concentrating, blurred vision, excessive yawning, and pallor (Headache Classification Committee of HIS, 2018).

Research has shown that there are a wide variety of triggers for migraines. Overall, triggers typically come from environmental, hormonal or dietary factors. Environmental triggers could include sleep disorder, stress levels, or strong odors; examples of hormonal triggers can be related to one's menstrual cycle, pregnancy, or menopause. Diet contributions could come from any number of food sources (Özön, Karadaş, & Özge, 2018). The onset of a migraine could occur within 48 hours of the introduction of these factors (Rockett et al., 2012a).

Bunner et al. (2014) conducted a study looking into the efficacy of a low fat, high fiber vegan diet as well as an elimination diet on menstrual migraines. Of the many food items that were part of the elimination diet, wheat, barley, and rye were all included. Evidence suggests that migraines are associated with neurogenic inflammation and neurogenic vasodilation. A vegan diet can be high in anti-inflammatory foods since many plant-based foods are high in antioxidants and anti-inflammatory composites. A limitation with the study was the difficulty to discern the effect of the vegan diet versus the elimination diet. At the conclusion, 35 out of 40 participants felt improvement after the vegan diet period, however, 20 out of 40 additional participants also reported feeling better after the placebo supplement. Those that felt better from the diet period indicated that there was a significant decrease in headache intensity, duration and the number of headaches that required medication (Bunner et al., 2014).

There are a couple of proposals considered in regard to the origins of a migraine, including their prodromes. The full pathogenesis has yet to be fully discovered and understood; however, there is evidence to suggest that inflammation of the meninges may be a contributor as will be demonstrated in the first proposal presented. The first explanation suggests that due to the hypothalamus' important role in regard to maintaining homeostasis, it is in the position to regulate the parasympathetic and sympathetic neurons that are currently firing. Within the superior salivatory nucleus, the pre-ganglionic parasympathetic neurons are firing, and in the spinal intermediolateral nucleus, the sympathetic pre-ganglionic neurons fire. The super salivatory nucleus is capable of stimulating the release of acetylcholine, vasoactive intestinal peptide, and nitric oxide from the meningeal terminals. This release occurs in the sphenopalatine ganglion. The results of this release create a dilation of intracranial blood vessels, plasma protein extravasation, and a local release of inflammatory molecules. These inflammatory molecules have the capacity to activate the meningeal nociceptors. Furthermore, the meningeal blood vessels are densely innervated by the parasympathetic fibers. The activation of this stimulation release within the sphenopalatine ganglion will initiate the activation of the meningeal receptors. These receptors solidify the change of homeostasis to the predominance of the parasympathetic tone, resulting in the development of a migraine. However, if the sphenopalatine ganglion is blocked, which can happen with certain migraine medications, there will not be a release of the meningeal nociceptors and the migraine will either be partially or fully blocked (Burstein et al., 2015; Gooriah, Mimeri, & Ahmed, 2015).

Essentially, when there are physiological and emotional changes in the body's homeostasis, the hypothalamic neurons will respond and activate the meningeal nociceptors because of an altering in homeostasis between the parasympathetic and sympathetic tones for the meninges. This alteration creates a tone of sympathetic dominance (Burstein et al., 2015; Gooriah et al., 2015).

The second proposal suggests the brainstem neurons and hypothalamic neurons have direct input to the trigeminothalamic neurons that are within the sensory thalamic nuclei. These neurotransmitters (noradrenaline, serotonin; and dopamine, histamine, orexin, and melanin concentrated hormone) within the neurons can influence the activity level of thalamic neurons. There are two activity modes: burst to tonic, which is excitatory, and tonic to burst, which is inhibitory. The brainstem and hypothalamic neurons are able to create the high and low set points of the allostatic load by creating these two modes. However, there can be opposing factors that affect the rate of firing from the trigeminovascular neurons where these modes may be disregarded. This effect on the firing relay of these neurons would be the cause behind the inconsistencies of migraine triggers. When the allostatic load is concurrent with the right phase of the circadian rhythm, the hypothalamic and thalamic neurons; the triggers for a migraine occurs. Essentially, the hypothalamus and brain stem both regulate the system when there is a deviation from homeostasis, physiological or emotional. In response, they can transmit more nociceptive trigeminovascular signals from the thalamus to the cortex by lowering the level at which the signal will begin to send. The further the threshold is decreased, the earlier signals for pain can transmit and induce a migraine (Burstein et al., 2015; Gooriah et al., 2015).

The etiology of auras that accompany migraines is also still under investigation. An aura is an attack of neurological symptoms. They can be of a visual, sensory, or speech nature. Individuals that experience auras prior to a migraine can exhibit vertigo, diplopia, allodynia, syncope, or hemiparesis. Auras typically last between five minutes to one hour (Burstein et al., 2015; Charles, 2017; Corbelli et al., 2012; Martin & Seaman, 2015).

It is believed that cortical spreading depression is the origin of an aura. It is a slow wave of cortical neurons that first go through a depolarization stage, followed by hyperpolarization. The hyperpolarization inhibits, so the threshold for stimulus increases. The delayed activation of the trigeminal pathway leads to the migraine. The trigeminovascular pathways are activated which prompts the pulsing throb due to the neuron sensitization. It spreads to the spinal trigeminal nucleus which creates scalp hypersensitivity. It continues to advance to the thymus that can create extracephalic hypersensitivity. The extreme sensitivities to homeostatic changes are because of the molecular, anatomical, and functional abnormalities. The abnormalities make it difficult for the body to adapt to the fluctuations that induce and increase the amount of migraines. When allodynia occurs, it is signaling a lower threshold for trigeminovascular sensitization that leads to more migraines (Burstein, et al. 2015; Gooriah et al., 2015).

Gluten

Gluten makes up the greatest amount of the protein within a single wheat kernel. Each kernel can vary according to composition, the protein can be from 7% to 22% protein, and within that percentage 85% to 90% of that composition is gluten. The remaining protein is composed of albumin/globulin. Gluten can be broken down into

hundreds of similar proteins; however, monomeric gliadins and polymeric glutenins are the main focus (Biesiekierski, 2017; Nijeboer et al., 2013). The human gastrointestinal system has difficulty digesting gliadin when there are loose junctions within the gastrointestinal (GI) tract, for example, in celiac patients. Zonulin is an intestinal peptide that is an important factor when it comes to tight junction regulation in the GI tract. It is believed that zonulin is at least partially to blame in increased permeability that can develop in the gut. Glutamine and proline-rich gluten enter the gut but are only partially hydrolyzed by the proteases. Then if there is a gap in the junctions, these partially hydrolyzed components of gluten approach the lamina propria via either transcellular or paracellular transport. During transport, tissue transglutaminase (tTG) modifies these proteins, by deamination or transamination, which allows them to become toxic and immunogenic to patients with the isomers of Human Leukocyte Antigen (HLA)-DQ2 or DQ8. The immune response is developed due the DQ molecule finding the deaminated proteins on dendritic cells and presents the proteins to the T cells. This immune response could be innate or adaptive, which is T cell mediated. The adaptive immune response can cause a cascade of events, starting with intestinal inflammation which then builds to atrophy of the intestinal villi, crypt hyperplasia, an increase of infiltration by intraepithelial lymphocytes, weight loss, and chronic diarrhea (Balakireva & Iven, 2018).

Gliadins are broken down into three separate groups. Furthermore, within a single gliadin, there are 50 or more peptide sequences, also known as epitopes, that create the gut-permeating capabilities as well as immunomodulatory and cytotoxic actions. These events create an inability of the gut to fully digest the proteins. Gliadins are comprised of glutamine, prolines, and other amino acids. This genetic makeup is the

cause for difficult digestion (Biesiekierski, 2017; Nijeboer et al., 2013). Gliadin proteins are able to covalently bond with tTG and create new epitopes that are able to trigger the immune response (Balakireva & Iven, 2018).

There was a single case study documented by Pascual and Leno (Pascua & Leno, 2005) regarding a woman with daily headaches lasting 12-24 hours with throbbing, light and sound sensitivity, as well as nausea and vomiting. Over the course of 14 months, the patient was seen by her primary care physician and then neurologists to determine the root cause. It was discovered that the daily consumption of a specific wheat biscuit every morning was causing these daily attacks. It was concluded that dietary factors are a crucial element when determining cause of migraines (Pascua & Leno, 2005).

There have been larger studies observing gluten and other foods containing IgG antibodies that may be a migraine trigger (Alpay et al., 2010). Evidence is supporting the idea that prophylactic medication cannot be the sole solution for migraines as there are too many lifestyle factors that have a role in migraine causation. To help gain true relief from a migraine, an individual is going to need to make lifestyle changes whether it is sleep, exercise, stress, diet, etc. (Rockett et al., 2012a).

Alpay et al. (2010) performed a double-blind, randomized, cross-over, controlled clinical trial with 30 patients with headaches. The patients kept record of their headache frequency, number of days, duration, severity, and medication usage during the course of the study. There were three phases within the study that started at a baseline diet, then to a provocation diet and elimination diet for the two groups. The provocation diet consisted of foods that had been enzyme linked immunosorbent assay (ELISA) tested to be IgG positive and negative to create a balanced diet. The elimination diet consisted of only

foods that were IgG negative. Gluten and wheat fell under their "food additives" category of which there were 21 patients that tested positive. It was determined that when both groups went through the elimination diet period, the results were statistically significant regarding the decrease of the number of headache days and how many headaches the patients had. It also showed a decrease in the number of headaches needing acute medication as well as a decrease of medication usage overall. It did not appear to affect the severity or duration of the headaches (Alpay et al., 2010).

There have been other similar research studies examining migraine patients, recording their migraines and all the aspects associated, and putting them on a varied diet. Özön et al. (2018) split the 50 participants into two groups. When testing for trigger sensitivity of gluten, group 1 had 52% test positive and group 2 had 56% positive. Gluten was considered to be the highest trigger. Their findings showed that the frequency and severity of headaches were affected by which diet patients were put on for the month, and those categories had statistically significant lower results for the months where the groups had to consume the elimination diet. The researchers also found that the patients tended to have more than one trigger for their headaches (Özön, Karadaş, & Özge, 2018).

Rockett et al. (2012a) studied migraine patients, their frequency of migraines, and if they were consistently related to a specific trigger. The researchers found that caffeine, Chinese food, chocolate, ice cream, cheese, colas, teas, and milk were the most commonly found triggers. While majority of those items do not contain gluten, it is probable that the Chinese food would contain gluten due to soy sauce being used. They discussed that most patients had reported having at least five triggers for their migraines,

and these triggers usually fell under the environmental and hormonal categories. Stress was frequently the leading trigger for migraines (Rockett et al., 2012a).

There is a small pool of research that has been conducted concerning migraines and dietary triggers. Within the data given, there has not been research conducted, of this researcher's findings, concerning solely gluten as the dietary triggers. As previously mentioned, there have been studies conducted looking at a large variety of dietary triggers of which gluten is considered. Evidence shows that there are dietary triggers, and gluten may be one; the mechanism pathway of how gluten is creating these extra-intestinal manifestations is still under debate. More research is needed to provide better understanding of the pathology of migraines and gluten.

Gluten-Free Diet

Some researchers believe that a GFD could be deemed unhealthy due to being restrictive nutritionally, possibly resulting in deficiencies. Fiber is a concern because processed gluten-free items are generally made with starches or refined flours that typically have low fiber content. Furthermore, it could lead to deficiencies in vitamin C, B_{12}, vitamin D, and folic acid. These deficiencies could be associated to lack of absorption due to the damage of the villi atrophy, mainly in the CD patients, but it could also be due to low quality gluten-free foods. There are also concerns with obesity and excessive weight gain while on a GFD (Balakireva & Zamyatnin Jr., 2016; Leccioli et al., 2017). The researchers of these articles appear to be considering only that the individual is consuming processed gluten-free items. However, if they were to consider the ease of eating whole foods when gluten-free, such as the inclusion of vegetables, then the risk of nutritional deficiencies would be much lower, if existent.

CHAPTER III

METHODOLOGY

Purpose of Study

The primary objective of this case study series was to determine the efficacy of a gluten free diet (GFD) for individuals with chronic migraines. Participants were asked to fill out records for their migraines with information including date of occurrence, duration, severity, 24-hr diet recall, location, and symptoms. A diet history questionnaire, body composition measurements, blood pressure, and blood sugar were all measured to evaluate the effect of a GFD on other health aspects.

Research Aims

The aims of this study were (1) can a GFD decrease the incidence of migraines in migraine sufferers? And (2) can a GFD positively impact body composition, blood pressure and glucose levels in migraine sufferers? The third aim of the study was asking if (3) there is a level of gluten which is tolerated without experiencing migraines in sensitive individuals?

Participants

All research participants had to be 18 years or old and could be male or female. They had to have chronic migraines of which severity would be confirmed by two questionnaires: Headache Impact Test (HIT) (Quality Metric, Inc.) and Migraine

Disability Assessment Scale (MIDAS) (AstraZeneca Pharmaceuticals). Participants also needed to be able to complete all parts of the study: diet history questionnaire II (DHQ-II), body composition measurements, blood glucose, blood pressure, migraine diary, and a gluten free diet. If the participants had one or more of the following, then they were excluded from participation: pregnant, confirmed diagnoses of celiac disease, less than 18 years of age, inability to read or write in English, and migraines due to menstrual cycles.

All participants, excluding one, were female. There was a single male in the research study. As shown in Table 3.1, all participants were greater than 18 years of age and Caucasian.

Table 3.1 Demographics

	Race	Gender	Age (years)
Participant 1	Caucasian	Female	22
Participant 2	Caucasian	Female	25
Participant 3	Caucasian	Female	21
Participant 4	Caucasian	Female	24
Participant 5	Caucasian	Female	33
Participant 6	Caucasian	Male	20

Institutional Review Board Approval

This research study was approved by the Institutional Review Board at Mississippi State University (Appendix A). The study number was IRB-17-095. All research was conducted either at Mississippi State University's Nutrition-Performance-Assessment-Composition-Testing (NPACT) lab on campus or the Exercise Physiology lab on the campus of Mississippi University for Women. This research study was approved for up to 100 participants for a five-month longitudinal study. However, recruitment proved to be a challenge, and the study was completed with six participants.

Procedure

The goal was to recruit 30 participants for the study; the IRB had allowed up to 100. The researcher created a flyer (Appendix E) to advertise for the study and posted it in a few local businesses, the University, social media, and had it sent through departmental email. It proved to be difficult to recruit enough participants due to the requirement of removing gluten from the diet. During the study, the researcher submitted an amendment to allow long-distance conduction of the study with the objective of gaining additional participants. The slight change in study, as well as a new advertisement flyer (Appendix F), were approved. Despite these efforts, only six participants volunteered for this research study. This development caused the researcher to reevaluate the study from a longitudinal study to a case series.

On the first visit, participants were first asked to fill out two questionnaires, HIT (Appendix B) and MIDAS (Appendix C), to determine if they qualified for the research study. Once confirmed, they were asked to sign an informed consent document. Body composition was measured using the TANITA TBF-300A (Arlington Heights, Illinois). Blood pressure was measured by an Omron Blood Pressure Monitor HEM-907XL (Kyoto, Japan). Blood glucose was sampled using a Unistick 3 comfort single-use, 28 gauge safety lancet and read by the LTC Assure Platinum, Blood Glucose Meter (Minneapolis, MN). The researcher met individually with each client to assess their understanding of nutrition and ability to observe a restrictive diet during the course of the study. The researcher also assessed their migraine history, occupation and location. Participants were asked to complete the web-based NIH DHQ-II within the first month, in order to gather information about the previous month's food and drink consumption,

with portion sizes. For their first month, they were asked to maintain their normal diet and lifestyle, but to keep a record of their migraines in their migraine diaries (Appendix D). The researcher explained the format of the migraine diary and the different sections including: date and time of the migraine, duration of the migraine, the intensity of the migraine, a 24-hour dietary recall, the subject's location when the migraine was first noticed, symptoms experienced during the migraine, any interventions (including medication), to reduce the symptoms or severity of the migraine and any additional information that they wished to provide. The researcher explained the intensity pain scale which was represented by the visual analogue scale (VAS). The VAS is a scale of increasing intensity from 1-10, where a one would indicate a headache, but the symptoms are barely noticed and easily forgotten. A five on the scale would indicate that they have a migraine, which cannot be ignored, but the pain is still at a tolerable level. A ten would indicate the pain is so intense that they need to seek medical attention due to the severity of symptoms. Each subject's initial visit would last a minimum of thirty minutes, with the possibility of additional time for questions regarding the research study. The web-based DHQ-II to be completed after the first visit would take them around thirty minutes to complete.

The participants would return to the lab at the conclusion of the first month and repeat body composition, blood pressure and blood glucose measurements. They also turned the migraine diary from the first month. During this second visit, they were given a small information packet (Appendix G). In this packet the participants were informed of what constitutes a gluten-free diet including: foods allowed, foods to avoid, and examples of allowable products available from a local grocery store. The second visit averaged

approximately twenty minutes per participant. Length of time varied depending on the amount of understanding and previous exposure to a GFD as well as the overall understanding of nutrition. For months 2-4, participants were asked to maintain a gluten-free diet, avoid lifestyle changes, and maintain an accurate record of any migraines or migraine symptoms in their study provided migraine diaries. They were also asked to record any ingestions of gluten during the GFD period of the study. The intent of this record was to inform the researcher of any potential effect the gluten ingestion may have on the participant during the study. Participants were asked to return to the lab at the beginning of each following month to record the participant's physical measurements and return the previous month migraine diary. Visits 2-4 were conducted within 15 minutes. During the fourth month, the researcher asked the participants to complete the web-based DHQ-II for a second time to evaluate if they changed their eating habits while on a GFD.

At the beginning of the fifth month, participants returned to the lab and were provided with instructions to add gluten to their diet in the prescribed amount, to have their measurements taken, and to return the latest migraine diaries. As part of the introduction of gluten in the diet, participants were instructed to gradually increase the amount of gluten each week of the study. Participants were given four separate bags of pre-measured Bob Redmill's Vital Wheat Gluten (Milwaukie, Oregon). Each bag represented a one-week intake of gluten. The protocol for adding gluten to the diet was as follows: Week 1-3 grams of gluten per day; Week 2-5 grams of gluten per day; Week 3-10 grams of gluten per day; and Week 4-20 grams of gluten per day. Participants were instructed to purchase a gluten-free mix (e.g. brownies, cookies, cornbread, etc.) and add the predetermined amount of gluten for each week. They would then divide the baked

product into 7 equal portions, consuming one baked product each day to meet the daily protocol intake of gluten. Participants were instructed to avoid additional sources of gluten during this phase of the study. Participants were instructed to return to the laboratory at the end of the four weeks to return their final migraine diary and have their measurements recorded for a final time prior to completing the study. Both visits during month 5 only lasted approximately 15 minutes. After the conclusion of the study, the researcher contacted all participants to ask additional questions (Appendix H) to gain a better understanding of each participant's experience. These additional questions included family history of migraines, at which age their migraines began, stress levels during the study, fasting regard to triggering a migraine, and if they discovered any additional triggers during the study. Questions were also asked to ensure accuracy of their migraine diary information, such as common symptoms, prophylactic treatment during the study (if any), and acute medication treatment.

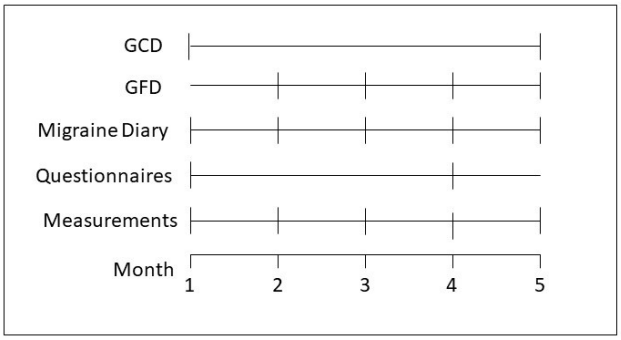

Figure 3.1 Study Design

GCD: gluten-containing diet; GFD: gluten-free diet; M: measurements (body composition, blood pressure, blood glucose); Q: questionnaires (HIT & MIDAS); MD: migraine diary.

Education

During each visit, the researcher gave participants the opportunity to ask questions regarding the diet or the research study. At the beginning of the study, the researcher gave a quick overview of what was expected in the study, including the GFD. The researcher created an informational packet (Appendix G) to provide to each participant. Included in this packet, the participant was provided with a definition of gluten, foods containing gluten, and foods considered to be gluten-free and therefore allowed as part of a GFD. Participants were provided the option to take the packet at the conclusion of the first visit or wait until starting the GFD during the second month. If the participant's GFD period occurred during a holiday, the researcher sent out e-mails to

remind the participant to maintain the GFD and suggested recommended foods and substitutions considered safe for anyone following GFD. The researcher also offered to provide each participant with assistance if needed during any phase of the diet study.

CHAPTER IV

CASE STUDY INFORMATION AND RESULTS

Results

Each participant's study experience will be documented in a case study format. All the data from their migraine journals will be presented as well as the data from the body composition measurements (body fat percentage [%], weight [lbs], fat free mass [%], and body mass index[kg/m^2]), blood pressure (mmHg) and blood glucose (mg/dL) results. It is important to note that some participants recorded a starting time and ending time for their migraines while others stated how long they lasted (duration). Any gluten exposure during their gluten-free period is noted in the proceeding sections. There will also be a table presenting the participant's results from the web-based DHQ taken prior to the start of the study and again at the conclusion of the gluten-free period of the study. These results will be compared with the USDA's RDA's.

Participant 1

Summary: Participant 1, 22-year-old college student at the time of the study, approached the researcher showing interest in participating in the research study due to recently realizing the pain and discomfort she had felt since she was 18 was from migraines.

History: Participant denied any family history of migraines. She noted several migraine-related symptoms including: photophobia, allodynia, ringing in the ears, pinching sensation behind the eyes, sonophobia, and light headedness. She did not have any

prophylactic treatment for the migraines, but for acute onset of a migraine she reported taking 440 mg Aleve© pills.

Demographics

Occupation: College student, undergraduate

Ethnicity: Caucasian

Sex: Female

Age: 22 years old

Height: 5'4.5" (64.5in)

Diagnosis: Participant 1 completed the HIT and MIDAS questionnaires and was qualified for the study. She signed the consent form and began the research study.

Measurements

Table 4.1 Body Composition Measurements

	BF%	Weight (lbs)	FFM (%)	BMI (Kg/m^2)
Month 1	25.9	139	73.4	23.8
Month 2	26.6	139.4	73.3	23.6
Month 3	24.7	136.2	75.3	23
Month 4	24.9	136.8	75.1	23.1
Month 5a	24.3	137.8	75.8	23.3
Month 5b	23.4	139.6	76.6	23.6

BF%: body fat percentage; lbs: pounds; FFM: fat free mass; BMI: body mass index; kg/m^2: kilograms per meters squared

Table 4.2 Blood Pressure and Blood Glucose

	BP (mmHg)	BG (mg/dL)
Month 1	113/64	95
Month 2	114/77	96
Month 3	119/67	91
Month 4	116/66	109
Month 5a	112/58	94
Month 5b	101/56	78

BP: blood pressure; BG: blood glucose; mmHg: milligrams of mercury; mg/dL: milligrams per deciliter

Gluten Exposure

The participant was asked to record any instances of gluten exposure while she was asked to be strictly gluten-free. Participants were not asked to disclose whether or not the gluten exposure was accidental or intentional. If this information was provided to the researcher, it is disclosed as part of the case study.

Table 4.3 Month 1: Gluten-Containing Diet

Migraine Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
11/30/17	2.5	4	Ad lib
12/5/17	4	6	Ad lib
12/11/17	7	5	Ad lib
12/13/17	8	8	Ad lib
12/24/17	3	6	Ad lib
12/29/17	5	4	Ad lib
1/9/18	6	5	Ad lib

Month 2

During the second month of the study, the participant reported five gluten exposures. This participant lived in a sorority house located on the university campus where meals were prepared by a central kitchen staff. It was discovered by the participant

that those preparing the meals were not following gluten-free protocol due to a lack of education regarding gluten-containing foods. The initial accidental ingestion was a veggie burger which had been inaccurately labeled as "gluten-free", that upon further inspection was determined not to be gluten-free.

Table 4.4 Month 2: Gluten-Free Diet

Migraine Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
2/10/18	4 (2 pm-6 pm)	7	1/19, 20, 25, 26/18, 2/4/18
2/14/18	7 (4 pm-11pm)	5	None

Month 3

During the third month, the participant reported six gluten exposures. She had a mission trip scheduled to a third world country during spring break. Due to the unique circumstances, it was suggested by the researcher to bring a variety of gluten-free snacks and to avoid gluten during the trip. Due to her location, the participant noted that her food options were limited, and there was no procedure for verifying the foods consumed were gluten free or to document the amount of gluten consumed during that week of the study.

Table 4.5 Month 3: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
2/24/18	3 (9 am-12 pm)	4	2/23/18
2/26/18	5 (12 pm-5 pm)	6	2/25/18
3/5/18	7 (8 am- 3 pm)	4	None
3/19/18	8 (time frame n/a)	6	3/14-17/18

n/a: not available

Month 4

In the fourth month, she reported two gluten exposures.

Table 4.6 Month 4: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
3/20/18	5 (time frame n/a)	3	None
4/10/18	10 (2 pm-12 am)	7	4/6/18
4/17/18	4 (7 pm-11 pm)	4	None
4/23/18	3 (3 pm-6 pm)	5	4/12/18

Month 5

In the fifth month, she reported two gluten exposures.

Table 4.7 Month 5: Gluten-Free Diet & Re-Introduction

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
4/15/18	6 (1 pm-7 pm)	6	5/5, 12/18
5/22/18	4 (3 pm-7 pm)	7	None
5/26/18	3 (6 pm-9 pm)	3-4	None
5/27-28/18	3 (1 pm-4 pm); 17 (10 pm-3 pm next day)	5; 8	None
5/22/18	4 (3 pm-7 pm)	7	None
5/26/18	3 (6 pm-9 pm)	3-4	None

Diet History Questionnaire Results

The results from the DHQ-II showed that over the course of the study, the participant increased her consumption of energy (kcals), fat and protein. Conversely, her consumption of carbohydrates decreased as well as her overall sugar consumption. Table 4.8 displays that Participant 1was able to meet almost all recommended dietary allowances while on a GFD.

Table 4.8 DHQ Data

Micronutrients	RDA (females)	Month 1 (gluten)	Month 4 (GF)
Fiber (g/d)	25	29	26
Vitamin C (mg/d)	75	191	116
Vitamin D (mcg/d)	15	4.9	3.8
B_{12} (mcg/d)	2.4	4.14	4.19
Folate (mcg/d)	400	672	556
Calcium (mg/d)	1000	993	1078
Iron (mg/d)	18	19	18
Magnesium (mg/d)	310	494	530

RDA: recommended dietary allowances; G: grams; D: day; Mg: milligrams; Mcg: micrograms; GF: gluten-free

Follow-up

A follow-up questionnaire (Appendix H), which was aimed at gathering uniform information from all the participants, was issued after the conclusion of the study. When asked if fasting or skipping meals triggered migraines, the participant confirmed that skipped meals or fasting can potentially induce a migraine. When asked if she discovered any new potential migraine triggers over the course of the study, she reported that consuming certain foods appeared to trigger the onset, especially an excess of sugar or gluten.

After the conclusion of the study the participant reported her migraine occurrences had decreased greatly due to increased sleep, reduced stress, and a greater understanding of her individual migraine triggers.

Participant 2

Summary: Participant 2, a 25-year-old graduate student, decided to participate in the research study due to the lack of efficacy of prophylactics for her migraines.

History: She reported having migraines since the age of nine, along with paternal migraine history. She noted several migraine-related symptoms including: photophobia, sonophobia, osmophobia, nausea, and shoulder/neck stiffness. Immediately prior to beginning the study, the participant had been put on Propranolol as a prophylactic treatment. She reported taking one Excedrin migraine© (250 mg acetaminophen, 250 mg aspirin, and 65 mg caffeine) or 600 mg of ibuprofen for acute treatment of the onset of a migraine. The participant also reported starting a high intensity work out program two to three months into the study after previously not being active.

Demographics

Occupation: College student, graduate

Ethnicity: Caucasian

Sex: Female

Age: 25 years old

Height: 5'2" (62")

Diagnosis: Participant 2 completed the HIT and MIDAS questionnaires and qualified for the study. She signed the consent form and began the research study.

Measurements

Table 4.9 Body Composition Measurements

	BF%	Weight (lbs)	FFM (%)	BMI (Kg/m^2)
Month 1	16	101	84	18.5
Month 2	18.4	104	81.5	19
Month 3	17.8	105.4	82.2	19.3
Month 4	19.8	107	80	19.6
Month 5a	19.3	109	80.7	19.9
Month 5b	18.9	109.4	81.2	20

BF%: body fat percentage; lbs: pounds; FFM: fat free mass; BMI: body mass index; kg/m^2: kilograms per meters squared

Table 4.10 Blood Pressure and Blood Glucose

	BP (mmHg)	BG (mg/dL)
Month 1	120/78	86
Month 2	113/68	129
Month 3	102/57	85
Month 4	117/61	132
Month 5a	102/59	98
Month 5b	118/64	86

BP: blood pressure; BG: blood glucose; mmHg: milligrams of mercury; mg/dL: milligrams per deciliter

Gluten Exposure

The participant was asked to record any instances of gluten exposure while she was asked to be strictly gluten-free. Participants were not asked to disclose whether or not the gluten exposure was accidental or intentional. If this information was provided to the researcher, it is disclosed as part of the case study.

Table 4.11 Month 1: Gluten-Containing Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
2/27/18	Estimated 8.5 (10 pm- woke up with h/a gone)	4	Ad lib
2/28/18	Estimated 7 (11:30 pm- woke up with h/a gone)	5	Ad lib
3/2/18	14.5 (4 pm- woke up with h/a gone)	5	Ad lib
3/14-15/18	16 (10 pm – 2 pm)	6	Ad lib
3/17-19/18	40 (8 pm- 12 pm)	9, "at it's worst"	Ad lib

h/a: headache

Table 4.12 Month 2: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
3/20-22/18	52 (6 am- 10 am)	4-9	None
3/25/18	7 (6 am- 1 pm)	5	None
4/1-2/18	17(9 pm- 2 pm next day)	5	None
4/4/18	Estimated 8 (6 am- end time not provided)	7	None
4/6/18	7 (2 pm- 9 pm)	6	None
4/12-13/18	19 (11 pm- 6 pm)	4	None
4/14/18	Estimated 13.5 (5 pm- woke up with h/a gone)	6	None
4/16/18	6 (8 am- 2 pm)	6	None
4/19/18	8.5 (6:30 am- 3 pm)	3-4	None
4/20/18	11 (5 am- 4 pm)	4	None

h/a: headache

Month 3

The participant reported two occurrences of gluten exposure during month three. The first instance was due to a smoothie that contained wheat grass. She drank one-third

of the smoothie before realizing the contamination and did not finish it. For the second instance she was at a family gathering, and despite her efforts of explaining she couldn't have certain items because of the gluten, she resigned and ate two bites of cake, small portion of pasta salad, and one chocolate chip cookie.

Table 4.13 Month 3: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
4/27/18	4.5 (12 pm- 4:30 pm)	3	None
4/28/18	5 (11 am- 4 pm)	2-3	6
5/14/18	6.5 (6:30 am- 1 pm)	7	None
5/20/18	Estimated 11.5 (7 pm- woke up with h/a gone)	6	19
4/28/18	5 (11 am- 4 pm)	2-3	6
5/14/18	6.5 (6:30 am- 1 pm)	7	None
5/20/18	Estimated 11.5 (7 pm- woke up with h/a gone)	6	19

h/a: headache

Month 4

The participant reported one occurrence of gluten exposure during month four. She explained to the researcher that when she had bought graham cracker snacks, she had mistakenly grabbed the wrong box. Some brands will make both a gluten-containing and gluten-free product and the boxes can look similar. She reported of eating 6-10 bite size graham cracker snacks before she realized they weren't gluten free and she did not finish the rest.

Table 4.14 Month 4: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure
6/1/13	9.5 (3:30 am- 1 pm)	6	None
6/3/18	5 (2 pm- 7 pm)	4	None
6/8-11/18	Estimated 96 (non-stop all four days, woke up with h/a gone on12)	4-7	None
6/17/18	6 (1 pm- 7 pm)	7	6/17/18

h/a: headache

DHQ Results

The results from the DHQ showed that over the course of the study, the participant decreased her consumption of energy (kcals), fat and carbohydrates. Her protein consumption stayed consistent between a diet containing gluten and a GFD. Her consumption of overall sugar decreased. She increased her intake of fiber and vegetables when on a GFD. The researcher specifically looked at the nutrients that research (Balakireva & Zamaytnin Jr., 2016; Leccioli et al., 2017) has claimed a gluten-free diet to be deficient in, and those results are recorded in table 4.15. This participant kept all nutrients consistent. The only nutrient intake that was decreased was her her vitamin C intake; however, it is important to note that her intake levels were not at the recommended level on either diet.

Table 4.15 DHQ Data

Micronutrients	RDA (females)	Month 1 (gluten)	Month 2 (GF)
Fiber (g/d)	25	5.4	5.9
Vitamin C (mg/d)	75	35.2	23.4
Vitamin D (mcg/d)	15	0.78	0.92
B_{12} (mcg/d)	2.4	1.1	0.96
Folate (mcg/d)	400	138.4	142.8
Calcium (mg/d)	1000	297.6	297
Iron (mg/d)	18	4.6	4.1
Magnesium (mg/d)	310	116.8	123

RDA: recommended dietary allowances; G: grams; D: day; Mg: milligrams; Mcg: micrograms; GF: gluten-free

Follow-up

A follow-up questionnaire (Appendix H) which was aimed at gathering uniform information from all the participants was issued after the conclusion of the study. The participant reported her stress levels being about average during the course of the study. When asked about fasting or skipping meals as a migraine trigger, she was unsure but reported that it could be possible. When inquired about other potential triggers at the completion of the study, she did not have knowledge of any, but found a desire to evaluate different lifestyle factors that could be affecting her.

After the conclusion of the study it was the researcher's understanding the participant did not continue to be gluten-free. She is looking into different lifestyle factors that could be affecting her migraines. The researcher also asked if the participant felt like the Propranolol, that she was prescribed at the beginning of the study, was making an impact. The participant felt as though the medication did not make a difference in her migraines.

Participant 3

Summary: Participant 3, a 21-year-old nursing student with a history of migraines since the age of about 17, asked to take part in the research study to see if this could help her migraines.

History: She reported that she is the only individual in her family with migraines, chronic or otherwise. She noted several migraine-related symptoms including: spots in vision, fatigue, nausea, photophobia, and sonophobia. The participant did not take any prophylactic treatment for her migraines; however, at the onset of a migraine she would often take 1000 milligrams of Naproxen.

Demographics

Occupation: College student, undergraduate

Ethnicity: Caucasian

Sex: Female

Age 21 years old

Height: 5'3" (63")

Diagnosis: Participant 3 completed the HIT and MIDAS questionnaires and qualified for the study. She signed the consent form and began the research study.

Measurements

Table 4.16 Body Composition Measurements

	BF%	Weight (lbs)	FFM (%)	BMI (kg/m^2)
Month 1	14.4	104	85.6	18.4
Month 2	13.5	105	86.5	18.6
Month 3	13.7	103.6	86.3	18.4
Month 4	15	104.2	85	18.5
Month 5a	15	105	84	18.8
Month 5b	15.9	106.4	87.4	18.6

BF%: body fat percentage; lbs: pounds; FFM: fat free mass; BMI: body mass index; kg/m^2: kilograms per meters squared

Table 4.17 Blood Pressure and Blood Glucose

	BP (mmHg)	BG (mg/dL)
Month 1	118/74	94
Month 2	116/70	86
Month 3	120/67	96
Month 4	109/71	83
Month 5a	114/69	74
Month 5b	106/64	77

BP: blood pressure; BG: blood glucose; mmHg: milligrams of mercury; mg/dL: milligrams per deciliter

Gluten Exposure

The participant was asked to record any instances of gluten exposure while she was asked to be strictly gluten-free. Participants were not asked to disclose whether or not the gluten exposure was accidental or intentional. If this information was provided to the researcher, it is disclosed as part of the case study. She did not have any gluten exposures recorded.

Table 4.18 Month 1: Gluten-Containing Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
2/23/18	3 (7 pm-10 pm)	5	Ad lib
3/1/18	3 (2 pm- 5 pm)	6	Ad lib
3/10/18	2 (1 pm- 3 pm)	4	Ad lib
3/19/18	4.5 (11:30 am- 4 pm)	4	Ad lib
3/27/18	3 (12 pm- 3 pm)	5	Ad lib

Table 4.19 Month 2: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
4/1/18	2 (9 am- 11 am)	5	None
4/16/18	3 (7 pm-10 pm)	6	None

Table 4.20 Month 3: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
5/14/18	3.5 (8:30 am- 12 pm)	3	None
5/18/18	8 (7 am- 3 pm)	5	None

Table 4.21 Month 4: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
6/5/18	3 (7 pm-10 pm)	4	None
6/14/18	3 (11 am- 2 pm)	4	None

Table 4.22 Month 5: Gluten-Free Diet & Re-Introduction

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
7/6/18	3 (7 pm-10 pm)	3	None
7/11/18	3 (8 am- 11 am)	2	None

DHQ Results

The participant was not compliant in completing the two diet questionnaires over the course of the study, so it will not be possible to determine the effect of a GFD on her overall nutritional intake.

Follow-up

A follow-up questionnaire (Appendix H) which was aimed at gathering uniform information from all the participants was issued after the conclusion of the study. In regard to the questions the researcher sent participants at the conclusion of the study, this participant reported having a large amount of stress during the course of the study due to nursing school. She also reported having discovered that fasting or skipping meals is also a trigger for her migraines. When asked if she discovered any additional potential migraine triggers over the course of the study, she reported that certain foods, particularly

starchy items, and staring at electronic screens all day without any physical activity also were a migraine trigger.

Participant 4

Summary: Participant 4, a 24-year-old graduate student, was immediately interested in participating in the research study once she heard about it. She has had migraines since the age of 20.

History: She has a family history of migraines. She noted several migraine-related symptoms including: nausea, irritability, body aches, and fatigue.

Demographics:

Occupation: College student, graduate

Ethnicity: Caucasian

Sex: Female

Age 24 years old

Height: 5'3" (63")

Diagnosis: Participant 4 completed the HIT and MIDAS questionnaires, and qualified for the study. She signed the consent form and began the research study.

Measurements

Table 4.23 Body Composition Measurements

	BF%	Weight (lbs)	FFM (%)	BMI (Kg/m^2)
Month 1	22.6	129.2	77.4	22.9
Month 2	26.1	132.8	74	23.5
Month 3	26.8	132	73	23.4
Month 4	26.2	129	73.6	22.9
Month 5a	27.9	138.2	72	24.5
Month 5b	28	137	72	24.3

BF%: body fat percentage; lbs: pounds; FFM: fat free mass; BMI: body mass index; kg/m^2: kilograms per meters squared

Table 4.24 Blood Pressure and Blood Glucose

	BP (mmHg)	BG (mg/dL)
Month 1	125/76	115
Month 2	103/69	91
Month 3	144/88	99
Month 4	127/81	116
Month 5a	114/77	109
Month 5b	125/75	115

BP: blood pressure; BG: blood glucose; mmHg: milligrams of mercury; mg/dL: milligrams per deciliter

Gluten Exposure

The participant was asked to record any instances of gluten exposure while she was asked to be strictly gluten-free. Participants were not asked to disclose whether or not the gluten exposure was accidental or intentional. If this information was provided to the researcher, it is disclosed as part of the case study.

Table 4.25 Month 1: Gluten-Containing Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
9/14/18	8 (10 am- 6 pm)	6	Ad lib

Month 2

This participant had two recorded gluten exposures, both in month two. It is of the researcher's belief that the participant didn't have a full understanding of the importance of being strictly gluten free.

Table 4.26 Month 2: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
11/6/18	4 (12 pm- 4 pm)	7	10/20-21/18

DHQ Results

The results from the DHQ, Table 4.27, displayed that over the course of the study, the participant had a decrease of all macronutrients ingested as well as micronutrients. The single value increased between the two questionnaires was caffeine intake. Her initial energy output, in kilocalories (kcal), was 424 kcals/day in the first month and it decreased to 104 kcals per day in the fourth month. The researcher is inclined to believe that the participant did not give accurate responses to the questionnaire, which affected all other values.

Table 4.27 DHQ Data

Micronutrients	RDA (females)	Month 1 (gluten)	Month 4 (GF)
Fiber (g/d)	25	7.7	1.5
Vitamin C (mg/d)	75	74	9
Vitamin D (mcg/d)	15	0.25	0.07
B_{12} (mcg/d)	2.4	0.32	0.07
Folate (mcg/d)	400	156.6	29.3
Calcium (mcg/d)	1000	360.8	39.9
Iron (mg/d)	18	3.74	0.49
Magnesium (mg/d)	310	144.1	28.28

RDA: recommended dietary allowances; G: grams; D: day; Mg: milligrams; Mcg: micrograms; GF: gluten-free

Follow-up

A follow-up questionnaire (Appendix H) which was aimed at gathering uniform information from all the participants was issued after the conclusion of the study. The participant reported her stress levels as being moderate over the course of the study. She also reported that fasting or skipping meals can trigger migraines. She also reported that not drinking enough water can be a migraine trigger for her.

It appears dehydration was the primary trigger for this participant's migraines. She learned that if she drank water before her morning coffee and frequently drank it all day, then she would have no migraine symptoms.

Participant 5

Summary: Participant 5, a 33-year-old woman, saw the research flyer in a local pharmacy and emailed the researcher to inquire about joining the research study.

History: She reported having a family history of migraines, mother and maternal aunt. She also reported that her migraines began at about the age of 15. She noted several migraine-related symptoms including: auras prior to a migraine, photophobia, nausea,

and vomiting. She was taking no prophylactic treatment, but her acute treatment of a migraine consisted of either 600 mg of ibuprofen or 50 mg Imitrex (also known as Sumatriptan).

Demographics

Occupation: Corporate finance

Ethnicity: Caucasian

Sex: Female

Age: 33 years old

Height: 5'7" (67")

Diagnosis: Participant 5 completed the HIT and MIDAS questionnaires and qualified for the study. She signed the consent form and began the research study.

Measurements

Table 4.28 Body Composition

	BF%	Weight (lbs)	FFM (%)	BMI (Kg/m^2)
Month 1	35.3	152.4	64.7	23.9
Month 2	35.3	155.6	64.7	24.4
Month 3	35.4	153	64.6	24
Month 4	34.8	148.6	65.1	23.3
Month 5a	34.8	147.8	65.2	23.1
Month 5b	35.4	147.6	64.6	23.1

BF%: body fat percentage; lbs: pounds; FFM: fat free mass; BMI: body mass index; kg/m^2: kilograms per meters squared

Table 4.29 Blood Pressure and Blood Glucose

	BP (mmHg)	BG (mg/dl)
Month 1	126/72	91
Month 2	131/81	90
Month 3	124/74	113
Month 4	110/67	105
Month 5a	120/87	106
Month 5b	117/76	102

BP: blood pressure; BG: blood glucose; mmHg: milligrams of mercury; mg/dL: milligrams per deciliter

Gluten Exposure

The participant was asked to record any instances of gluten exposure while she was asked to be strictly gluten-free. Participants were not asked to disclose whether or not the gluten exposure was accidental or intentional. If this information was provided to the researcher, it is disclosed as part of the case study. She did not have any gluten exposures recorded.

Table 4.30 Month 1: Gluten-Containing Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
9/16/18	1 (10 am- 11 am)	8	Ad lib

Table 4.31 Month 2: Gluten-Free Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
10/7/18	1 (10 am- 11 am)	5	None
10/14/18	1 (10 am-11 am)	4	None

DHQ Results

The results from the DHQ showed that over the course of the study, the participant decreased her consumption of energy (kcals) and all macronutrients. Her consumption of sugar stayed the same. She decreased her intake of fiber. Her vegetables intake stayed the same between being on a diet with gluten and a GFD. However, her caffeine intake increased dramatically between the two diets. Table 4.32 gives details regarding her micronutrient intake.

Table 4.32 DHQ Data

Micronutrients	RDA (females)	Month 1 (gluten)	Month 2 (GF)
Fiber (g/d)	25	15.8	12.2
Vitamin C (mg/d)	75	119.8	60.2
Vitamin D (mcg/d)	15	6.2	2.2
B_{12} (mcg/d)	2.4	4	2.4
Folate (mcg/d)	400	418.8	307.2
Calcium (mg/d)	1000	516.6	603.9
Iron (mg/d)	18	12.57	8.34
Magnesium (mg/d)	310	313.8	276.2

RDA: recommended dietary allowances; G: grams; D: day; Mg: milligrams; Mcg: micrograms; GF: gluten-free

Follow-up

A follow-up questionnaire (Appendix H) which was aimed at gathering uniform information from all the participants was issued after the conclusion of the study. At the conclusion of the study when asked about her stress levels over the course of the study, these levels ranged between very low to moderate. She reported that skipping meals or fasting did not trigger migraines. She also did not discover any new triggers over the course of the study. However, during the appointments through the course of the research study, she would mention that she decreased the amount of alcohol she was drinking,

specifically red wine. She said that she tended to have migraines if she consumed too much alcohol.

Participant 6

Summary: Participant 6, a 20-year-old college student, overheard the researcher telling colleagues about the research study and began inquiring about the requirements to join. He became interested due to the severity of his migraines and the desire to try anything to help with the migraines.

History: He reported to the researcher that his immediate family does not have a history of migraines, and that his migraines began around the age 15. He noted several migraine-related symptoms including: photophobia, sonophobia, neck stiffness, pain behind the eyes. He reported consuming no prophylactic treatment for his migraines. He also stated that he does not take any medication with the onset of a migraine; however, during the last week of the fourth month he began to try cannabis derivative cannabidiol (CBD) oil on two separate occasions with the onset of a migraine.

Demographics

Occupation: College student, undergraduate

Ethnicity: Caucasian

Sex: Male

Age: 20 years old

Height: 5'7.5" (67.5")

Diagnosis*:* Participant 6 completed the HIT and MIDAS questionnaires and qualified for the study. He signed the consent form and began the research study.

Measurements

Table 4.33 Body Composition Measurements

	BF%	Weight (lbs)	FFM (%)	BMI (kg/m^2)
Month 1	21.2	170.4	78.8	26.3
Month 2	21.7	171.8	78.4	26.5
Month 3	19.1	164.6	80.9	25.4
Month 4	18.4	161.2	81.6	24.9
Month 5a	17	155	82.9	23.9
Month 5b	14.6	153	85.4	23.6

BF%: body fat percentage; lbs: pounds; FFM: fat free mass; BMI: body mass index; kg/m^2: kilograms per meters squared

Table 4.34 Blood Pressure and Blood Glucose

	BP (mmHg)	BG (mg/dL)
Month 1	129/80	83
Month 2	125/68	78
Month 3	130/68	105
Month 4	113/73	81
Month 5a	132/76	94
Month 5b	140/77	91

BP: blood pressure; BG: blood glucose; mmHg: milligrams of mercury; mg/dL: milligrams per deciliter

Gluten Exposure

The participant was asked to record any instances of gluten exposure while he was asked to be strictly gluten-free. Participants were not asked to disclose whether or not the gluten exposure was accidental or intentional. If this information was provided to the researcher, it is disclosed as part of the case study. He had two recorded gluten exposures.

Table 4.35 Month 1: Gluten-Containing Diet

Occurrence Date	Duration (hours)	Severity (1-10)	Gluten Exposure Date
10/13-14/18	18 (8 am- 2 am next day)	4-7	Ad lib
10/14/18	Estimated 8.5 (9 pm- woke up with h/a gone)	1	Ad lib
10/17/18	3 (4 pm- 7 pm)	6	Ad lib
10/19-20/18	9 (4 pm- 1 am)	6-10	Ad lib
10/24/18	4 (6 pm- 10 pm)	3	Ad lib
11/1/18	3 (12 pm- 3 pm)	3	Ad lib
11/3/18	2 (4pm- 6 pm)	4	Ad lib
11/4/18	2 (3pm- 5 pm)	5	Ad lib
11/8/18	3 (1 pm- 4 pm)	2	Ad lib
11/11/18	4 (7 am- 11 am)	6	Ad lib
10/13-14/18	18 (8 am- 2 am next day)	4-7	Ad lib

h/a: headache

Month 2

This participant had one gluten exposure in the second month. He told the researcher that someone had brought a pumpkin roll to class, which he loves, and automatically picked up a piece for himself. After the first bite he realized that he was not supposed to have it, so he did not finish the pumpkin roll.

Table 4.36 Month 2: Gluten-Free Diet

Day	Duration (hours)	Severity (1-10)	Gluten Exposure Date
11/13/18	3 (3 pm- 6pm)	6	None
11/15/18	6 (4 pm- 10 pm)	4	None
11/21/18	4 (7 pm- 11 pm)	6	11/21/18
11/27/18	4 (12 pm- 4 pm)	3	None
12/1/18	3 (6 pm- 9 pm)	4	None
12/3/18	5 (11 am- 4 pm)	9	None

Month 3

There was one gluten exposure in the third month. He reported that he was used to eating the nacho flavor of Doritos©, but decided to change flavor to the sweet spicy chili flavor. It wasn't until he finished the small, personal-size bag that he realized that specific flavor was not gluten-free.

Table 4.37 Month 3: Gluten-Free Diet

Day	Duration (hours)	Severity (1-10)	Gluten Exposure Date
12/11/18	5 (7 pm- 12 pm)	6	None
12/13/18	3 (9 am- 12 pm)	5-7	12/13/18
12/18/18	4 (7 pm- 11 pm)	6	None
12/26/18	4 (4 pm- 8 pm)	3-7	None
1/1/10	4 (8 am- 12 pm)	3-7	None
1/11/19	3 (3 pm- 6 pm)	8	None

Table 4.38 Month 4: Gluten-Free Diet

Day	Duration (hours)	Severity (1-10)	Gluten Exposure Date
1/15/19	4 (3 pm- 7 pm)	4-8	None
1/21/19	5 (4 pm- 9 pm)	3-5	None
1/28/19	4 (7 am- 11 am)	5-8	None

Table 4.39 Month 5: Gluten-Free Diet & Re-Introduction

Day	Duration (hours)	Severity (1-10)	Gluten Exposure Date
2/6/19	6 (12 pm- 6 pm)	3-7	None
2/15/19	3.5 (8:30 am- 12 pm)	4-6	None
2/23/19	6 (5 pm- 11 pm)	3-7	None
2/24-25/19	5 (8 pm- 1 am)	3-6	None
2/26/19	5 (8 am- 1 pm)	4-6	None
2/27/19	5 (5 pm- 10 pm)	5	None
2/28/19	4 (2 pm- 6 pm)	3-6	None

DHQ Results

The results from the DHQ showed that over the course of the study, the participant decreased his consumption of energy (kcals) and all macronutrients. His consumption of overall sugar decreased. His vegetable intake stayed the same, but fiber intake decreased slightly. He had some difficulty consuming enough food, especially protein. Table 4.40 gives the macronutrient levels of the concern nutrients involving a GFD.

Table 4.40 DHQ Data

Micronutrients	RDA (males)	Month 1 (gluten)	Month 4 (GF)
Fiber (g/d)	38	14.9	11.9
Vitamin C (mg/d)	90	47	59.5
Vitamin D (mcg/d)	15	2.87	4
B_{12} (mcg/d)	2.4	3.3	3.5
Folate (mcg/d)	400	323	314.1
Calcium (mg/d)	1000	649.3	585.9
Zinc (mg/d)	11	9.6	7.5
Magnesium (mg/d)	400	258.2	185.9

RDA: recommended dietary allowances; G: grams; D: day; Mg: milligrams; Mcg: micrograms; GF: gluten-free

Follow-up

A follow-up questionnaire (Appendix H) which was aimed at gathering uniform information from all the participants was issued after the conclusion of the study. At the conclusion of the study, participant 6 reported that his stress levels during the course of this study were moderate. He thought that skipping meals or fasting could sometimes trigger a migraine, but not on a consistent basis. When he was asked of any potential migraine triggers he discovered during the study, he responded that stress, screen time, and anxiety were all additional triggers for his migraines.

Discussion

Of the six participants, five were female and one was male. All participants were less than 35 years of age. Five participants were enrolled in a 4-year university. Four of the six participants indicated some background in nutrition.

In the research conducted by Özön et al. (2018) and Rockett et al. (2012a), they both discussed stress being a potential trigger for migraines. Rockett et al. (2012a) continued to emphasize the effect of lifestyle factors contributing to migraines stating, "Although a wide variety of prophylactic medications is available for headaches, most patients do not show a significant decrease in frequency and severity of symptoms without appropriate changes in their lifestyle. These changes include dietary alterations, regular aerobic exercise and sleep, and stress monitoring" (Rockett et al., 2012a). The stress of being a student, undergraduate or graduate, could have been a contributing factor for the participants' migraines. All the student-participants reported that their stress levels during the course of this study were moderate to high. Over the course of the research study, some of the participants began to question the causation of their

migraines. As previously mentioned, many of the participants identified personal triggers during the course of the research study. It is known that individuals may have multiple triggering factors, especially food, for their migraine attacks (Özön, Karadaş, & Özge, 2018). All participants had a reduction in migraine occurrence, the direct effect of the gluten free diet will be discussed.

Aim 1: Can a gluten free diet decrease the incidence of migraines in migraine sufferers?

The main objective and first aim of this research was to determine if a GFD can help decrease the incidence of migraines in chronic migraine sufferers. Due to the limited amount of data available, this hypothesis cannot be tested. All participants had a reduction of migraines during the study. It was anticipated that, during the reintroduction of gluten in month five, participants would experience an increase in the frequency, severity, or duration of migraine; however, only two participants noted an increase during this period. It is important to note that individuals often have more than one migraine trigger, and since this study was conducted over a 5-month period, participants may have identified triggers over the course of the study. These discoveries may have led to lifestyle changes, intentional or unintentional, which could have affected the overall results, including the re-introduction period. As shown in table 4.1, participants 3-6 had an overall decrease in the duration of migraines during the first four months of the study. It should be noted that participant 2 had an increase in month 4 due to a single migraine lasting 96 hours, which was unusual compared to the rest of the migraine days. As shown in table 4.2, all participants, excluding number six, had a decrease in severity; however,

the average decrease was marginal, at less than or equal to 1.3 points on the VAS, as shown on table 4.3

Table 4.1 Number of migraines per month

	Month 1	Month 2	Month 3	Month 4	Month 5
Participant 1	7	2	4	4	5
Participant 2	6	10	4	7	0
Participant 3	5	2	2	2	2
Participant 4	1	1	0	0	0
Participant 5	1	2	0	0	0
Participant 6	10	6	6	4	7

Table 4.2 Average duration of migraines

	Month 1	Month 2	Month 3	Month 4	Month 5
Participant 1	5.1	4	7.5	5	3.8
Participant 2	17.2	14.8	6.8	29	0
Participant 3	3.1	2.5	5.75	3	3
Participant 4	8	4	0	0	0
Participant 5	1	1	0	0	0
Participant 6	3.9	4.2	3.8	3	4.9

Duration of migraines are documented in hours.

Table 4.3 Average severity of migraines

	Month 1	Month 2	Month 3	Month 4	Month 5
Participant 1	5.4	6	5	4.75	5.9
Participant 2	6	5	4.6	5.25	0
Participant 3	4.8	5.5	4	3.5	2.5
Participant 4	6	7	0	0	0
Participant 5	8	8	0	0	0
Participant 6	4.35	5.3	5.8	5.5	4.4

Severity of migraines are according to the VAS, which is on a scale of 1-10.

While the participants were asked to maintain a strict GFD, there were still some accidental exposures. Participant 1 had the greatest amount of exposures due to eating on campus where food was incorrectly labeled. In addition, she traveled to a third world country during spring break for a mission trip where meal choices were limited. While she tried to maintain a GFD while in a foreign country, it was difficult for her to verify the contents of the food consumed as gluten-free. Due to that, it is impossible to know the true effect of gluten on her digestive and nervous system. It is difficult to determine the efficacy of a GFD for Participant 2 due to beginning the prophylactic treatment near the beginning of the study as well as beginning an exercise program in the middle of the study. Post research feedback indicates that despite her continual prophylactic treatment, she is under the impression that it is not effective. It is the researcher's belief that her improvement was due to her developing attention to lifestyle factors. The researcher is inclined to believe that gluten could be a potential migraine trigger for Participant 3. Her migraines decreased greatly during the gluten-free period. However, the migraines did not increase during the gluten re-introduction. It is possible Participant 3 identified additional triggers to her migraines which could indicate why her migraines did not increase during month 5. The researcher spoke with Participant 4 at the conclusion of the study to discuss the potential reason for the reintroduction period not having any effect. During the study, the participant realized her lack of hydration status on a daily basis. Once she began to drink water on a more consistent basis, her migraines were consistently fewer, and eventually, nonexistent. Participant 5 realized in the course of the study that when she drank alcohol, she frequently had migraines. When she drank very little to none, her migraines decreased also. Participant 6 had a 33% decrease in his

migraines over the course of the first four months. He reported that within a few days of beginning the re-introduction period, he could tell the difference by the way his body was reacting to the food change.

In conclusion, based on the variety of responses in conclusion to the research study, the specific effect of gluten on migraines cannot be determined.

Aim 2: Can a GFD positively impact body composition, blood pressure, and glucose levels in migraine sufferers?

The second aim to the research study was to determine if a GFD can positively impact body composition, blood pressure, and glucose levels. Blood pressure, fasting glucose, and non-fasting glucose measurements were taken, but none varied significantly during the research study. With regard to body composition, the researcher examined the participants' body fat percentage (BF%), weight (lbs), and fat free mass (FFM). Participant 1 reduced BF%, weight, and increased her FFM over the course of the study. Participants 2 and 4 gained BF% while on a GFD. Participant 2 lost 0.4% in the fifth month. Participants 3, 5, and 6 all lost BF% during the gluten free period, and Participants 3-5 gain BF% in the fifth month. Participant 6 decreased his BF%, weight and FFM over the course of the study. While the weight loss was intentional, the participant had difficulty maintaining FFM, partially due to a lack of adequate calories and lack of a consistent physical activity regimen. Participants 2-4 gained weight during the gluten free period, and 1-3 gained FFM. Participants 1, 5, and 6 all lost weight during the research study.

In conclusion, it is impossible to interpret the body composition effects of a gluten free diet since several participants did not adhere to a strict GFD over the course of

the study along with the presence of external factors such as increased exercise and nutrition changes not part of this study.

Table 4.4 Body Fat Percentage

	Month 1 BF%	Month 2 BF%	Month 3 BF%	Month 4 BF%	Month 5a BF%	Month 5 b BF%
Participant 1	25.9	26.6	24.7	24.9	24.3	23.4
Participant 2	16	18.4	17.8	19.8	19.3	18.9
Participant 3	14.4	13.5	13.7	15	12.6	15.9
Participant 4	22.6	26.1	26.8	26.3	27.9	28
Participant 5	35.3	35.3	35.4	34.8	34.8	35.4
Participant 6	21.2	21.7	19.1	18.4	17	14.6

Body fat percentage measurements during each month of the study. A and B in month 5 indicate the meeting at the beginning of the month and then at the conclusion of the study.

Table 4.5 Weight (in lbs)

	Month 1 (wt in lbs)	Month 2 (wt in lbs)	Month 3 (wt in lbs)	Month 4 (wt in lbs)	Month 5a (wt in lbs)	Month 5 b (wt in lbs)
Participant 1	139	139.4	136.2	136.8	137.8	139.6
Participant 2	101	104	105.4	107	109	109.4
Participant 3	104	105	103.6	104.2	105	106.4
Participant 4	129	132.8	132	129	138.2	137
Participant 5	152.4	155.6	153	148.6	147.8	147.6
Participant 6	170.4	171.8	164.6	161.2	155	15.3

Weight measurements during each month of the study. A and B in month 5 indicate the meeting at the beginning of the month and then at the conclusion of the study.

Table 4.6 Fat Free Mass (%)

	Month 1 (%)	Month 2 (%)	Month 3 (%)	Month 4 (%)	Month 5a (%)	Month 5 b (%)
Participant 1	73.4	73.3	75.3	75.1	75.8	76.6
Participant 2	84	81.5	82.2	80	80.7	81.2
Participant 3	86	86.5	86.3	85	87	84
Participant 4	77.4	74	73	73.6	72	72
Participant 5	64.7	64.7	74.6	65.1	65.2	64.6
Participant 6	78.8	78.4	80.9	81.6	82.9	85.4

FFM% from the beginning of the research study to the end of the research study.

The participants were instructed to complete the DHQ in order to evaluate their dietary choices while gluten-free versus being allowed to eat gluten. As referenced earlier, there are some concerns of acquiring nutritional deficiencies while on a GFD. When evaluating the results of each participant's DHQ and those aforementioned micronutrients, the data from the case studies in this research study suggests that following a GFD does not necessarily lead to a nutrient deficiency due to eliminating gluten from the diet, especially if the individual is implementing a variety of foods, including vegetable intake. Participant 1's results showed that she met the RDA requirement for fiber, vitamin C, B_{12}, folate, calcium, iron, and magnesium while she was consuming either a GFD or gluten-containing diet. Results of the questionnaire showed that this participant increased calcium and magnesium intake while on a GFD. Vitamin D was the only nutrient, which did not meet the requirement regardless of diet. Participant 2 did not meet any of the RDA requirements for either diet period. It is important to note that while consuming a GFD, her estimated intake of fiber, B_{12}, folate, calcium, and iron were similar to her estimated intake during her gluten-containing period. Participant 4's results are more difficult to judge since she began with an unusually low caloric intake and ended with an even lower intake. Her results showed that she did not meet RDA

requirements during either diet period. Participant 5 also had slightly unusual reported caloric intake which might affect the results. For vitamin C, she met the RDA requirement while consuming gluten, while her intake of vitamin C dropped during the GFD period. Similar occurrences are observed with folate, and magnesium. However, she met both goals for B_{12} in both diet periods. While she did not meet the requirements for calcium in either diet period, she was able to increase the levels during the GFD period. Participant 6 did not meet any of the RDA requirements for any of the nutrients except for B_{12}. However, he was able to increase the levels of vitamins C and D during the GFD period.

Aim 3: Is there a level of gluten which is tolerated without experiencing migraines in sensitive individuals?

The third aim of the study was evaluating if a level of gluten can be tolerated without experiencing migraines from the sensitive individual. Only Participants 1 and 6 showed a changed in migraines during the reintroduction period. It is difficult to determine the true effect of the reintroduction period for Participant 1 since she had several accidental exposures to gluten. For Participant 6, the quantity of his migraines increased by more than double of his results from the gluten free period. Both Participant 1 and Participant 6 did not have a major increase of migraines until the third and fourth week of the re-introduction periods, when they were consuming 10 grams of gluten per day and 20 grams of gluten per day, respectively. For participant 1, they were slightly more spread out over the two-week period, but for participant 6, he had migraines two days in a row, skipped a day, and then again for three more days in a row in the last week of the re-introduction.

Limitations

There are several limitations to this research study. The sample size is small. Despite the recruitment efforts of the researcher and maintaining two different data collection locations, it proved difficult to obtain a sufficient sample size for the study.

It is difficult to know if participants were accurate with respect to their DHQ's, adherence to a GFD diet, or recording and reporting of all gluten exposures.

Another potential limitation is the accuracy of each participant's migraine journal. Any migraine treatment medication could affect the duration and/or severity of the migraines, which could create an inaccurate representation of average migraine duration hours. Since the VAS is subjective and based on each individual's perception of pain, these results must be viewed as an overall increase or decrease by the individual participant. Furthermore, since multiple triggers are commonly reported by migraineurs, it is important to consider other dietary, environmental, and hormonal triggers, beyond gluten.

Any lifestyle changes that the participants made during the study could have also affected the results. Given the length of the study, it is possible that participants may not have realized these were changes that could affect their participation in the study.

It was difficult for the researcher to adequately convey to participants the importance of adhering to the GFD and how deviation may affect the results of the study.

For future studies, it might be recommended to implement serological testing periodically to help keep participants accountable for any gluten intake. It is also possible that the initial dose of gluten during the re-introduction phase was too low and perhaps a

higher amount, i.e. 20 grams/day, would be more appropriate considering the estimated average intake of gluten in the Western diet (Pascua & Leno, 2005).

Body composition measurements have potential for inaccuracy due to human error and lack of standardized timing and conditions of the measurements. Due to the variety of participants' schedules, it was impossible to meet with them at the same same time of day each month. For future studies, it would be helpful to note menstrual cycles since this can influence water weight, body composition and potential for migraines.

CHAPTER V

CONCLUSION

The purpose of this study was to determine the efficacy of a gluten free diet on individuals with chronic migraines. Additional information regarding their body composition, diet history, blood pressure, and blood glucose levels were also gathered. Due to the low number of participants, the researcher decided to examine the results from a case study point of view. Individually, during the 5-month study each participant's number of migraines decreased; however, it is impossible to conclude if the change can fully be attributed to a GFD. Participant 6's migraines decreased greatly in the gluten-free period of three months, as well as being able to lose weight. He also admitted to feeling better overall after going gluten free. During the gluten re-introduction period, participant 6's migraines increased during the last week of the gluten re-introduction.

It is evident there is more research needed in the area of migraines and triggers. The pathology of NCGS has many hypotheses which needs further evaluation to understand the underlying mechanisms. The diagnosis criteria have developed over the years, but without a definitive standard method, it is difficult to determine if a person truly has NCGS. While this study has a variety of limitations, some of which can be controlled and others that cannot, there is an opportunity for this study to aid future research regarding migraines and dietary triggers.

REFERENCES

Alpay, K., Ertas, M., Orhan, E.K., Üstay, E.K., Leiners, C., & Baykan, B. (2010). Diet restriction in migraine, based on IgG against foods: a clinical double-blind, randomized, cross-over trial. *Cephalalgia, 30* (7), 829-837. doi: 10.1177/0333102410361404.

Balakireva, A. V. & Zamyatnin Jr., A.A. (2016). Properties of gluten intolerance: gluten structure, evolution, pathogenicity and detoxification capabilities. *Nutrients,8*, 644. doi: 10.3390/nu8100644.

Biesiekierski, J.R. & Iven, J. (2015). Non-coeliac gluten sensitivity: piecing the puzzle together. *United European Gastroenterology Journal, 3*(2), 160-165. doi: 10.1177/2050640615578388.

Biesiekierski, J.R. (2017). What is gluten? *Journal of Gastroenterology and Hepatology, 32*, 78-81. doi: 10.1111/jgh.13703.

Bunner, A.E., Agarwal, U., Gonzales, J.F., Valente, F., & Barnard, N.D. (2014). Nutrition intervention for migraine: a randomized crossover trial. *The Journal of Headache and Pain, 15*(69). doi: 10.1186/1129-2377-15-69.

Burstein, R., Noseda, R., & Borsook, D. (2015). Migraine: Multiple, Processes, Complex Pathophysiology. *The Journal of Neuroscience, 35*(17), 6619-6629. doi: 10.1056/NEJMcp1605502.

Corbelli, I. et al. (2012). Migraine with aura in the locker room: three case reports. *Journal of Headache Pain, 13,* 91-93. doi: 10.1007/s10194-011-0369-6.

Czaja-Bulsa, G. (2015). Non coeliac gluten sensitivity – a new disease with gluten intolerance. *Clinical Nutrition, 34*, 189-194. doi: 10.1016/j.clnu.2014.08.012.

Ford, Rodney P.K. (2009). The Gluten Syndrome: A Neurological Disease. *Medical Hypotheses.* doi: 10.1016/j.mehy.2009.03.037.

Gooriah, R., Nimeri, R., & Ahmed, F. (2015). Evidence-Based Treatments or Adults with Migraine. *Pain Research and Treatment,* 1-13. doi: 10.1155/2015/6293382.

Hadjivassilou, M et al. (2006). Neuropathy Associated with Gluten Sensitivity. *J Neurol Neurosurg Psychiatry*; *77*: 1262-1266. doi: 10.1136/jnnp.2006.093534.

Headache Classification Committee of the International Headache Society (IHS). (2018). The International Classification of Headache Disorders. *Cephalgia,38*(1), 1-211. doi: 10.1177/0333102417738202.

Leccioli, V., Oliveri, M., Romeo, M., Berretta, M., & Rossi, P. (2017). A new proposal for the pathogenic mechanism of non-coeliac/non-allergic gluten/wheat sensitivity: piecing together the puzzle of recent scientific evidence. *Nutrients, 9*, 1203. doi: 10.3390/nu9111203.

Lionetti, E., Pulvirenti, A., Vallorani, M., Catassi, G., Verma, A.K., Gatti, S., & Catassi, C. (2017). Re-challenge studies in non-celiac gluten sensitivity: a systematic review and meta-analysis. *Frontiers in Physiology, 8*, 621. doi: 10.3389/fphys.2017.00621.

Liu, Z. & Udenigwe, C.C. (2019). Role of food-derived opioid peptides in the central nervous and gastronintestinal systems. *Journal of Food Biochemistry, 43*. doi: 10.1111/jfbc.12629.

Losurdo, G. et al. (2018). Extra-intestinal manifestations of non-celiac gluten sensitivity: an expanding paradigm. *World Journal of Gastroenterology, 24*(14), 1521-1530. doi: 10.3748/wjg.v24.i14.1521.

Martin, B.R. & Seaman, D.R. (2015). Dietary and Lifestyle Changes in the Treatment of a 23-Year-Old Female Patient with Migraine. *Journal of Chiropractic Medicine* (14), 205-211. doi: 10.101/j.jcm.2015.09.001.

Nijeboer, P., Bontkes, H.J., Mulder, C.J.J., a&nd Bouna, G. (2013) Non-celiac gluten sensitivity. Is it in the gluten or the grain? *J Gastrointestin Liver Dis, 22*(4), 435-40. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/24369326.

Pascual, J. & Leno, C. (2005). A woman with daily headaches. *Journal of Headache Pain(*9), 1-92. doi: 10.1007/s10194-005-0158-1.

Rockett, F.C., Castro, K., de Oliveira, V.R., da Silveira A., Chaves, M.L.F., & Perry, I.D.S. (2012a). Perceived migraine triggers; do dietary factors play a role? *Nutr Hosp. 27(*2), 483-489. doi: 10.3305/nh.2012.27.2.5512.

Rockett, F.C., de Oliveira, V.R., Castro, K., Chaves, M LF, Perla, A.S., & Perry, I.DS. (2012b). Dietary Aspects of Migraine Trigger Factors. *Nutrition Reviews* 70(6), 337-356. doi: 10.1111/j.1753-4887.2012.00468.x.

Semenov, Irene A. (2015). Migraine Headaches. *Disease-a-month, 61,* 218-222. doi: 10.1016/j.disamonth.2015.03.003.

Sources of Gluten. (n.d.). Retrieved from https://celiac.org/gluten-free-living/what-is-gluten/sources-of-gluten/.

Zioudrou, C., Streaty, R.A., & Klee, W.A. (1979). Opioid peptides derived from food proteins. The exorphins. *The Journal of Biological Chemistry, 245*(7), 2446-2449. Retrieved from http://www.jbc.org/content/254/7/2446.full.pdf+html.

Zis, P., Julian, T., & Hadjivassiliou, M. (2018). Headache associated with coeliac disease: a systematic review and meta-analysis. *Nutrients, 10*, 1445. doi: 10.3390/nu10101445.

Özön, A.Ö., Karadaş, Ö., & Özge, A. (2018). Efficacy of diet restriction on migraines. *Arch Neuropsychiatry, 55*, 233-237. doi: 10.5152/npa.2016.15961.

APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

MISSISSIPPI STATE UNIVERSITY

Office of Research Compliance

Institutional Review Board for the Protection of Human Subjects in Research
P.O. Box 6223
53 Morgan Avenue
Mississippi State, MS 39762
P. 662.325.3294

www.orc.msstate.edu

NOTICE OF APPROVAL FOR HUMAN RESEARCH

DATE:	July 06, 2017
TO:	Terezie Mosby, Food Sci Nutrition Hlth Promo, Brent Fountain;Diane Tidwell
FROM:	Kari Reeves, Assoc Dean/Assoc Prof, MSU Expedited
PROTOCOL TITLE:	A study to determine if a gluten free diet can help relieve migraines in chronic migraine patients
PROTOCOL NUMBER:	IRB-17-095
APPROVAL PERIOD:	Approval Date: July 06, 2017 Expiration Date: June 15, 2018

Under an expedited review procedure, the research project identified above was approved for one year on July 06, 2017 by the Mississippi State University Institutional Review Board (MSU IRB). The application qualified for expedited review under CFR 46.110, Category 2.

This memorandum is your record of the IRB approval of this study. Please maintain it with your study records.

Please note that the MSU HRPP accreditation for our human subjects protection program requires an approval stamp for consent forms. The approval stamp will assist in ensuring the HRPP approved version of the consent form is used in the actual conduct of research. **If applicable, you must use the stamped consent form for obtaining consent from participants.**

The MSU IRB approval for this project will expire on June 15, 2018. If you expect your project to continue beyond this date, you must submit an application for renewal of this HRPP approval. HRPP approval must be maintained for the entire term of your project.

If, during the course of your project, you intend to make changes to this study, you must obtain approval from the HRPP prior to implementing any changes. Upon becoming aware of an unanticipated problem that suggests participants or others are at greater risk of harm than was previously known or recognized, a problem report must be submitted to the HRPP as soon as possible, but always within 10 days. Serious problems must be reported verbally within one business day, in addition to the submission of the written Problem Report.

You are required to maintain complete records pertaining to the use of humans as participants in your research. This includes all information or materials conveyed to and received from participants as well as signed consent forms, data, analyses, and results. These records must be maintained for at least three years following project completion or termination, and they are subject to inspection and review by the HRPP and other authorized agencies.

Please notify this office when your project is complete. Upon notification, we will close our files pertaining to your project. Reactivation of the HRPP approval will require a new HRPP application.

If you have any questions relating to the protection of human research participants, please contact the HRPP by phone at 325.3994 or email irb@research.msstate.edu. We wish you the very best of luck in your research and look forward to working with you again.

Kari Reeves

Approval Period:	July 06, 2017 through June 15, 2018
Review Type:	EXPEDITED
IRB Number:	IORG0000467

APPENDIX B

HIT QUESTIONNAIRE

HIT-6™ Headache Impact Test

HIT is a tool used to measure the impact headaches have on your ability to function on the job, at school, at home and in social situations. Your score shows you the effect that headaches have on normal daily life and your ability to function. HIT was developed by an international team of headache experts from neurology and primary care medicine in collaboration with the psychometricians who developed the SF-36® health assessment tool. This questionnaire was designed to help you describe and communicate the way you feel and what you cannot do because of headaches.

To complete, please circle one answer for each question.

When you have headaches, how often is the pain severe?

never ▽ rarely ▽ sometimes ▽ very often ▽ always ▽

How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?

never ▽ rarely ▽ sometimes ▽ very often ▽ always ▽

When you have a headache, how often do you wish you could lie down?

never ▽ rarely ▽ sometimes ▽ very often ▽ always ▽

In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?

never ▽ rarely ▽ sometimes ▽ very often ▽ always ▽

In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?

never ▽ rarely ▽ sometimes ▽ very often ▽ always ▽

In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

never ▽ rarely ▽ sometimes ▽ very often ▽ always ▽

☐ +	☐ +	☐ +	☐ +	☐
COLUMN 1 6 points each	COLUMN 2 8 points each	COLUMN 3 10 points each	COLUMN 4 11 points each	COLUMN 5 13 points each

To score, add points for answers in each column.

If your HIT-6 is 50 or higher:

You should share your results with your doctor. Headaches that stop you from enjoying the important things in life, like family, work, school or social activities could be migraine.

☐ TOTAL SCORE

APPENDIX C

MIDAS QUESTIONNAIRE

The Migraine Disability Assessment Test

The **MIDAS** (Migraine Disability Assessment) questionnaire was put together to help you measure the impact your headaches have on your life. The information on this questionnaire is also helpful for your primary care provider to determine the level of pain and disability caused by your headaches and to find the best treatment for you.

INSTRUCTIONS

Please answer the following questions about ALL of the headaches you have had over the last 3 months. Select your answer in the box next to each question. Select zero if you did not have the activity in the last 3 months. Please take the completed form to your healthcare professional.

_____ 1. On how many days in the last 3 months did you miss work or school because of your headaches?

_____ 2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school.)

_____ 3. On how many days in the last 3 months did you not do household work (such as housework, home repairs and maintenance, shopping, caring for children and relatives) because of your headaches?

_____ 4. How many days in the last 3 months was your productivity in household work reduced by half of more because of your headaches? (Do not include days you counted in question 3 where you did not do household work.)

_____ 5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?

_____ Total (Questions 1-5)

What your Physician will need to know about your headache:

_____ A. On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day.)

_____ B. On a scale of 0 - 10, on average how painful were these headaches? (where 0=no pain at all, and 10= pain as bad as it can be.)

Scoring: After you have filled out this questionnaire, add the total number of days from questions 1-5 (ignore A and B).

MIDAS Grade	Definition	MIDAS Score
I	Little or No Disability	0-5
II	Mild Disability	6-10
III	Moderate Disability	11-20
IV	Severe Disability	21+

If Your MIDAS Score is 6 or more, please discuss this with your doctor.

APPENDIX D

MIGRAINE JOURNAL/DIARY

MIGRAINE JOURNAL

Date	Time & Duration	Intensity*	Food & Drinks 24 Hours Prior	Location	Symptoms**	Other Notes***

*Pain scale 1-10: 1 (hardly hurts, easy to ignore), 5 (hard to ignore, but bearable), 10 (ready to go to the ER)

** Any auras; sensitivity to light, smell, or sound; nausea; vomiting; tenderness in the neck and scalp skin and/or muscles, etc.

If you have further comments that cannot fit into the box, please continue to write on the backside of this page but be sure to indicate the date of occurrence with the information.

APPENDIX E

FIRST RECRUITMENT ADVERTISEMENT

Poster ad:

Are you a chronic migraine sufferer?

We would love to invite you to join this study and perhaps we can help you! This is a research study to see if just changing your diet will decrease, or perhaps eliminate, your migraines – no pharmaceuticals needed! Information you need to know is below:

You must be:

- 18 years old and above
- Sufferer of chronic migraines (which will be confirmed by our evaluation tools)
- Ability and willingness to complete all parts of the study (Diet History questionnaire (DHQ), body composition measurements, blood glucose testing, blood pressure measurement, headache diary, and gluten free diet)

You cannot:

- Have a confirmed diagnoses of Celiac Disease by blood test and/or intestinal biopsy
- Less than 18 years of age
- Be pregnant
- Inability of reading or writing in English
- People with chronic disease need permission from their primary physician
- Have migraines due to menstrual cycles

This study will take place over the course of 5 months. You will be asked to come to Mississippi State University to take measurements once per month. You also will be asked to partake in a complete gluten free diet during the majority of this study. *Being able to comply with all the parts of this study, including being completely gluten free for 3 months, is the key!*

Potential benefits from this study is a partial to complete reduction to your chronic migraines in addition to possible benefits to your overall wellness, blood pressure, blood glucose, and body composition.

If you have questions and would be interested in participating, please contact the study coordinator:

Kristen Ensor
Phone: 662.341.6413
E-mail: kensor601@gmail.com

APPENDIX F

SECOND RECRUITMENT ADVERTISEMENT

Are you a chronic migraine sufferer?

MSU HRPP Full Review/Exempt | Approved: 10/1/18 | Expires: 5/15/19 | IRB # 17-095

Will you participant in this research study to see if we can help reduce your migraines?! No pharmaceuticals needed!

You must be:
- ◊≥18 years old
- ◊Sufferer of chronic migraines
- ◊Ability and willingness to complete all parts of the study

You cannot:
- ◊Have a confirmed diagnoses of Celiac Disease
- ◊Be pregnant
- ◊<18 years of age
- ◊Unable to read or write in English
- ◊Migraines due to menstrual cycles
- ◊Already eating a gluten free diet

This study will take place over the course of 5 months. You will be asked to come to the University of your choosing (to take measurements once per month) or you can participate long-distance (no measurements involved). You also will be asked to partake in a complete gluten free diet during the majority of this study.

Participating Universities:
-Mississippi State University
-Mississippi University of Women

Measurements involved:
-Blood pressure
-Blood glucose
-Body composition

Potential benefits

- Decrease occurrence of migraines
- Improved overall wellness
- Improved body composition
- Improved blood glucose
- Improved blood pressure

If you have questions and would be interested in participating, please contact the study coordinator:

Kristen Ensor
Phone: (662-341-6413)
E-mail: kensor601@gmail.com

APPENDIX G

GLUTEN PACKET

What is Gluten?

"Gluten is a general name for the proteins found in wheat (wheatberries, durum, emmer, semolina, spelt, farina, farro, graham, KAMUT® khorasan wheat and einkorn), rye, barley and triticale – a cross between wheat and rye. Gluten helps foods maintain their shape, acting as a glue that holds food together. Gluten can be found in many types of foods, even ones that would not be expected."
Read more at https://celiac.org/live-gluten-free/glutenfreediet/what-is-gluten/#Ozs2plsVJGARQa7w.99

- The most common ingredients you will see is wheat, barley and rye.
- You MUST be vigilant with reading ingredient labels. Usually it will say "contains: wheat" if there's wheat in there, but read through the ingredients regardless. If it says "certified gluten free" then you can know that it's perfectly safe to eat (note: does not also include if it is labeled as "wheat free", if so, you still need to read the label)
- Oatmeal. Technically it doesn't fall under the gluten label, but it is usually grown/processed in locations the same as wheat so it needs to be specifically labeled as gluten free if you're going to eat it.
- Be careful for cross contamination. If you go out to eat, just tell the server that you need a GF menu and the food needs to be GF. Don't be afraid to ask if something is GF! It is becoming much more common in the last few years.
- I know eating GF for the first time is intimidating, but I want to make it as easy as possible. Once you know what to look for and find things you like, it becomes much easier. If you ever have questions about food items please call, text or email me!
- Sometimes items will say they are gluten free or just don't have wheat in the ingredients, but the label states that they were produced in a facility or on the same equipment as wheat. If that's the case, it is best to avoid those items from that brand.

Common Foods Containing Gluten (and what you can eat instead)

1. Pastas (there are gluten free made noodles, usually uses mostly rice flour)
2. Noodles (there are GF options, also could use zucchini or spaghetti squash)
3. Breads and Pastries
4. Crackers
5. Baked Goods
6. Cereal & Granola
7. Breakfast Foods
8. Breading and Coating mixes
9. Croutons
10. Sauces and Gravies (often wheat flour is used as thickener, look for arrowroot powder or antahn gum)
11. Flour tortillas (corn tortillas are an option as well as specific GF tortillas)
12. Beer (aim for GF and try to avoid gluten reduced kinds. E.g. Buck Wild Pale Ale, Rustic Badger, Hollywood Nights, Copperhead, Kickback, Headless Imperial Pumpkin Ale, Sunset Belgian Tripel, Bard's Gold, Redbridge Lager). Some beers are naturally gluten free, you can look up https://www.celiac.com/articles.html/safe-gluten-free-food-list-unsafe-foods-

amp-ingredients/gluten-free-alcoholic-beverages-r218/ for more specific information regarding any alcoholic beverage and gluten free.
**Wines and hard liquor/distilled beverages are usually gluten-free. **
another source in regards to other alcoholic beverages:
http://celiacinthecity.weebly.com/gluten-free-diet.html

13. Brewer's yeast

Foods That Might Contain Gluten (read the labels!)

1. Energy bars (watch for oats that aren't GF)
2. French Fries
3. Potato Chips
4. Processed Lunch Meats
5. Candy and Candy Bars
6. Soups (watch the cream based ones)
7. Multi-grain or "artesian" tortilla chips (go for corn tortilla chips)
8. Salad dressings and marinades (watch for malt vinegar, soy sauce and flour)
9. Starch or dextrin (Unless it specifies it's not from wheat)
10. Brown rice syrup
11. Meat substitutes (i.e. vegetarian burgers, imitation foods)
12. Soy Sauce (tamari or coconut aminos are soy sauce substitutes that are GF)
13. Self-basting poultry
14. Pre-seasoned meats
15. Cheesecake filling
16. Eggs served at restaurants – some restaurants put pancake batter in their scrambled eggs and omelets, but on their own, eggs are naturally gluten-free
17. Herbal or nutritional supplements
18. Vitamins and supplements

While there is a rather long list of things to avoid and look out for, there are still PLENTY options of **things you CAN eat**!

1. Fresh (unbreaded, batter coated, or marinated) meats, poultry and seafood
2. Fresh fruit and vegetables
3. Beans, nuts and seeds (if pre-seasoned, make sure to check the label
4. Majority of dairy product (e.g. if ice cream has something mixed in, make sure it's GF)
5. Certified Gluten Free pre-made food items (breads, pastas, crackers, cookies, etc)
6. GF baking mixes (pancakes, brownies, cornbread, etc)

If you accidently eat some gluten, don't finish the food, record *what* you ate and *how much* and *when* you ate it!!

Restaurants & Eating GF

- Definitely feel free to check with the restaurant first! Also, there's always the possibility your server doesn't know about being GF and you may have to talk to a manager.
- They may not have an extra menu for just GF items, but you can still ask which items on the regular menu are GF.

Ready-Made GF Foods (brands**)

Keep in mind, this is not an exhaustive list, but a decent one of the foods provided at the Columbus Kroger. Other grocery stores may have more or less options.

Breakfast

1. Waffles – Van's, Eggo GF Waffles, Kashie
2. Pancake Mixes – Pamela's, Among Friends, Bob's Red Mill
3. Breads – Rudi's
4. Cereals – Love Grown, Mom's Best, Nature's Path, Chex, Cheerios, Lucky Charms, Special K GF Cereal Touch of Brown Sugar, Kashi (Simply Maize, Indigo Morning, Clusters- Vanilla Pepita)
5. Applegate Breakfast Sausage

Lunch Items

1. Sandwich meats – most are okay, just check for additives
2. Crackers – Van's, Absolutely, Glutino, Harvest Stone, RW Garcia
3. Frozen meals – Love (spelled backwards), Amy's Cooked Perfect, Lean Cuisine
4. BBQ sauce – Sweet Baby Rays

Dinner

1. Frozen Pizzas – Udi's, Sonoma, Amy's
2. Applegate (brand) – Chicken nuggets, corn dogs, chicken tenders
3. Quorn (brand)
4. Pastas – Jovial, Pow!, Simple Truth Organic
5. Mac & Cheese – Horizon, Daiya
6. Bob's Red Mill – Pizza crusts, corn bread mixes, bread mixes, baking flour
7. Pamela's – Brownie mixes, Cornbread mixes, baking mix
8. Among Friends – Cake mix

Snacks

1. Granola bars – Nature's valley, Nutri Gain Fruit & Nut Bars, Special K Nourish Chewy Nut Bars, Kashi (Salted Dark Chocolate & Nuts, Dark Chocolate Cashew Chia Plant Powered Bars, Basil White Bean & Olive Oil Savory Bars, Quinoa Corn & Roasted Pepper Savory Bars)
2. Pudding
3. Applesauce
4. Popcorn
5. Chips: Doritos, corn tortilla chips, ruffles, fritos, Cheetos, most Lays, Cape Cod, Kettle Brand, Terra potato chips, Way Better multigrain chips, Special K Popcorn Chips

Alcoholic Beverages

1. Angry Orchard
2. White Claw Hard Seltzer
   **There are others that I am continually finding out about. Just check labels and make sure it says gluten free (avoid those that say gluten reduced).

**Make sure to check labels regardless of the brands listed here. Some of the brand do not exclusively sell GF items, but a mixture, so make sure what you are getting is actually GF.

APPENDIX H

POST-STUDY QUESTIONS

Does any of your immediate family have a history of migraines (chronic or otherwise)?

Does any of your immediate family have a history of IBS or any other gastrointestinal issues?

How old were you when your migraines started? (or your best guess)

Do you ever experience auras, what symptoms do you usually experience? They typically last anywhere from 5 minutes to one hour prior to a migraine, symptoms can be visual (spots in vision, squiggly lines, etc), sensory (extra skin sensitivity) or speech (difficulty speaking/getting words out, stuttering) symptoms.

During the study, did you take any preventative medications for your migraines?

During the study, did you take any medications at the onset of a migraine? If so, what did you take and average dose?

How were your stress levels for the duration of the study?

Is it common for you to get a migraine after you have been fasting for several hours/skipped a meal?

Did you discover any potential other triggers during the study?