

Diet and autism: no gluten, no casein, no difference?

*The Gluten-Free/Casein-Free Diet:
A Double-Blind Challenge Trial in
Children with Autism* 



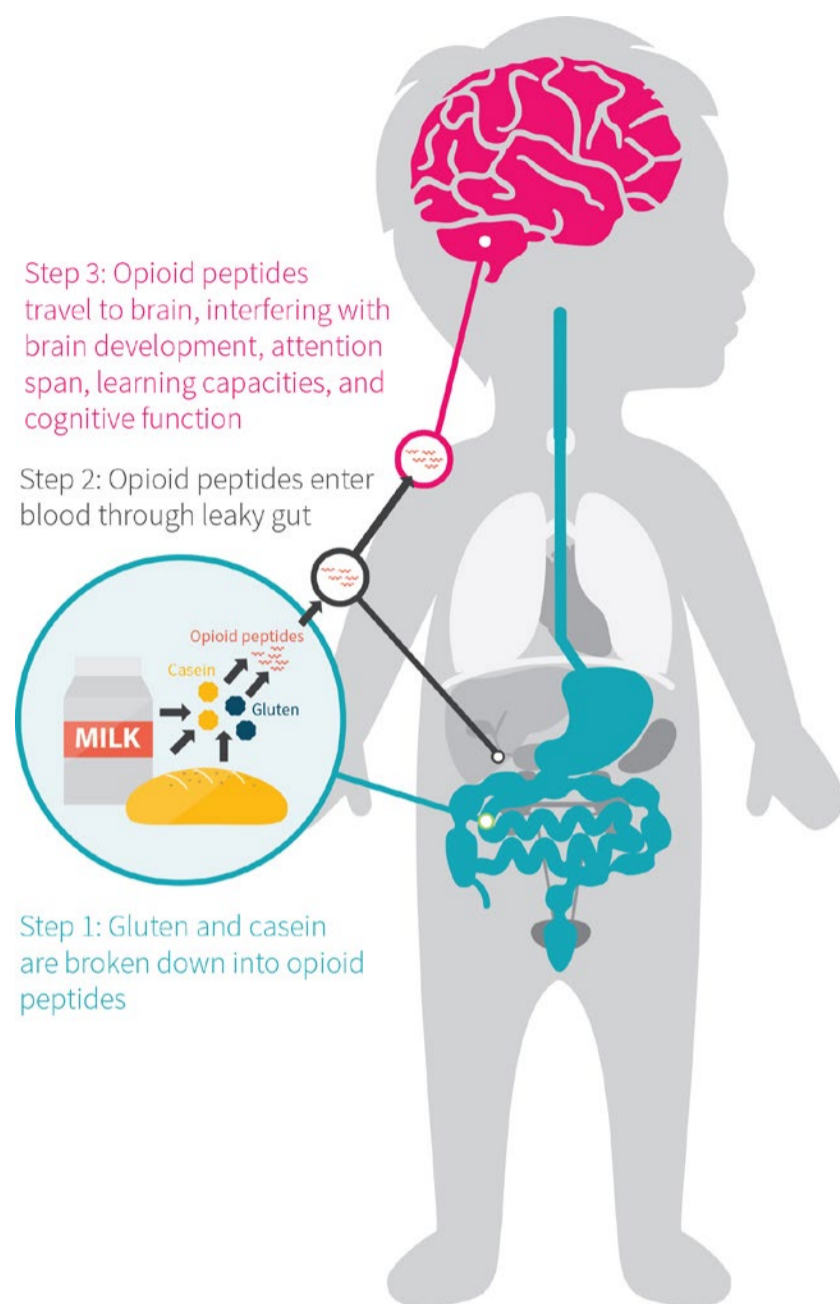
Introduction

Interest surrounding gluten-free/casein-free (GFCF) diets for children with autism spectrum disorder (ASD) has been growing for decades. The first trial to test a gluten-free diet on children with ASD was [published in 1971](#). A few years later, a [1977 case study](#) from The Johns Hopkins University School of Medicine was the first to eliminate both milk and gluten products from the diet, in this case of a 9-year-old boy with ASD.

Since then, GFCF diets have become one of the most popular dietary treatments chosen by parents who have children with ASD. Many surveys have attempted to determine the prevalence of GFCF diets as an alternative treatment, but results have been [wide ranging](#). An average of these rates gives us an estimated 35% prevalence of GFCF diets, including both current and previous use. Parents with ASD children on a GFCF diet often report [seeing improvements](#) in behavior.

The prevailing concept in support of a GFCF diet is the ‘[opioid-excess theory](#)’ of ASD, depicted in Figure 1. This theory states that the incomplete breakdown of gluten and casein proteins into excess opioid peptides can trigger symptoms in people with ASD. Gluten proteins are found in products like wheat, barley, and rye, while casein proteins are found in dairy products. When ingested, gluten and casein are broken down into peptides (short chains of amino acids) such as glutomorphin/gliadorphin or beta-casomorphin. These peptides [could potentially cross through](#) an abnormally permeable intestinal border, often referred to as a ‘leaky gut’, fully intact and undigested. If sufficient quantities were produced, these peptides could [theoretically cross the blood-brain barrier](#), affecting the central nervous system and interfering with brain development, attention span, learning capacities, and cognitive function in people with ASD. It is therefore hypothesized that removal of these proteins from the diet could cause the behavioral symptoms of ASD to improve.

Figure 1: The opioid excess theory of ASD



Like any theory, the opioid-excess theory of ASD does have its weak points. The biggest issue is a lack of consistent results. For example, [some studies](#) have noted an [increased presence of gut permeability](#) in people with ASD, while others have seen [no difference](#). Further trials have seen increased gut permeability, but only in a [specific subset of children](#) with ASD. Additional doubt has been cast on this theory due to the consistent [lack of detectable concentrations of opioid peptides in urine samples](#) of patients with ASD using highly-sensitive measurement techniques. If significant amounts of opioid peptides were making it past the gut and into the bloodstream, urine tests would reveal their high levels as the body worked to eliminate them.

Regardless of the points for or against the opioid-excess theory, the biggest question is: does the dietary elimination of casein and gluten actually help to alleviate symptoms in people with ASD? The present rigorously-controlled study aims to shed further light on that matter.

Gluten-free/casein-free (GFCF) diets are a popular alternative treatment among parents who have a child with autism spectrum disorder (ASD). Many parents have reported seeing behavior improvements when their child is on a GFCF diet. The opioid-excess theory of ASD proposes that the opioid peptides produced from incomplete breakdown of gluten and casein proteins cross into the body and alter brain functions, causing the symptoms of ASD. The study under review uses rigorous methodology to test if a GFCF diet can provide ASD symptom relief.

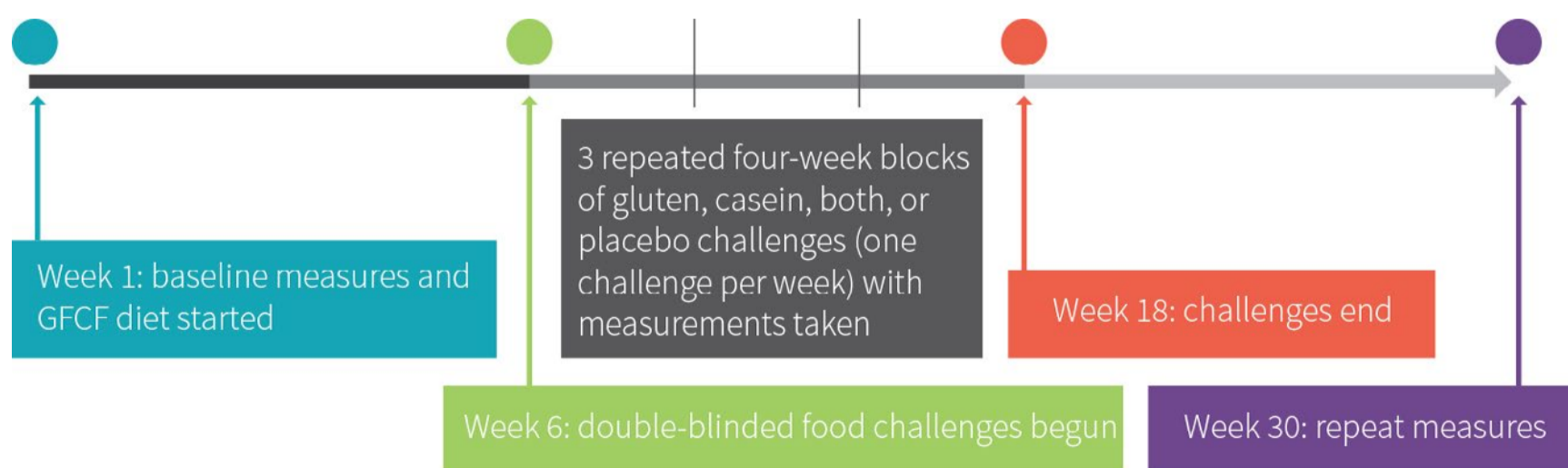
Who and what was studied?

This study is the most well-controlled trial looking into the efficacy of GFCF diets to relieve behavioral symptoms of ASD to date. It's basic design is outlined in Figure 2. The researchers employed a double-blind, pla-

cebo-controlled design that introduced the casein and gluten food challenges in a randomized, counterbalanced method. Twenty-two children with a confirmed diagnosis of ASD were recruited for the study. Fourteen were able to complete the trial (12 males, two females). Children who had confounding medical conditions, such as celiac disease, were excluded. The study ran for 30 weeks (7.5 months) and was broken up into three phases: implementation, challenge, and maintenance.

The implementation phase lasted six weeks and allowed the families to become accustomed to and maintain a GFCF diet with the help of a registered dietitian, who also provided nutrition support throughout the trial. Baseline measurements of behavioral and nutritional status were taken at the beginning of week one. The challenge phase lasted 12 weeks. During this phase, food challenges were administered to the participants once a week via various snacks. Four types of challenges were used: foods that had only gluten, only casein, both gluten and casein, or neither (placebo). The child, family, child's instructors and caregivers and the research personnel that recorded behavioral data were all blinded to the type of food being given. These snacks were administered by the research team to ensure they were being consumed.

Figure 2: Study design



Continuous sleep and stool diaries, weekly 24 hour diet recalls, applied behavioral analysis data

The order in which each child received these foods was randomized and counterbalanced. The counterbalancing of the food challenges consisted of three four-week blocks where the food order was randomized for each block. The study team was blinded to the fact that blocks were part of the study design. During each block, the children received all four food types (one per week). If all of one type of food were administered at the beginning or end of the study, we might see the effect of the ongoing behavioral therapy or natural history of the disorder and could misinterpret it as an effect of the diet.

The last phase, the maintenance phase, ran for 12 weeks, and the families were free to “maintain, modify, or abandon the GFCF diet.” The children were then put through a final assessment at the end of this period. Throughout the entire trial, food recalls, sleep patterns, physiologic functions (stool frequency and consistency), and measures of behavior changes were recorded.

Of particular interest was how much time and effort the research team spent developing the gluten and casein-containing snacks the children had to eat during the food challenges. As many ASD children [can be picky eaters](#), every snack was created with the personal tastes of

each child in mind. The tricky part was that all versions of the snack had to be indistinguishable from the other. The gluten-free foods had to taste and smell the same as the gluten-containing foods, as did the casein-containing and casein-free foods. A variety of snacks were created, including banana bread, cookies, brownies, breakfast pastries, smoothies, puddings and egg mixtures. Two of the researchers, Dr. Patricia Stewart and Robin Peck, R.D., have discussed how the snacks were developed and administered in a [YouTube video](#).

This is the most well-controlled GFCF diet trial performed to date. Fourteen children with confirmed ASD were rotated through various food challenges using snacks containing only gluten, only casein, both gluten and casein, or neither (placebo). The trial was designed in a way that each child’s individual response to the diet could be measured to ascertain if some children with ASD respond better to a GFCF diet. Particular care was placed on developing the GFCF versions of the gluten- and casein-containing snacks so that they were indistinguishable from the real thing.

The Conners’ scale

During the study, the parents, children’s instructors, and research assistants all completed the Conners’ Abbreviated Rating Scale. This 28-question rating scale is used to assess a child’s behavior on a four-point grading system, from zero to three. Traditionally, the Conners’ rating scale has been utilized as one of the many tools employed to diagnose and evaluate treatment options for children with attention deficit hyperactivity disorder (ADHD). In this study, this scale was employed to assess and monitor changes in behavior surrounding the food challenges.

The questions in the survey mainly focus on monitoring hyperactivity, impulsivity, and inattention. The 28-question format offers a quick and easy method to ensure that specific behaviors are being monitored. Observations to be scored in the Conners’ scale include items like “restless or overactive” and “mood changes quickly and drastically.” These questionnaires can also offer a means of tracking the severity and frequency of behaviors changes over time. Noticeable shifts in behavior are what the researchers of this paper were attempting to closely monitor with this scale both before and after administration of the food challenges.

What were the findings?

The main conclusion of the study was that the GFCF diet did not appear to change measures of “physiologic function, behavioral disturbance (sleep disruption and over activity), or ASD-related behaviors.” Although no statistically significant effects were found between food challenges, a few interesting and surprising trends were observed. On the days that gluten and casein were administered, some children experienced fewer negative social relationship symptoms. This would indicate that casein and gluten actually improved social behaviors. When the gluten challenge was administered, there was also a positive trend seen in the reduction of language symptoms.

Due to the study’s design, the researchers were able to go back and look at the children’s individual data for the trends that had been identified in the group as a whole. The purpose of this was to see if a subgroup of the participants consistently responded unfavorably (or favorably) to the gluten and casein challenges. The researchers were not able to identify any consistent patterns within individual conditions or across them. Because the individual data showed no clear pattern of dietary challenge impact on any outcome measured, the research team was able to confirm that the overall group results had not masked any child’s individual response.

No statistically significant effects of the GFCF diet were seen in any of the measured outcomes of the children. However, some non-statistically significant trends were seen within the group as a whole. When the individual results for each child were examined, these trends were shown to be inconsistent and did not yield any statistically significant results across differing food challenges.

What does the study really tell us?

The design and execution of this study gives us a clearer understanding of what the effects of a GFCF diet may be. The research team went to great lengths to eliminate factors that were potential confounders and limitations in previous studies. For example, certain children were placed on iron, calcium, or vitamin D supplements when deficiencies were noted by the dietitian. Dietitians also closely monitored the children’s dietary intake and nutritional status throughout the duration of the trial. Inadequate nutrient intake can be a considerable confounder in studies of this nature. In addition, all of the children were in stable educational and behavioral programs to ensure that fluctuations in ASD behaviors were not too heavily influenced by external environmental factors.

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However, the results of the study should be interpreted carefully. Although 22 children were initially enrolled, only 14 were able to complete the study (equating to a 36% drop-out rate). While the majority of these participants were male, it should be noted that ASD is [almost five times more common](#) in boys (one in 42) than among girls (one in 189). With the above-mentioned limitations in mind, the study findings did not support the widespread use of a GFCF diet in children with ASD. Additionally, the results cannot be fully extrapolated to children with gastrointestinal symptoms. That being said, the use of a GFCF diet should be safe for ASD children with or without gastrointestinal problems, as long as it is implemented correctly and the children's nutritional status is monitored.

Many of the methodological restraints of previous studies were controlled for in this trial. Dietitians ensured that the children's nutritional needs were being met both before and during the trial. All participants were in stable educational environments for the entire study. The results did not support the general use of a GFCF diet. Further research into ASD children with gastrointestinal conditions will be needed to clarify the potential role of a GFCF diet for this subset of children.

The big picture

Since the early 1970s, there have been more than 30 trials conducted to try and ascertain what, if any, role a GFCF diet could play in ASD therapy. But, [many of these studies](#) have been limited in their [methodological quality](#). Some lacked a control group, while others were single-blinded or not blinded at all. Studies also had very small sample sizes and short intervention durations, and often the parents were the only group reporting changes in behavior. When parents are the sole group responsible for reporting behavior changes, it is possible they could be susceptible to confirma-

tion bias, if they know or suspect that their child is on the GFCF diet. If the parents believe the GFCF diet will be good for their child, it increases the chances of them reporting positive benefits. This could result in a false positive in the study's findings. Performing a double-blinded test helps reduce the chances of biased reporting, even if the parents are the sole reporters.

To get a better picture of where the weight of the evidence presently stands on the question of GFCF diets, we can examine the most rigorously controlled trials currently available: those that are double-blinded, randomized, and placebo-controlled. Other than the study discussed in this article, only two other trials meet these inclusion criteria. Both of these studies had the added benefit of incorporating a crossover design, where all participants receive both treatments at different periods and essentially acted as their own control group. The first trial, conducted by [Elder et al.](#), examined 13 children with ASD for 12 weeks. Standard assessment questionnaires and urinary peptide levels were taken. No significant changes were observed at any endpoint. The second study by [Seung et al.](#) also examined 13 children with ASD for 12 weeks. Video recorded sessions of the children were taken throughout the experiment and were used to assess verbal and nonverbal communication. These assessments were conducted by a blinded third party. The GFCF diet did not result in any differences on any of the measured communication variables. A third, larger study was [completed earlier this year](#) that looked specifically at the use of GFCF diets in children with ASD who have gastrointestinal disorders. To date, the results have not yet been published.

Based on the three highest quality studies presently available, a GFCF diet does not seem to assist in reducing the symptoms of ASD, at least within typical study timeframes. So, what might explain anecdotal success stories of children switching to GFCF-type diets? There are many factors at play, but an important one is that

this was a highly controlled study, specifically testing the gluten and casein components against placebo. In contrast, parents who make sweeping changes to their children's diets often cut out a variety of unhealthy junk foods in addition to boosting intake of healthy foods. That's why it's quite possible to reconcile negative studies like this with positive changes seen by parents in the real world.

Not to mention the simple fact that children can vary in genetics, gut health, and environments. We know a little bit about which factors influence the risk of ASD (some of them are shown in Figure 3), but very little about how factors influence response to diets aimed at ASD. In fact, previous research has indicated [there may be a subgroup](#) of people with ASD that could respond well to this diet. Thus it's critical to keep in mind that the broad question of autism and diet is difficult to "answer" in any one trial, or even in a large collection of studies.

A [consensus report](#) published by the American Academy of Pediatrics also concluded that "available research data do not support the use of a casein-free diet, a gluten-free diet, or combined gluten-free, casein-free (GFCF) diet as a primary treatment for individuals with ASDs." They went on to warn that "parents need information to help plan a balanced diet within the restrictions imposed by the chosen [GFCF] diet. Given the real hardships associated with implementation of a strict GFCF diet, additional studies are needed to assess risk factors and possible markers that identify individu-

als who might benefit from these diets."

GFCF diets have been investigated for use in children with ASD since the 1970s. Only three of these studies have been randomized, double-blind, and placebo-controlled. All three studies indicate that GFCF diets are not effective at relieving behavioral symptoms associated with ASD. The American Academy of Pediatrics has also concluded that available research does not support the use of a GFCF diet in the primary treatment of ASD. A forthcoming study will examine if a GFCF diet could be effective in ASD patients who have gastrointestinal disorders.

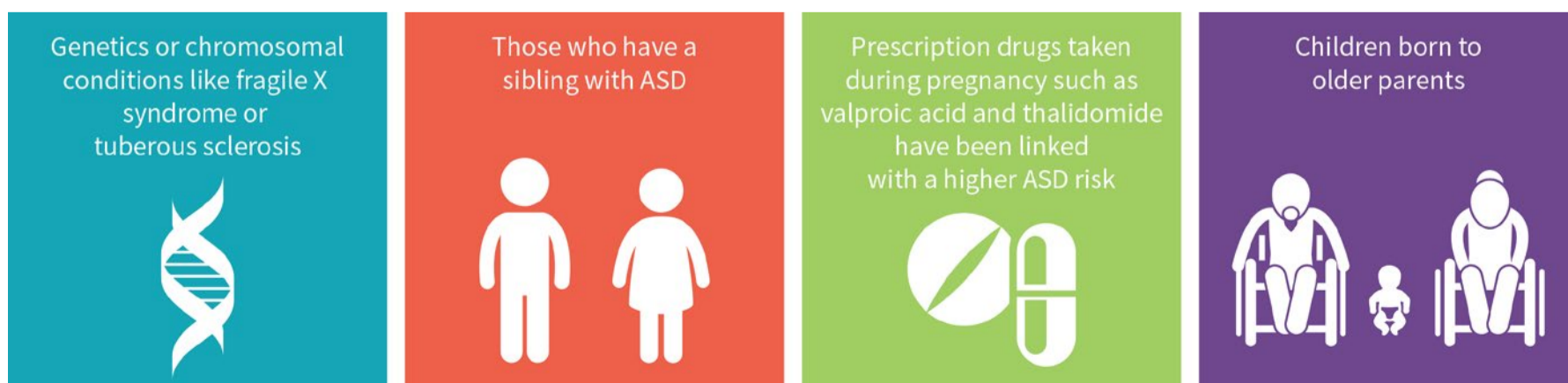
Frequently asked questions

What nutrient concerns would need to be monitored for a child on a GFCF diet?

Any diet that decreases food variability has the potential to increase the risk of nutrient deficiencies if it is not well planned. With a GFCF diet, nearly all dairy, many grains, and grain-based products will be eliminated, primarily wheat, barley, and rye. The removal of dairy and gluten-containing foods can subsequently decrease the intake of vitamins and minerals these products contain naturally and are typically fortified with. Namely, vitamin D, calcium, fiber, and the B-vitamins.

While it may seem simple for an adult to just get wheat or dairy associated nutrients from other foods, nutri-

Figure 3: Known risk factors of ASD



ent intake issues can be tricky in developing children, who typically don't make their own eating decisions, and especially children with specific conditions. One study found that [boys with ASD](#) had lower bone mineral density and vitamin D intake from food as well as measured in serum. With the elimination of dairy, particular attention is needed to ensure adequate intakes of calcium and vitamin D are being consumed to maintain bone health.

What should I know?

At present, a GFCF diet does not appear to be supported for reducing behavioral symptoms associated with ASD. Within the current study, no significant findings were seen when the trial results were looked at as a whole or on a case-by-case basis. Implementing a GFCF diet can be both expensive and time-consuming. Given the current weak evidence of GFCF efficacy, emphasis on other behavioral therapies may provide greater benefit than gluten and dairy cutting.

The more than 30 trials that have looked into the GFCF diet are a good illustration of why it can be so difficult to get a specific answer to a question like "Do GFCF diets work to relieve ASD symptoms?" There are many variables at play that can make it hard to find a concrete answer. Conducting rigorous, well-controlled studies in humans is a hefty challenge. The authors of this study succeeded in controlling important confounding variables, and contributed to the body of literature indicating that simply cutting out gluten and casein isn't likely to be helpful in the treatment of ASD. ♦

There are few issues as controversial as the cause(s) of autism. But at least we're learning more and more about autism spectrum disorder treatment. Talk this paper over at the [ERD Facebook forum](#).

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