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The Gluten-Free, Casein-Free Diet and Autism

Limited Return on Family Investment

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The gluten-free, casein-free (GFCF) diet is widely used by families of children with autism spectrum disorders (ASD). Despite its popularity, there is limited evidence in support of the diet. The purpose of this article was to identify and evaluate well-controlled studies of the GFCF diet that have been implemented with children with ASD. A review of the literature from 1999 to 2012 identified five studies meeting inclusion criteria. Research rigor was examined using an evaluative rubric and ranged from *Adequate* to *Strong*. In three of the studies, no positive effects of the diet were reported on behavior or development, even after double-blind gluten and casein trials. Two studies found positive effects after 1 year but had research quality concerns. Reasons why families continue to expend effort on GFCF diets despite limited empirical evidence are discussed. Recommendations are that families should invest time and resources in more robustly supported interventions and limit GFCF diets to children diagnosed with celiac disease or food allergies.

Keywords: *gluten-free, casein-free, elimination diet, autism spectrum disorders*

The gluten-free, casein-free (GFCF) elimination diet is a popular intervention for children with autism spectrum disorders (ASD). Elimination diets are commonly used in the ASD community, in which half of families of children with ASD have tried them (Smith & Antolovich, 2000) in an effort to improve their child's functioning or behavior. This widespread use of the GFCF diet implies its efficacy; but in fact, as this article will describe, empirical support for the diet is limited. An analysis of the research that has been completed on GFCF diets for children with ASD is provided herein, along with a discussion of implications for researchers, families, and individuals.

Connections Between the GFCF Diet and ASD

A GFCF diet is an elimination diet in which a person does not eat anything that contains gluten or casein. On this regimen, all foods with gluten, which is a protein found in wheat, barley, and rye, and all foods containing casein, a protein found in dairy products such as milk, yogurt, and cheese, are removed from the diet, leaving other edibles like meat, eggs,

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nuts, fruits, and vegetables as permissible. Many children with ASD have been on GFCF diets at one time or another, some for years at a time (Pennesi & Klein, 2012). In a survey of the treatments they were currently using, 27% of parents reported that their child with ASD was at that moment on an alternative diet (Green et al., 2006) and half had tried a special diet at one time or another (Smith & Antolovich, 2000).

The GFCF diet appears frequently in the popular media and occasionally in research. Families of children with ASD may be exposed to success stories through parent testimonials (e.g., Pennesi & Klein, 2012), autism websites (e.g., www.autism.com), personal stories (e.g., www.tacanow.org), and dozens of books with titles like *The Autism Cookbook: 101 Gluten-Free and Dairy-Free Recipes* (Delaine, 2010) and *Healing and Preventing Autism: A Complete Guide* (McCarthy & Kartzinel, 2010), in which the authors credit a GFCF diet and other alternative therapies with the recovery of a child with autism. Anecdotally the diet is often credited for successful outcomes, which may interest families as they consider intervention options for their children.

There are many reasons that families of young children newly diagnosed with ASD choose the GFCF diet. Above all, the diet is easily accessible. It can be implemented at home and be used concurrently with other interventions (Green et al., 2006). This means the diet can be initiated without reaching the top of long waiting lists for therapist or doctor appointments and can begin whenever a family feels ready to try it. In addition, the rules of the diet are relatively straightforward, so it may be easier to follow than some other therapies with less concrete guidelines. For example, professional guidance may be required to correctly use functional analysis to identify the cause of a child's tantrums (Hurwitz & Minshawi, 2012) or to understand how to use a "mand" to teach new words in Verbal Behavior Therapy (Sautter & LeBlanc, 2006). This accessibility helps to explain why the diet is so prevalent.

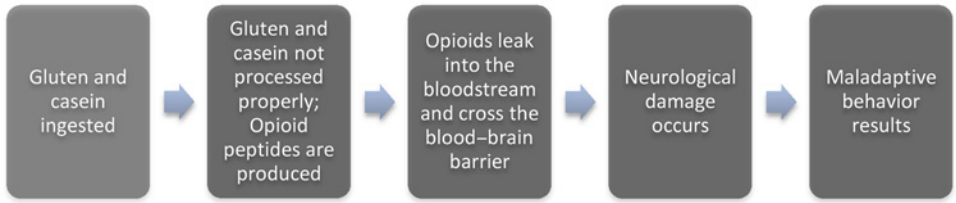
However, there are some hidden challenges to maintaining a GFCF diet. A diet such as this requires careful advanced planning, including extra effort to prepare special foods every day for many months. It also requires a financial commitment because GFCF foods such as rice pasta, GF bakery mixes, vegan cheese, and almond milk typically cost more than twice as much as their regular counterparts (Stevens & Rashid, 2008). Also, families must take special care to balance the nutritional needs of their growing children while eliminating many food staples, risking reduced bone density (Hediger et al., 2008) and other nutritional concerns. Finally, being on a special diet can have unintended negative social consequences when children are not able to participate conventionally in birthday celebrations and class treats or eat in restaurants or other people's homes.

Given the effort, time, and money that the GFCF diet requires, knowing whether this investment will pay off would be valuable. As Christison and Ivany (2006) pointed out,

> If these diets are not beneficial, such efforts may be creating false hope and diverting attention away from more fruitful approaches. If actual benefit undergirds the popularity of these diets, such benefit needs to be clearly documented and its implications and mechanisms studied. (p. S169)

The important question is whether the anecdotal stories of success and the easy accessibility that help make the GFCF diet so popular for children with ASD are backed by empirical support.

Figure 1
The Chain of Events Suggested by the Opioid-Excess Theory of Autism, Which Proposes that Eating Gluten and Casein Affects the Behavior of People with Autism Spectrum Disorders



Theories Supporting GFCF Diets for Children With ASD

There are several theories that propose a link between diet and behavior for people with ASD. The most common is called the opioid-excess theory of autism, which suggests that gluten and casein consumption cause some of the negative behavioral and developmental outcomes seen in the disorder. An alternate explanation is that gastrointestinal (GI) discomfort from food allergies or celiac disease might make the child feel ill and thus exhibit maladaptive behaviors. Both theories postulate that by changing a child's diet, his or her behavior can change (Knivsberg, Reichelt, Høien, & Nødland, 2002).

The opioid-excess theory of autism. Proponents of the opioid-excess theory of autism have found high levels of opioid peptides in the urine of some children with ASD that they ascribe to gluten and casein malabsorption (Knivsberg et al., 2002). They propose that gluten and casein in grains and dairy products enter the body but are not properly metabolized by the digestive system, which produces urinary peptides as a by-product (Reichelt & Knivsberg, 2009). These peptides are thought to leak out of the intestines into the bloodstream—referred to as the "leaky gut hypothesis" (White, 2003)—and are carried by the blood around the body and up to the brain. In the brain, they are thought to attach to opioid neuroreceptors and negatively impact neurotransmission (Mulloy et al., 2010), resulting in behavior problems and increased symptoms of ASD (Whiteley, Rodgers, Savery, & Shattock, 1999). Figure 1 contains a schematic of the process suggested by the opioid-excess theory.

The opioid-excess theory was originally proposed by Panksepp (1979), who postulated that if the opioids could be reduced or blocked from reaching the brain, symptoms could improve. In other words, according to the theory, removing gluten and casein from the diet of a child with ASD should interrupt the chain of events by reducing the level of opioids produced by the body and consequently improving behavior and symptomology. This theory has been the foundation for many dietary interventions for people with ASD. Although it has been around for many years, the theory remains inconclusive.

GI difficulties. GI difficulties stemming from dietary intake can cause bloating and discomfort. It has been suggested that children with ASD, who have communication delays, may have trouble conveying that they feel unwell when they experience GI problems. Instead

of language, they might express their discomfort through maladaptive behaviors, like tantrums or self-injury, in effect communicating their unhappiness without using words (Schroeder et al., 2001). Although children with ASD are commonly thought to have a high prevalence of GI symptoms (e.g., Horvath & Perman, 2002), they have not been found to have GI issues at rates that are any different from those of typically developing children (Erickson et al., 2005) nor is there any "unique gastrointestinal pathophysiology specific to ASDs" (Buie et al., 2010, p. S5).

Nevertheless, children of all kinds can have GI discomfort, and the possibility remains that behavior problems can ensue for children with ASD. Common roots of GI symptoms include celiac disease and food allergies/sensitivities. Celiac disease is an inflammatory disorder that is caused by eating foods that contain gluten (Lynette et al., 2010). It is a chronic genetic disorder resulting in GI discomfort, weight loss, nutritional deficiencies, and sometimes, neurological impairment (Kagnoff, 2004). This disease is present in about 1% of the general pediatric population and may be as high as 3.3% in children with ASD (Barcia, Posar, Santucci, & Parmeggiani, 2008). Celiac disease may be overlooked among children with ASD, so screening is recommended for children who are involved in research (Barcia et al., 2008), those who are at risk due to family history, or those with suggestive symptoms. If detected, the treatment for celiac disease is a GF diet wherein GI symptoms are typically reduced and neurological complications are prevented.

Food allergies and sensitivities can also cause digestive problems as the body reacts poorly to certain foods, like nuts or lactose. Of all children, 6% to 8% have allergies or intolerances, with children with ASD experiencing these issues at similar rates (Buie et al., 2010). If GI problems exist, allergy testing is recommended to identify whether there are foods that are at fault so they can be removed from the diet.

Research on the GFCF Diet and ASD

In earlier clinical diet research, the opioid-excess theory was used as a justification for putting children with ASD on a GFCF diet. Theories and case reports such as this can be suggestive of new interventions to try, but to determine efficacy, the treatment must be tested with controlled, experimentally designed studies (Reichow, Barton, Sewell, Good, & Wolery, 2010). Therefore, to endorse the continued use of the diet, evidence demonstrating a link between diet and behavioral change is needed.

Experimentally Rigorous GFCF Studies in ASD

There have been relatively few studies of the GFCF diet and even fewer experimentally rigorous ones. In their review of all GFCF diet studies completed through 2009, Mulloy et al. (2010) found only 14 studies that examined GFCF diets in children with ASD. These included case reports and nonexperimental design studies, as well as studies with some experimental control, as exemplified by single-subject and control-group designs. Of the 14 articles reviewed in the Mulloy article, "only three studies were of sufficient experimental rigor to qualify at the preponderant level of certainty" (p. 335; that is, they used experimental designs). This dearth of data is supported by earlier reviews (Christison & Ivany, 2006;

Millward, Ferriter, Calver, & Connell-Jones, 2004) that identified only 1 well-controlled study (Knivsberg et al., 2002) in their analyses of GFCF trials.

Experimental control is important in research studies to learn whether changes would have occurred even without the intervention. The gold standard in research is the randomized, double-blind, placebo-controlled trial that involves random assignment to either an intervention or a control condition (Goin-Kochel, Mackintosh, & Myers, 2009). Only a few experimentally rigorous studies were identified in the previous reviews of the GFCF literature; many others were case studies or group designs without control groups in which all of the children received the dietary intervention. Without a control group, studies are vulnerable to parental and clinician expectations being raised and potentially impacting their objectivity (Christison & Ivany, 2006).

The previous reviews focused on a wide range of studies completed prior to 2010, and several new studies have been conducted since then. This article expands on previous reviews by examining the new studies, along with the older ones, using a focused approach. Because randomized controlled trials provide the most careful assessment of an intervention, I examined GFCF diet studies for rigor and experimental control in an attempt to more definitively determine their efficacy for children with ASD.

As it is currently not clear whether the diet is genuinely worthwhile for some children or whether its popularity is due to the diet's accessibility and anecdotal reports of success, the purpose of this study was to identify rigorous experimental studies of the GFCF diet that would determine whether there were positive changes in behavior, language, or social functioning of children with ASD when on the diet.

Method

Literature Search Procedure

Systematic searches were conducted to identify all articles related to GFCF diets with individuals with ASD. Searches were completed in the following databases: PsychINFO, ERIC via EBSCO, and PubMed. In addition, the reference lists from two earlier review papers on this topic were examined, and a search in Google Scholar with particular focus on the past 2 years (2010-2012) was conducted to identify any recent articles that were not yet listed in the other databases. The searches were limited to articles published in English language peer-reviewed journals from 1999 to 2012. The terms *autism, diet*, and *gluten* were entered, identifying 90 results.

Inclusion Criteria

To be included in this study, each article had to incorporate four components: (a) at least one child (less than age 18) with ASD, (b) an examination of a GF or a GFCF diet, (c) dependent measures related to behavioral or developmental outcomes (e.g., autistic symptoms, communication, social skills), and (d) studies using a group design with random assignment to a control or diet condition.

Eliminating the articles that did not focus on GF or GFCF diets with individuals with ASD identified a total of 55 studies. These studies had a range of foci including studies

with biomedical outcomes (14 studies), reviews of ASD interventions that included but were not primarily about diets (14 studies), surveys or case reports (6 studies), examinations of the diet for celiac disease or nutritional interests unrelated to ASD symptomology (12 studies), or studies that tested the diet but did not meet other criteria like random assignment (2 studies). The studies that were excluded from this analysis were reviews, studies that measured outcomes unrelated to behavior or development (e.g., sampling urinary peptides or blood levels), and case studies.

Thus seven studies met all of the inclusion criteria. After reading them carefully, it was apparent that two pairs of articles reported results from the same groups of children (i.e., Seung, Rogalski, Shankar, & Elder, 2007, was a follow-up to Elder et al., 2006; Knivsberg, Reichelt, Høien, & Nødland, 2003, was a follow-up to Knivsberg et al., 2002) so only one study from each data set was included here. Hence, from the entire search, there were five studies that focused on GFCF diets using randomized groups of children with ASD. These five were analyzed further.

Analysis

Each of the five studies that met the inclusion criteria was analyzed using an evaluative rubric developed by Reichow, Volkmar, and Cicchetti (2008). This rubric is used to assess the rigor of research studies by evaluating 14 quality indicators. The rubric provides operational definitions and a scoring mechanism for each quality indicator and then synthesizes them to get an overall strength rating score for each study. A description of the quality indicators used in this evaluative method appears in Table 1.

Under this evaluative system, there are six primary quality indicators that are considered critical components of a research study and are essential for establishing its validity (Reichow, 2011). They include indicators that examine how well the participants are described (e.g., age, gender, diagnosis) and how well the independent and dependent variables are defined (i.e., whether there is enough detail for replicable precision). The primary quality indicators are scored as one of three levels: *high quality, acceptable quality*, or *unacceptable quality*. There are also eight secondary quality indicators, which are elements of the study design that are considered important but not necessary for the establishment of the study's validity (Reichow, 2011). These examine whether research elements such as random assignment, blind raters, and measures of treatment fidelity are included in the study design. The secondary quality indicators are scored as being either present or not present.

The overall strength rating for each study is rated as *Strong, Adequate*, or *Weak. Strong* research reports receive high-quality grades on all of the primary indicators and show evidence of several of the secondary quality indicators. *Adequate* research reports receive high scores on at least four of the quality indicators, with no unacceptable grades and evidence of some of the secondary indicators. *Weak* research reports receive fewer than four high-quality grades on the primary indicators and evidence of very few secondary indicators.

The benefit of using this rubric is that it allows research strengths and weaknesses to be compared across studies. The studies included in this article are assessed using the quality indicators and given final strength rating scores.

Table 1
Quality Indicators Used to Evaluate Rigor for Group Research Studies

Primary quality indicators	Explanation
Participant characteristics	Was there a complete description of participants, including diagnostic information and age
Independent variable	Was the treatment described with replicable precision
Comparison condition	Were the conditions for the comparison group described with replicable precision
Dependent variable	Was the dependent variable described with replicable precision and were measures linked to it
Link between research question and data analysis	Was there a strong link between data analyses and research question
Statistical tests used	Were statistical analyses conducted correctly, with adequate power, and a sample size of *n*
Secondary quality indicators	**Explanation**
Random assignment	Were participants randomly assigned to treatment condition
Interobserver agreement	Was interrater agreement above .80 and at least *Good* reliability
Blind raters	Were raters blind to treatment condition
Fidelity	Was treatment fidelity assessed continuously
Attrition	Did attrition differ between conditions (by more than 25%) and was it less than 30% at final outcome
Generalization and/or maintenance	Were outcome measures collected after final data collection to assess generalization/maintenance
Effect size	Were effect sizes reported and ≥.40
Social validity	Was this study socially important to society, time and cost-effective, and completed in the natural environment

Source: Adapted from Reichow, Volkmar, and Cicchetti (2008). The original article has more detailed descriptions of quality indicators.

Results

Five controlled studies of the GFCF diet were analyzed. To broadly summarize, all of them focused exclusively on children with ASD and compared diet and no-diet conditions. What follows is a detailed description of the primary quality indicators and broader one for some of the secondary indicators. Table 2 contains detailed information about each of the studies.

Participant Characteristics

Four of the five studies received *high-quality* ratings for their descriptions of the participants they enrolled and one study received an *acceptable quality* rating. Every study focused exclusively on children diagnosed with autism or Pervasive Developmental Disorder—Not Otherwise Specified (PDD-NOS) who ranged in age from 2 to 16 years. Two studies included participants within a relatively small age range of 3 to 5 years, while the other three studies included a much wider span, ranging from as young as 2 to as old as 16 (mean age approximately 7.5 years). Diagnostic tools varied across studies. Three studies used the Autism

Table 2
Descriptions of GFCF Diet Studies That Include Children With ASD

		Participants						
Authors	Rigor	*n*	Diagnosis	Age (years)	Design	Results	Strengths	Limitations
Elder et al. (2006)	Adequate	13 (received both conditions)	ASD	2-16	Children provided with all food in a randomized double-blind, placebo-controlled, crossover manner; duration 12 weeks	No differences between treatments on autistic symptoms or urinary peptide levels	Double-blind, meals and snacks provided to families	Small, heterogeneous sample (n = 13)
Hyman et al. (2010)	Strong	14 (received both conditions)	ASD	2.5-5.5	Children placed on GFCF diet and given double-blind, placebo-controlled food challenges; duration 12 weeks	No effects of gluten or casein food challenges on attention, sleep, or activity	Children screened for celiac and food allergies; double-blind food challenges	Small sample (n = 14)
Johnson, Handen, Zimmer, Sacco, and Turner (2011)	Adequate	22 (8 diet, 14 control)	ASD	3-5	Children randomized into GFCF diet and healthy diet control groups, administered by parents; duration 3 months	No group differences in developmental or behavioral outcomes	Clinician attention provided equally to families in both groups	Small sample (n = 8 in diet group)
Knivsberg, Reichelt, Høien, and Nødland (2003)	Adequate	20 (10 diet, 10 control)	ASD	4-10	One member of each matched-pair randomly assigned to GFCF or nondiet control group, administered by parents; duration 12 months	Parents of children in diet group reported more improvement in autistic traits than controls	All children had urinary peptide abnormalities, may represent a specific subgroup of ASD	Results based on parent questionnaire, parents not blinded, small sample size (n = 10 per group)
Whiteley et al. (2010)	Adequate	55 (26 diet, 29 control)	ASD	4-10	Children randomized to GFCF diet and no-intervention control group, administered by parents; duration 12 months	Diet group improved on social interaction, inattention and hyperactivity; controls improved on daily living skills	Large sample size	High attrition rate (29% from GFCF group, 15% from control group)

Note: GFCF = gluten-free, casein-free; ASD = autism spectrum disorders. "*n*" represents the number of children who completed the study. Rigor ratings are derived using the evaluative method for determining evidence-based practices in autism (Reichow, Volkmar, & Cicchetti, 2008) and range *Strong, Adequate*, or *Weak*.

Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 2002) or the Autism Diagnostic Interview—Revised (ADI-R; Lord, Rutter, & LeCouteur, 1994), one study used the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10; World Health Organization, 1993), and one study simply reported that children had been diagnosed by professionals in the field but did not describe the precise method of diagnosis or whether the researchers confirmed this diagnosis, so this study (Knivsberg et al., 2003) got only an *acceptable quality* rating.

With one exception, the studies included a relatively small number of participants. Four studies were quite small, enrolling only 8 to 14 children per group. The largest study (examined by Whiteley et al., 2010) included 38 children who received the GFCF diet and 34 children who were in a no-diet control group (due to attrition, the study ended with 26 and 29 children per group, respectively). There were many more boys enrolled in the studies than girls, with ratios ranging from 4:1 to 8:1 (boys:girls).

Comparison Condition

All five studies randomized participants to diet or control conditions (an inclusion criteria for this analysis), and all received a score of *high quality* for the comparison condition quality indicator.

Independent Variable

Investigators took different approaches to how they implemented the dietary intervention. Two of the studies used double-blind, placebo-controlled designs in which researchers provided some or all of the food to the participants and saw the children three or more times over the course of a 3-month study to complete assessments. Two of the studies were not blinded as parents implemented the diet at home and research staff evaluated participants from the intervention and control groups at the end of 8 to12 months. The final study had parents implement the intervention at home, but the researchers were in regular contact with the families via telephone, and they evaluated the participants from the intervention and control groups after 3 months.

Most of the studies were designed so the families themselves were responsible for carrying out the intervention because maintaining an elimination diet requires providing participants with many meals over many months. To be more detailed, in three of the studies (Johnson, Handen, Zimmer, Sacco, & Turner, 2011; Knivsberg et al., 2003; Whiteley et al., 2010), children were randomized to diet or control groups, and their parents provided them with the appropriate food for 3 to 12 months. One drawback to having families implement the diet was that the parents were not blind to treatment condition (although sometimes the researchers were); this aspect is discussed later in this article.

Although they provided excellent detail about the study design and measures used, Whiteley et al. (2010) included scarce information about the intervention itself, stating only that "participants were allocated to gluten- and casein-free diet . . . or no diet intervention" (p. 91) and they formally met the families after 8 to 12 months. Likewise, Knivsberg et al. (2003) wrote that a dietician met with parents in the GFCF diet group prior to starting the yearlong study to give them information, but no other details were given about what happened during the length of the intervention itself. For this reason, these two studies received *adequate quality* ratings for the independent variable score.

Johnson and colleagues (2011) had families implement the diet as well but more clearly explained their intervention procedures. Participants from the intervention and control groups met with a dietician prior to implementing the diet, and their progress was monitored via biweekly phone conversations during which a 24-hr Dietary Recall Interview was conducted to monitor nutritional intake and adherence to the diet. Assessments were administered after 3 months. This study more clearly explained their intervention and received a *high-quality* rating for the independent variable score.

The other two studies (Elder et al., 2006; Hyman et al., 2010) used double-blind, placebo-controlled designs when implementing the diet. In these studies, neither the families nor the researchers knew which condition the children were experiencing. In the Elder et al. (2006) study, the participants began on either a GFCF diet or a placebo diet for 6 weeks and then were switched to the other condition for the next 6 weeks. A special kitchen provided participants with all of their meals and snacks, and the foods were made to look similar across treatment conditions. Assessments were completed at baseline, 6 weeks, and 12 weeks.

In the Hyman et al. (2010) study, the children were placed on a GFCF diet for at least 4 weeks and then they were given weekly food challenges, which consisted of a snack that was disguised so that no one could tell what ingredients it contained. The food challenges incorporated either wheat flour, evaporated milk, both wheat and milk, or neither wheat nor milk. They were given to the children in a blinded, randomized order until each child had received each type of challenge three times (for a total of 12 challenges) while they remained on the GFCF diet the rest of the day. Assessments were conducted 2 and 24 hr after each challenge. The Elder et al. (2006) and Hyman et al. studies were well-described, and the interventions were uniquely designed so both received a *high-quality* rating for the independent variable quality indicator.

Dependent Variable and Link Between Research Question and Data Analysis

All five studies investigated whether ingesting gluten and casein affected ASD severity, language, or development. Most of the studies used a combination of standardized measures, parent interviews, and coded videos of play sessions to look for change from pre- to postintervention. Examples of the measures were autism screening and assessment measures such as the ADOS (Lord et al., 2002) and the Gilliam Autism Rating Scale (GARS; Gilliam, 1995), developmental and social functioning assessments such as the Mullen Scales of Early Learning (Mullen, 1995), and parent questionnaires and interviews such as the Diagnosis of Psychotic Behavior in Children (DIPAB; Haracopos & Kelstrup, 1975). Two of the studies also collected urinary peptide samples. One caveat is that some of the studies did not report results on all of the measures that they collected; for example, the Knivsberg et al. (2003) article reports outcomes only on the parent interview and not the other language, developmental, and urinary peptide measures they collected. All five studies received *high-quality* ratings for their detailed descriptions of the dependent variables. They also received *high-quality* ratings for their clear link between the research questions posed and the data analysis used.

Statistical Analysis

Due to the small sample sizes, several of the studies received *adequate ratings* for the statistics quality indicator. Johnson et al. (2011) and Knivsberg et al. (2003) had 10 or fewer children in the GFCF diet group, and it is unclear whether the authors had adequate statistical power. Elder et al. (2006) followed 13 children, but their sample was heterogeneous in age (ranging from 2 to 16 years) and other characteristics and was small enough in size that the authors themselves considered it a pilot study. The Hyman et al. (2010) study had only 14 participants, but their participants were less heterogeneous in age, diagnostic criteria, and allergies and they may have had adequate power, so this and the other remaining study (Whiteley et al., 2010), which had a larger more homogeneous sample, received *high-quality* scores.

Strengths and Weaknesses as Seen in Secondary Indicators

The Blind Raters indicator was a notable outcome in these studies. After implementing an intervention for up to a year, parents in some studies had invested a great deal of time and effort into maintaining the diet and may have been looking for improvements in their children's behavior. It is possible that their opinions were impacted, and placebo effects may have been at play. The Johnson et al. (2011), Knivsberg et al. (2003), and Whiteley et al. (2010) studies were scored as lacking on this element as parents were not blind. However, the food provided/food challenges in the Elder et al. (2006) and Hyman et al. (2010) studies were made to look and taste alike so that no one (not the child, the parents, or the researchers) knew which contained gluten or casein and which did not. In this way, the behaviors recorded after the challenges could not be impacted by preconceived ideas or biases.

The Whiteley et al. (2010) study was the only one to score as lacking on the Attrition indicator. They experienced a very high drop-out rate from the intervention group: 11 of the original 38 children (29%) in the diet group discontinued their participation in the 1st year, while only 4 children from the no-diet group withdrew (12%). The authors acknowledge that for some families the cost of the intervention (i.e., the effort that being on such a diet expends) outweighed the apparent benefits. If a family did not feel that their child was making strides on the diet, they may have been more likely to drop out of the study, thereby skewing the analysis toward those who believed their children were making progress.

Fidelity was assessed particularly well in the Johnson et al. (2011) study, in which families from both treatment groups participated in meetings with a nutritionist, dietary monitoring, and biweekly phone calls that included dietary recall interviews. By meeting with families from both groups, the authors ensured the intervention was implemented as planned, and in the process, controlled for clinician attention.

Finally, several of the studies examined children in advance for alternate explanations. Hyman et al. (2010) tested children for milk allergies, wheat allergies, and celiac disease so that individuals with these issues were screened out of the study. Knivsberg et al. (2003) included only children who tested positive for urinary peptide abnormalities, suggesting the possibility that those children represented a specific subgroup of ASD for whom diets might be more effective.

Study Outcomes

The researchers reported mixed effectiveness of the diet on behavioral and developmental outcomes. In three of the studies, they found no support for the diet; the children did not improve on measures of language, attention, activity level, sleep, or bowel habits. Two of these investigations (Elder et al., 2006; Hyman et al., 2010) disguised foods so the participating parents, research staff, and children could not know when they were given gluten or casein, strengthening the study results. However, one article (Whiteley et al., 2010) described group differences on several standardized behavioral measures. The other remaining study (Knivsberg et al., 2003) found that after a year on the diet, parents reported improvements in the autistic behaviors of their children.

Elder et al. (2006) also interviewed parents. At the end of their investigation, the parents were asked whether they thought their child was placed on the GFCF diet during the first 6-week period or the second one; five families guessed correctly while six were incorrect. Interestingly, despite finding no measurable differences or empirical support for the diet, families of nine of the children decided to continue the diet after the study ended. Those parents felt that there were improvements in language and decreases in hyperactivity and tantrums, and they attributed these changes to the GFCF diet. The authors suggest that this finding may be attributed to placebo effects.

The final strength rating scores ranged from *Adequate* to *Strong*, with no *Weak* scoring study. They are listed in Table 2 under "Rigor."

Discussion

This analysis of five well-controlled studies of the GFCF diet for children with ASD does not support the use of the diet for most children. All of the studies were conducted with an adequate level of research rigor to take their results seriously. Three of the studies found no support for the diet; the children did not improve on measures of language, attention, activity, sleep, or bowel habits. Moreover, two of these investigations disguised foods so that all participants were blind to treatment condition, strengthening their results. Sample sizes were small though, so replication is warranted.

In the two studies reporting positive results of the GFCF diet, families implemented the diet at home over the course of a full year. These studies had several considerable research quality flaws. Neither provided a fidelity check during this long intervention period so it is unknown what shape the diet took for each family. One of these studies experienced a high attrition rate from the diet group (much higher than from the control group), meaning that nonresponders may have withdrawn at high rates, thus biasing the results. The other study used a parent interview as their main outcome measure. As parents could not be blind to treatment condition, they may have felt invested in seeing results after all of their efforts; therefore, there are concerns that placebo effects might have been at play.

Explanations for Prevalence of the Diet

Placebo effects may be one reason that the GFCF diet continues to be so popular despite a lack of empirical support. Families may have high hopes for positive behavioral results

after investing the substantial resources required to implement an elimination diet. When improvement is seen, it can be nearly impossible to parse out whether a particular intervention, maturation, or mood is responsible for the progress or whether changes would have occurred even without any direct intervention.

> It is not unusual for a child to start a new diet in the midst of receiving intensive behavioral intervention at school, several sessions of speech therapy per week, visits from an occupational therapist who encourages a sensory-rich diet, and social skills training activities in the afternoons—all while continuing the natural process of growing, maturing, and interacting with family. And then we ask parents to gauge the impact of the diet. (Goin-Kochel et al., 2009, p. 529)

In cases of the placebo effect, parents attribute changes to the diet, in part due to the great effort they are putting into it, and they may discount the contribution of other treatments. The more effort parents expend, the larger the chance they will be biased toward seeing evidence of success (Christison & Ivany, 2006).

Another reason placebo effects perpetuate the GFCF diet is that parent perceptions may be so strong that they persist even when there is empirical evidence to the contrary. In the Elder et al. (2006) study described above, many of the parents reported seeing improvements in language and behavior that they attributed to the diet. This progress was not corroborated by the empirical data collected by the researchers. Although only 5 of the 13 families were able to guess correctly which treatment condition their child was in, the majority upheld that the diet helped. After the study ended, most of the families decided to continue the diet despite this lack of empirical corroboration. In cases where placebo effects exist, it is possible that parents are looking for positive changes in behavior and ignore or explain away negative ones (Sandler & Bodfish, 2000).

One final reason the GFCF diet is perpetuated despite such weak empirical support is that without a medically endorsed best-practice treatment path for ASD, families may choose to err on the side of trying indeterminate therapies rather than run the risk of overlooking a helpful intervention. To explain why families carry on with unsupported alternative treatments, Geraldine Dawson (2011), chief science officer at Autism Speaks, wrote, “Until science discovers the causes of autism and explains its dramatic increase, parents will continue to reach their own conclusions and desperately try a wide range of treatments, whether there is evidence to support them or not” (p. A24). Implementing GFCF diets may give parents a sense of empowerment and a feeling that they are doing something proactively that might benefit their children.

Implications for Research and Practice

The search for interventions to help their children with ASD provides families with many options. There are some established treatments that are evidence-based, meaning that they are supported by several well-controlled studies that have produced beneficial effects (National Autism Center [NAC], 2009) and others that are popular but are not supported by rigorous research. Although not all treatments work for all children, using evidence-based practices to inform therapy choices increases the likelihood of the chosen treatments being effective ones (Reichow et al., 2008). When it comes to the GFCF diet, there is currently not enough scientific support to recommend it.

Implementing a GFCF diet involves a lifestyle change, including significant family commitment of time and resources. These resources are better invested in evidence-based interventions that are more likely to result in successful outcomes. Resources exist to help families determine which treatments are evidence-based including (but not limited to) an evaluation of many educational and behavioral interventions by the National Standards Project (NAC, 2009), an overview and explanation of treatments provided by the research and advocacy group Autism Speaks (www.autismspeaks.org), and the searchable database developed by Research Autism (www.researchautism.net), a United Kingdom charity dedicated to evaluating ASD interventions.

For researchers, the GFCF diet could be revisited in different ways. This analysis does not support the opioid-excess theory of autism. Removing gluten and casein from the diet should have had measurable downstream effects on development and behavior, but several of the studies examined here did not have this result. The opioid-excess theory has remained inconclusive for over 30 years and consequently should no longer be used to promote the GFCF diet.

However, individuals with ASD are part of a heterogeneous group, and subgroups of children may be more sensitive to dietary intake than others. Certainly the children with celiac disease or food allergies and intolerances might benefit from special diets. Testing for these issues is recommended for children with ASD who demonstrate GI problems or discomfort, and for those with positive test results, a GF or CF diet may be appropriate. Larger studies that test prospectively for food intolerances might provide better insight into who will benefit from a diet.

Other subgroups might also benefit. Recent research, for example, has found that there is a small subset of children with autism and epilepsy that have a particular gene mutation causing an amino acid deficiency (Novarino et al., 2012). The authors suggest that dietary supplementation might replace the missing amino acids and improve functioning. This type of research suggests that a special diet may indeed play a role in ASD treatment in the future.

Conclusion

Based on these five well-controlled group studies, the effect of a GFCF diet on behavior is inconclusive at best. Although anecdotally there is word-of-mouth espousal for the GFCF diet, the research examined here does not substantiate this, nor does it support the opioid-excess theory of autism. In the studies reviewed, eliminating gluten and casein from the diet did not have the dramatic measurable decreases in autistic behaviors that the theory predicted. Three of the studies reported no positive effects of the diet and two of these are especially convincing because they compared children's behavior on the diet with blinded gluten and casein trials and found no differences. Only two studies reported some positive effects at the end of 1 year on the diet, but their results may have been impacted by placebo effects and high attrition rates.

Families of children with ASD are recommended to carefully weigh the pros and cons of a GFCF diet and to prioritize evidence-based interventions in their decision process. Investing time and energy in treatments that have been established as effective, including

those that focus directly on communication, behavior, and social interactions (NAC, 2009), are more likely to have positive outcomes than turning to therapies without sufficient scientific support, like the GFCF diet. One caveat is for children who have tested positive for celiac disease or allergies to milk or gluten and who may therefore derive benefit from a GFCF diet. In conclusion, it appears that the GFCF diet does not significantly change functioning or behavior for most children with ASD, and family resources would be better spent on interventions with stronger empirical support.

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