Critical Review: Do children with Autism Spectrum Disorders (ASD) have improved language and communication skills following implementation of a gluten- and/or casein-free diet?

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This critical review examines the effectiveness of gluten- and/or casein-free diets in improving the language and communication skills of children diagnosed with Autism Spectrum Disorder (ASD). Six studies including a single-blind randomized control trial (RCT), a randomized double-blind repeated measures crossover study, two single-group design studies, one cohort study, and one non-experimental single-group study were evaluated in the review. Significant improvements in the language and communication skills of children diagnosed with ASD were found within a few months to one year of beginning the dietary changes. Significant improvements in additional areas were also found. As a number of common weaknesses were identified across studies, evidence for the effectiveness of such diets should be interpreted with caution, as the reliability and validity of research to-date is considered to be equivocal. Recommendations for health-care professionals and suggestions for future research are provided.

Introduction

Autism Spectrum Disorders (ASD) fall under the umbrella term of *Pervasive Developmental Disorders (PDD)*, and include the diagnoses of *Autistic Disorder, Asperger Disorder, Atypical Autism, and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS)* (Wray Silove & Knott, 2005). Qualitative impairments in reciprocal social interaction, verbal and/or nonverbal communication, and varying degrees of stereotyped behaviors, interests, and activities comprise the core symptoms of ASD (Anderson & Shames, 2006).

In attempts to treat the symptoms of ASD, the number of caregivers turning to Complementary and Alternative Therapies (CAM) has been growing in recent years (Christison & Ivany, 2006). More specifically, some of the most popular CAM therapies involve diets that remove gluten and/or casein (proteins found in grains and dairy products, respectively) (Christison & Ivany, 2006; Knivsberg, Reichelt, Hoien & Nodland, 2002). However, their effectiveness in improving behavior and/or learning remains controversial among scientific researchers due to a lack of empirical evidence (Christison & Ivany, 2006; Harrison-Elder, Shankar, Shuster, Theriaque, Burns & Sherrill, 2006).

Nevertheless, a number of biologically-related theories suggest potential relationships between diet and brain functioning. (Christison & Ivany, 2006; Wray, Silove & Knott, 2005). According to the held theory, children with ASD have an abnormal leakage of gluten and casein metabolites from the intestines into the central nervous system (CNS). This leakage is thought to produce excessive brain opioid activity and alter brain functioning (Christison & Ivany, 2006; Knivsberg et al., 2002). Findings that support the held theory include increased urinary peptide levels, increased intestinal permeability, and abnormal intestinal mucosa in children with ASD (Christison & Ivany, 2006). Other proposed biological theories involve decreased levels/activity of specific peptidases, autoimmune mechanisms and/or faulty immune system functioning, as well as gastrointestinal abnormalities (Christison & Ivany, 2006).

Clinical Rationale

The language and communication impairments in children diagnosed with ASD are often the most devastating and are frequently of greatest concern to family members (Anderson & Shames, 2006). As gluten- and/or casein-free diets have become an increasingly popular treatment choice among parents and caregivers, health care professionals have a professional responsibility to be educated and prepared to accurately address queries about such interventions using the best available scientific evidence.

Objectives

The objective of this review is to critically examine the literature on the effectiveness of gluten- and/or casein-free diets on language and communication outcomes in children diagnosed with ASD.

Methods

Search Criteria
Computerized databases, including Cochrane Library, MEDLINE--OVID, PubMed, PsychINFO,

and ProQuest Research Library were searched using the following search strategy:

((Autism) OR (Autistic Disorder)) AND ((Diet Modification) OR (Elimination Diet) OR (Gluten-free diet) OR (Casein-free diet) OR (Gluten) OR (Casein))

The search was limited to articles written in English. No other limits were used.

Reference lists in obtained journal articles were also examined to seek out additional relevant sources.

Selection Criteria

Studies included in this review were required to examine the effectiveness of a gluten- and/or casein-free diet on language and/or communication skills in children diagnosed with ASD. Although the reviewed studies also examined the changes in additional skills and abilities following diet implementation, this review specifically addresses the language and communication outcomes.

Data Collection

Results of the literature search yielded the following types of articles: (1) one single-blind randomized control trial (RCT), (2) one randomized double-blind repeated measures crossover study, (3) two uncontrolled experimental single group studies, (4) one cohort study follow-up study, and (5) one non-experimental single group study. One review article was eliminated from this review, as it did not provide sufficient detail about the studies examined, and some studies included did not measure language outcomes. To address this issue, the studies in the eliminated review that addressed language and communication outcomes were obtained and examined in the current review.

Results

(1) Single-blind Randomized Control Trial

Knivsberg et al. (2002) examined the effectiveness of a 1-year gluten- and casein-free diet in 20 Norwegian children diagnosed with ASD and abnormal urinary peptide levels. All participants were randomly assigned to the experimental group (n=10, mean age = 91 mos., age range = 62-120 mos.) or control group (n =10, mean age = 86 mos., age range = 59-127 mos.). Parents volunteered their children after reading pertinent information about the study, which was included in journals and at school psychological services. Standardized observation

forms and tests were used to collect data on urinary peptide levels, autistic traits, attention, cognition, language and communication, social and emotional development, and sensory/motor abilities prior to and following the experimental period. Data were analyzed using non-parametric within- and between-group tests (Wilcoxon two-tailed paired tests and Mann-Whitney U-tests, respectively) due to small sample size and concern that the data would not be normally distributed. Significant *between* group differences were found in the number of children who showed traits suggestive of communication problems before and after the experimental period, as measured by nonverbal communication, abnormal eye contact, reaction when spoken to, presence of language peculiarities and peculiar interests. Significant *within* group differences in linguistic age in both groups was also found (mean increase of 11 months vs. 8 months, respectively). Furthermore, significant *within* group differences were found in the experimental group only for nonverbal communication, eye contact, reaction when spoken to, and language oddities (e.g. echolalia).

(2) Double-blind Repeated Measures Crossover

Harrison-Elder et al. (2006) designed a pilot study to examine the efficacy of a 12-week gluten- and casein-free diet in 15 children who were diagnosed with ASD based on Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria and Autism Diagnostic Interview-Revised (ADI-R) scores (mean age = 7.32 yrs., age range = 2-16 yrs.). All participants were chosen by "purposive sampling" (p. 415) from the Center for Autism and Related Disabilities (CARD) and/or the University of Florida's Department of Psychiatry and Brain Institute (Child Psychiatry Services), and were randomly assigned to one of two groups. Group A received a regular diet for the first six weeks followed by a gluten- and casein-free diet for the remaining six weeks, whereas group B received the opposite. Data were collected by direct observation (unstructured, in-home, 15-minute videotaped sessions) and two scales: *Childhood Autism Rating Scale (CARS)* and the *Ecological Communication Orientation Language Sampling Summary (ECOS)*. The outcome measures consisted of urinary peptide levels, severity of autistic symptoms, parent behavioral influence, as well as frequency of social initiation and responding, non-speech vocalizations, and intelligible words spoken. Data were collected at baseline, week 6, and week 12. Urine samples were obtained from each child five times across the experimental period. Data were analyzed for 13 of the 15 participants using two-tailed t-tests (the

remaining 2 participants' data were not accounted for). A "missing at random" model was used to account for incomplete data. Results indicated no significant differences on any dependent measures. However, anecdotal reports from parents indicated marked improvements in the language skills of seven children, while reports from two professionals (a teacher and respite worker) observed language improvements in two children.

(3) Single Group Study #1

Knivsberg, Wiig, Lind, Nodland and Reichelt (1990) investigated the efficacy of three reduction/elimination diets in a group of 15 Norwegian children from Madlavoll School (mean age = 10.5 yrs, age range = 6-22 yrs.). All participants were diagnosed with ASD and had abnormal urinary peptide patterns. Participants were individually assigned to a dietary condition involving the reduction and/or removal of gluten and/or casein for 1-year based on their urinary peptide patterns, as these patterns were thought to correspond to various types of autistic syndromes. No control groups were used in this study. Data were collected by means of direct observation, standardized and informal scales, and two standardized tests by two testers. Outcome measures in this study included urinary peptide levels, autistic symptoms, general cognitive ability, language skills, and play. Data were analyzed using the non-parametric Wilcoxon paired-ranking test and Spearman's rank-order correlation coefficient due to concern over the distribution of the data, given the small sample size. Results indicated statistically significant *within* group changes for language (for 10 participants whose data were reported), as measured by the Illinois Test of Psycholinguistic Ability (ITPA). One participant stopped the diet after 9 months and another broke the diet one-week prior to the final assessment, however, there was no mention of the missing data for the remaining 3 participants whose data were not included. In addition, correlation analyses revealed that as abnormally high urinary peptide levels decreased, increases in sociability and language were found (r = -0.63 and r = -0.02, respectively). No *between* group differences were analyzed.

(4) Single Group Study #2:Follow-Up Study

Knivsberg, Reichelt, Nodland and Hoien (1995) designed a follow-up study to examine the efficacy of three gluten- and/or casein- reduced and/or eliminated diets in the same participants from the Knivsberg et al. (1990) study. They re-tested the same group of children on only two of the previously administered tests 4 years following implementation of the diets. In addition, urine samples were not tested at the 4-year mark. The ITPA was one of the two re-administered tests. The same non-parametric tests that were used to analyze data in the Knivsberg et al. (1990) study were used in this study since the sample was not deemed to be random. Results from the ITPA data indicated a significant *within* group difference on mean test results for the 10 subtests, indicating further improvements in language ability for the same 10 participants, of more than one standard deviation, after 4 years of diet modification. Moreover, mean test results for each ITPA subtest indicated significant improvements in all but 3 subtests, as indicated by Wilcoxon values. It was noted that the ITPA could not be administered to the remaining 5 participants as their language abilities were either below or beyond what the ITPA could assess based on the test guidelines.

(5) Cohort Study

Reichelt, Knivsberg, Lind and Nodland (1991) discussed the effects of remaining on or abandoning a gluten and/or casein reduced/eliminated diet on urinary peptide levels, autistic symptoms, cognition, and language abilities in a follow-up study of 2 cohorts of children that were followed for more than two years. One cohort consisted of participants in the Knivsberg et al. (1990) study and the other consisted of participants in the Reichelt, Ekrem, and Scott (1990) study, which could not be obtained for use in this critical review. However, it was indicated that children in this second cohort had been referred to psychological services in Norway (n = 10, mean age = 7 yrs, age range = 3-17 yrs). Participants in both groups were diagnosed with ASD, had abnormal urinary peptide patterns, and were assigned to one of three identical dietary conditions based on their urinary peptide patterns. Furthermore, both cohorts included children who remained in and dropped out of a diet condition.

The results reported were based on those found in the Knivsberg et al. (1990) and Reichelt, Ekrem, and Scott (1990) studies. Statistically significant increases in mean scores were obtained on the ITPA for the 10 children who remained on their modified diet for 4 years (as indicated by significant Wilcoxon values). No comparison to the children in the drop-out group was reported. In addition, parent and teacher consensus reports of observed changes in the diet group (n=26) after 2 years indicated a 60% improvement in language, 49% improvement in eye contact, and a 41% improvement in ability to express emotions. Percentages were not given for the drop-out group.

(6) Non-Experimental Single-Group Study

Whiteley, Rodgers, Savery, and Shattock (1999) investigated the effects of a 5-month gluten-free diet in an experimental group of 31children diagnosed with Autism (n = 9, mean age = 68.1 mos.), Asperger Disorder (n = 4, mean age = 79.9 mos.), and ASD (n = 5, mean age = 40 mos.). Four additional children with semantic pragmatic disorder (mean age = 54.5 mos.), and dyspraxia (mean age = 102 mos.) were included in the experimental group. Age ranges were not given. Six children diagnosed with Autism acted as the control group (mean age = 64 mos., age range = 42-93 mos.), and 5 children with Autism formed a gluten-challenge group (mean age = 73 mos., age range = 56-106 mos.). These children went off of their gluten-free diets during the intervention phase. Information concerning participant recruitment was not provided. Data was collected by urinary samples, a questionnaire, a survey, a standardized observation scale, and a standardized psychometric test prior to, during, and following the intervention. The outcome measures consisted of urinary peptide patterns, autistic symptoms, behavior, cognitive abilities, as well as language and communication skills. The interview questionnaire, observation scale, and survey were the only measures of language and communication, and were completed by participants' parents and/or teachers. Parents were not blinded to the intervention. Data were analyzed for 22 participants who fully completed the intervention using a two-tailed paired t-test and correlational analyses. Results from the parental interviews indicated that 50% of parents who had a child in the intervention group observed improvements in their child's verbal and non-verbal communication abilities post intervention. However, parents of children in the gluten-challenge group observed a slight regression of communication skills in 3/5 children, and no information was provided about the control group. In addition, t-test analyses on parental observation schedule data revealed improvement, but no significant change in the parents' observation scores for verbal and non-verbal communication post intervention for the experimental group. Teachers completed observation schedules for 13/22 children in the experimental group, however, t-test analyses specifically addressing language and communication outcomes were not provided. Furthermore, correlations between parent and teacher observation scores for individual behavioral items indicated improvements in communicative effort for children in the experimental condition (r = 0.53). Finally, parental survey results indicated that, on average, parents of children in the experimental group saw no change or improvements in all areas examined in this study, and marked improvements were noted in the number of communicative attempts and initiations. Information pertaining to parental views of language and communication outcomes for children in the control and challenge groups was not provided.

Discussion

Subject Selection and Characteristics

Weaknesses in subject selection and characteristics were identified across all reviewed studies. The number of subjects in each condition was very small, potentially affecting the power to detect significant differences. Moreover, the likelihood of making a Type II error may have increased due to inadequate sample sizes. Furthermore, large age ranges were noted in all groups across all studies. It is unclear whether different results would have emerged had there been smaller age ranges. Specific to the Knivsberg et al. (2002) study, one major weakness existed as children in the diet group were significantly more impaired on autistic behaviors than the controls prior to dietary intervention, and thus diminished the credibility of the results.

Procedures

Of particular concern across the reviewed studies, with the exception of the Knivsberg et al. (2002) and Harrison-Elder et al. (2006) studies was the lack of control groups. This reduced the credibility of any significant findings, as it remained unclear whether findings were solely attributable to the diet modifications or whether possible confounding variables affected the results, such as general development, severity, and/or other concomitant disorders.

In addition, in many of the reviewed studies, there was no mention of monitoring participants' food intake or diet compliance. As a result, researchers would not have known whether prohibited food items were consumed, intermittently or consistently, by one or more participants in the experimental group during the intervention period. One strength of the Harrison-Elder et al. (2006) study was that parents were asked to record their child's dietary intake in an attempt to monitor compliance; however, the accuracy and reliability of such data is questionable.

Another weakness of the reviewed studies, with the exception of the Harrison-Elder et al. (2006) study, was that parents and researchers were not blinded to dietary group. Blinding parents to dietary

condition is very challenging in these types of studies; however, this weakness introduces the question of whether parental and/or experimental biases affected the results.

Measurement Tools and Outcome Measures

Content validity was another weakness among most of the reviewed studies. The language and communication skills of participants were often assessed using one or two measures, which did not provide comprehensive evaluations of these skills. In the Whiteley et al. (1999) study, only parental questionnaires, surveys and parent/teacher observations were used to assess language and communication changes. Although information from these sources is extremely valuable, researchers should complement this data using a variety of language and communication assessment measures. Both formal and informal measurement tools would be particularly useful in achieving this goal.

Statistical Analyses

Weaknesses pertaining to statistical analyses were also noted within and across studies. In the Harrison-Elder et al. (2006) study, researchers employed a two-tailed, two sample t-test to analyze the results and compare the two groups (n=15). An F-test (or another non-parametric test) may have been more appropriate and sensitive, since the researchers examined data from populations that were not 'normal' (McClave & Sincich, 2000). Moreover, the researchers noted that significant differences were not found in their study, possibly because of the small, varied sample. This could have contributed to a Type II error. In the Whiteley et al. (1999) study, 'intention to treat' was not used for nine participants who were either taken off the gluten-free diet, failed to completely implement the diet, or had incomplete data. In the Knivsberg (1995) study, the language measure was only given to 10 of the 15 participants pre-intervention, after 1 year on-diet, and 4 years post-intervention, as the test could not be administered due to the degree of their linguistic abilities.

Furthermore, the statistical results were not laid out clearly in the Reichelt et al. (1991) study to truly indicate how the drop-outs compared to the children who remained in the diet condition.

Finally, one weakness across studies was the lack of reported confidence intervals for data collected from standardized tests. As a result, it was difficult to ascertain whether post-intervention group scores were indicative of true gains following dietary intervention.

Nonetheless, strengths were noted in some of the studies. The statistical analyses in the Knivsberg et al. (1990) and (2002) studies were carried out with the researchers' acknowledgement that the data were not normally distributed due to small, heterogeneous samples. They used appropriate non-parametric tests to measure within and between group differences (e.g. Wilcoxon paired ranking test, Mann-Whitney U-test, respectively, as well as Spearman's Correlation Coefficient). In the Harrison-Elder et al. (2006) study, two blinded raters independently coded the videotaped observations to minimize bias. The inter-rated reliability was found to be high (0.82 – 1.0). They also used the Multi-Option Observation System for Experimental Studies (MOOSES) program to assist with coding and analyzing observational data.

Summary Statement

To date, no study has solely and comprehensively examined whether the implementation of a gluten- and/or casein-free diet improves the language and communication outcomes for children diagnosed with ASD. As a result, six studies that addressed these outcomes, in addition to a variety of other outcome measures, following diet intervention were examined and critiqued in this review. Although this review focused specifically on language and communication outcomes, it is important to highlight that significant findings in the additional outcome measures examined were found, and similarly to the language and communication outcomes, results varied across studies.

Each study had its own strengths and weaknesses; however, common weaknesses existed across most, if not all, studies, such as small sample sizes, large age ranges, as well as a lack of true control groups, blinding, monitoring of diet adherence, inclusion of comprehensive language measures, and reported confidence intervals.

Recommendations

Results from the reviewed studies should be interpreted with caution due to the identified weaknesses. Nonetheless, some studies found significant improvements in the language and communication skills of children diagnosed with ASD following implementation of a gluten- and/or casein diet. Some studies also found significant improvements in additional areas, such as cognition, attention, social/emotional development, and overall autistic symptoms. Additional research is needed to increase the reliability and validity of the results to-date. In sum, there is a growing interest in examining

the effectiveness of diet modification in this population; however, the available research is limited and inconclusive. It is recommended that further research be conducted, and that researchers attempt to implement the following in their studies: 1) larger sample sizes, 2) smaller age ranges, 3) control groups, 4) monitoring of dietary intake, 5) blinding researchers and parents to dietary assignment, 6) comprehensive language and communication assessment batteries.

Conclusions

Knowledge of the best available scientific research on gluten- and/or casein-free diets is of great value to health-care professionals who work closely with parents of children diagnosed with ASD, as they are popular treatment choices. Overall, research proposes some significant improvements in the language and communication skills, amongst others, following dietary intervention in children diagnosed with ASD. However, a number of common weaknesses were identified in the examined studies. Future research incorporating larger sample sizes, smaller age ranges, control groups, dietary monitoring, blinding, and comprehensive language and communication assessment batteries is needed to increase the reliability and validity of the current findings.

References

Anderson, N.B. & Shames, G.H. (2006). Human Communication Disorders: An introduction (7th Ed.). *Developmental Language Delay in Infancy and Early Childhood*, Chapter 11 (pp.325-351).

Christison, G. W. & Ivany, K. (2006). Elimination diets in autism spectrum disorders: Any wheat amidst the chaff? *J. Dev. Behav. Pediatr, 27*(2), April, 162-171.

Harrison-Elder, J., Shankar, M., Shuster, J., Theriaque, D., Burns, S., & Sherrill, L. (2006). The gluten-free, casein-free diet in autism: Results of a preliminary double blind clinical trial. *Journal of Autism and Developmental Disorders, 36*(3), April, 413-420.

Knivsberg, A.M., Reichelt, K.L., Nodland, M., & Hoien, T. (1995). Autistic syndromes and diet: A follow-up study. *Scandinavian Journal of Educational Research, 39*, 223-236.

Knivsberg, A.M., Wiig, K., Lind, G., Nodland, M., & Reichelt, K.L. (1990). Dietary intervention in autistic syndromes. *Brain Dysfunction, 3*, 315-327.

McClave, J.T. & Sincich, T. (2000). Statistics (8th Ed.). *Nonparametric Statistics*, Chapter 14 (pp. 745-788).

Reichelt, K.I, Ekrem, J, & Scott, H. (1990). Gluten, milk proteins and autism: Dietary intervention effects on behavior and peptide secretion. *Journal of. Applied. Nutrition,42*, 1-11.

Reichelt, K.L.., Knivsberg, A.M., Lind, G., & Nodland, M. (1991). Probable etiology and possible treatment of childhood autism. *Brain Dysfunction, 4*, 308-319.

Whiteley, P., Rodgers, J., Savery, D., & Shattock, P. (1999). A gluten-free diet as an intervention for autism and associated spectrum disorders: Preliminary findings. *Autism, 3*, 45-65.

Wray, J., Silove, N., & Knott, H. (2005). Language disorders and autism. *Medical Journal of Australia, 182*(7), 543-360.