Nutritional and Dietary Interventions Improve Anxiety, Depression and Other Symptoms in Autism Spectrum Disorder

James B. Adams, Tapan Audhya, Elizabeth Geis, Eva Gehn, Valeria Fimbres, Elena L. Pollard, Jessica Mitchell, Julie Ingram, Robert Hellmers, Dana Laake, Julie S. Matthews, Kefeng Li, Jane C. Naviaux, Robert K. Naviaux, Rebecca L. Adams, Devon M. Coleman and David W. Quig

NOURISHING HOPE — JULIE MATTHEWS

AUTISM RESEARCH INSTITUTE — Arizona State University — ZOOWALK FOR AUTISM RESEARCH

Introduction

In addition to the core symptoms of autism, children and adults with autism spectrum disorder (ASD) experience a wide variety of symptoms including: increased anxiety, depression, aggression, and lower non-verbal IQ, cognitive thinking, developmental age, attention/focus and sociability. Individuals with autism also experience physical symptoms and digestive distress, in which the severity of digestive symptoms correlates with the severity of autism. Many studies have demonstrated that people with autism often have significant nutritional deficiencies, food reactions, metabolic imbalances, poor sleep and digestive problems. Several short-term studies have demonstrated benefits in addressing these underlying conditions using either nutritional or dietary treatments, but none of them investigated whether combining these treatments over the long-term could be more effective.

The Present Study

This is a one-year, single-blinded study, with a total of 117 individuals aged 3 to 58. This study is unique, being the first to combine a comprehensive nutritional intervention with specific dietary modifications. Combinations of these treatments were expected to be synergistic, and longer-term treatment to result in greater benefits. The study was conducted over 12 months to assess the long-term effects of this combined approach - since nutritional interventions are often slower than those of pharmaceutical interventions. Addressing ASD with a combination of nutritional and dietary interventions could be more effective at improving the overall symptoms of autism, as well as additional physical and psychological symptoms such as anxiety and depression, and overall functioning in children

Enrollment Criteria

ASD: n=67	Neurotypical: n=50
Diagnosis of ASD (autism, PDD-NOS or Asperger's) Diagnosis verification of ADOS and CARS-2.	No diagnosed mental disorders, including ASD, ADHD, depression or anxiety.
No major changes in behavioural or medical treatments 2 months prior, and no such changes during the 12 months of the study.	No first degree relatives of individuals with ASD (no siblings or parents).
No usage of nutritional supplements (vitamins, minerals etc.) or special diets in the previous 2 months.	No usage of nutritional supplements (vitamins, minerals etc.) or special diets in the previous 2 months.

FIGURE 1: Participant Enrollment Criteria

Participants were mostly children, some adolescents and a few adults. Gender distributions were similar between groups and were mostly male (21 females, 96 males).

Key

ASD – Autism Spectrum Disorder
PDD-NOS - Pervasive Developmental Disorder - Not Otherwise Specified
ADOS - Autism Diagnostic Observation Schedule
CARS-2 - Childhood Autism Rating Scale-2
ADHD – Attention Deficit Hyperactivity Disorder
RIAS - Reynolds Intellectual Assessment Scales
PGI-2 – Parent Global Impressions-2
VABS-II – Vineland Adaptive Behaviour Scale II
HGCSF – Healthy Gluten, Casein and Soy-Free diet
SAS-Pro - Severity of Autism Scale
PDD-BI – Pervasive Developmental Disorders Behavior Inventory
ATEC – Autism Treatment Evaluation Checklist
ABC - Aberrant Behavior Checklist
SRS - Social Responsiveness Scale
SSP - Short Sensory Profile

Protocols

All Participants: n=117

Day 0 - Initial evaluation of ASD severity and overall function. Physical examination by a physician to assess health. Initial blood draw and first morning urine collection for testing.

ASD Treatment: n=37	ASD Non-Treatment: n=30
Day 0 - Begin vitamin/mineral Day 30 - Essential fatty acids Day 60 - Epsom salt baths Day 90 - Acetyl L-carnitine Day 180 - Digestive enzymes Day 210 - Start a healthy, gluten-casein-soy-free diet	No changes in medical, nutrition, therapy, or education treatments for 12 months.

Day 365 – Final assessment of ASD severity/overall function. Final blood draw and first morning urine collection for testing.

ASD Non-Treatment and Neurotypical Groups

67 participants with ASD began the study, and 50 neurotypical participants were assessed at baseline only. ASD participants with similar ages and gender were matched and then randomly assigned to either the Treatment or Non-treatment group.

Results

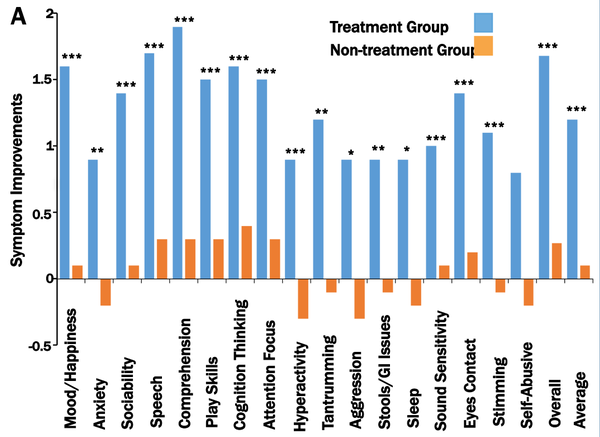

FIGURE 3: Treatment improved symptoms in 3 months

A: Parent Global Impressions (PGI-2) Average score showed significant improvements in the Treatment group compared to the Non-treatment group (1.2 ± 0.7 vs. 0.1 ± 0.5, $p=0.3x10^{-7}$). Notably, symptoms improved significantly for Mood/Happiness, Anxiety, Sociability, Speech, Comprehension, Cognition, Focus and Aggression. All symptoms were significantly improved except for Self-abusive.

B: PGI-2 average scores measured at 3, 6, and 9 months for the treatment group only, showed significant improvements in the Treatment group during the first three months. Error bars represent SD.

Y-axis: 0 (no change), +1 (slightly better), +2 (better), +3 (much better). *** p<0.05 ** p<0.01 *** p<0.001**

Results

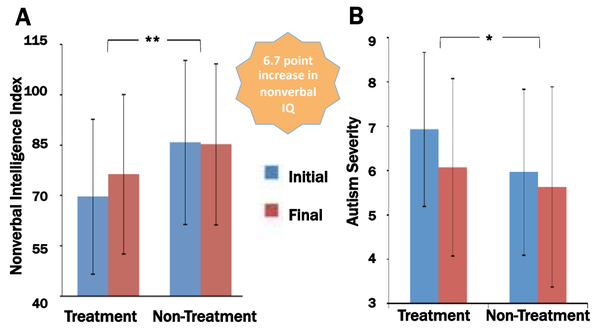

FIGURE 4: Improvement in non-verbal IQ scores and Autism Severity

A: The Treatment group show significant improvements in non-verbal IQ compared to the Non-treatment group (+6.7 ± 11.4 vs. −0.6 ± 10.7, p=0.009), using the Reynolds Intellectual Assessment Scales (RIAS). Scores are normalized so that 100 is an "average" IQ.

B: Severity of Autism Scale—Professional Evaluation (SAS-Pro) showed the treatment group improved significantly compared to the Non-treatment group (−0.93 ± 1.2 vs. −0.33 ± 0.12, p=0.04).

Y-axis: zero (no symptoms) to 10 (severe autism).
Error bars represent SD. *** p<0.05 ** p<0.01**

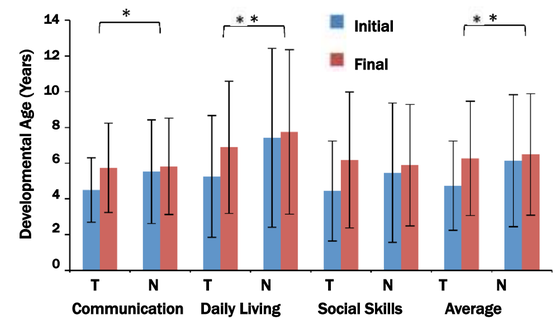

FIGURE 5. Improvement in developmental age

The Vineland adaptive behaviour scale (VABS-II) showed a 4.5 x developmental age improvement in the Treatment group (T). The Average developmental age for Communication, Daily Living and Social Skills of the Treatment group improved significantly more compared to the Non-treatment group, (N; 18.4 +/- 16 months vs. 4.3 +/- 16 months, p=0.008). Note: developmental age remained below the physical age, even after significant increases in the treatment group. Error bars represent SD. **p≤0.1 significant * p<0.05 ** p<0.01**

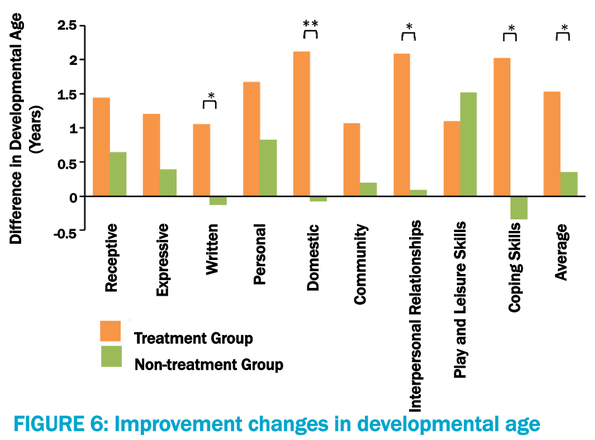

FIGURE 6: Improvement changes in developmental age

The Treatment group had significant improvements in all Vineland sub scales (VABS-II) compared to the Non-Treatment group except for Personal and Play/Leisure Skills. The Treatment group improved significantly more in Written, Domestic, Coping Skills and Interpersonal Relationships. **p≤0.1 significant * p<0.05 ** p<0.01**

Discussion

Autism has long been considered as a cluster of psychiatric/psychological behaviors caused by defective genes that induced structural changes in the brain before birth. However, we now know that autism is a whole-body disorder. Current research clearly shows that autistic individuals have suboptimal biochemical pathways that affect neurological function. The majority of children with autism have 'broken' Methylation, Transsulfuration and/or Sulfation Pathways, that can result in a cascade of symptoms (e.g. increased digestive issues/inflammation, gut flora imbalance, intestinal permeability, and decreased detoxification, etc.). All of these symptoms can significantly impact the brain since they impair nutrient absorption, cause oxidative stress, and increase inflammation. In addition, multiple studies indicate that children with ASD often have deficiencies in vitamins, essential fatty acids, sulfate, digestive enzymes and antioxidants like glutathione and often have abnormal immune responses to gluten, casein and soy.

Conclusions

The nutritional supplements and healthy gluten-free, casein-free, soy-free diet improved nutritional status. The HGCSF diet also removes potential food triggers, thereby reducing inflammatory proteins and supporting the immune system. By increasing nutrient density and decreasing the body burden, the brain's ability to function and learn is enhanced. This is demonstrated by the increase in non-verbal IQ (RIAS), and the substantial 18-month increase in developmental ability in communication, daily living skills, and social skills (VABS-II). In addition to biochemical reasons for improvement in mood, improvements in coping skills, community skills and interpersonal relationships would likely enhance mood and happiness, and contribute to the reduction in anxiety and depression symptoms seen within 3 months of starting the treatments (PGI-2).

- Many ASD symptoms, including significant improvements in happiness/mood and anxiety were alleviated in children and adults within 3 months.
- Supporting key biochemical pathways and correcting nutrient deficiencies with a HGCSF diet and specific supplements can improve ASD symptoms.
- Three unusual case reports, in which long-term problems (wheelchair dependence, catheterization, and pica) were eliminated, shows the power of comprehensive nutritional interventions in addressing complex, puzzling medical conditions, which may involve nutritional deficiencies.
- Parents report the vitamin/mineral supplement, essential fatty acids, and HGCSF diet to be the most beneficial, and were most likely to continue with these interventions in addition to the Epsom Salt Baths.
- The results suggest that comprehensive nutrition/diet protocol was safe and effective. It is recommended as a promising therapy for children and adults with ASD.

Acknowledgments

The Autism Research Institute and Zoowalk for Autism Research for funding this study. The participating families. Nordic Naturals, NOW, Houston Enzymes and Walgreens. A. Agrawal, S. Dessoy, C.Gutgsell, C.M. Lee, R. Smith, N. Tkacenko, S. Seitz, S. Ezcurra, M. McConnell and M. Adams.

Reference

Adams J.B., Audhya T., Geis E., Gehn E., Fimbres V., Pollard E.L., Mitchell J., Ingram J., Hellmers R., Laake D., Matthews J.S., Li K., Naviaux J.C., Naviaux R.K., Adams R.L., Coleman D.M., Quig D.W.. Comprehensive Nutritional and Dietary Intervention for Autism Spectrum Disorder-A Randomized, Controlled 12-Month Trial. Nutrients. 2018 Mar 17;10(3). pii: E369.

For more detailed information about this project please contact the presenting author Julie Matthews, Certified Nutrition Consultant and author of *Nourishing Hope for Autism*;
Julie@NourishingHope.com
Nourishing Hope, San Francisco, CA USA