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When the editor of Nutricula Magazine asked me if I wanted to write an article on autism, I immediately jumped at the chance since my son has Asperger syndrome, a disorder on the autism spectrum.

I also knew that I wanted the article to focus on the complementary treatment of autism and autism spectrum disorder (ASD). But I'm getting ahead of myself. Let me back up and begin with a quick overview of this group of disorders.

An overview of autism and ASD

Autism is a developmental disability characterized by problems with social interaction and communication. Typically, symptoms begin before age three and can cause delays or problems in different developmental skills.

ASD currently refers to autism, Asperger syndrome and Pervasive Developmental disorder. People on the spectrum can have very different symptoms, some more mild and others more serious. The symptoms in question include problems in:

- Verbal and non-verbal communication (unspoken, such as pointing, eye contact, and smiling)
- Sharing emotions, understanding how others think and feel, and holding a conversation
- Routines or repetitive behaviors such as repeating words or actions, obsessively following routines or schedules, and playing in repetitive ways

An obsessive interest in a single object or topic (often to the exclusion of others) is characteristic of Asperger syndrome. Furthermore, children with Asperger syndrome tend to have good vocabularies and grammar skills, unlike some children with ASD.

The focus of this article

In writing an article on this topic, there was a tremendous amount of material to pull from included research on dietary changes, behavior therapy and special education, and the use of nutraceuticals (dietary supplements). In the interest of limiting this article to a readable length, I have focused on the use of a few key dietary supplements: multivitamins, omega-3

fatty acids and iron. This is not to say that there aren't other dietary supplements that may be of benefit; just that these are the few that I have chosen to review.

Multivitamins

To determine the effect of a moderate dose multivitamin/mineral supplement on children with autistic spectrum disorder, a randomized, double-blind, placebo-controlled 3-month study was conducted in twenty children with autistic spectrum disorder, ages 3-8 years. Assessment was based upon a Global Impressions parental questionnaire.

The results were that the supplement group reported statistically significant improvements in sleep and gastrointestinal problems compared to the placebo group. An evaluation of vitamin B6 levels prior to the study found that the autistic children had substantially elevated levels of B6 compared to a control group of typical children (75% higher, $p < 0.0000001$). Vitamin C levels were measured at the end of the study, and the placebo group had levels that were significantly below average for typical children, whereas the supplement group had near-average levels.

The finding of high vitamin B6 levels is consistent with recent reports of low levels of pyridoxal-5-phosphate and low activity of pyridoxal kinase (i.e., pyridoxal is only poorly converted to pyridoxal-5-phosphate, the enzymatically active form). This may explain the functional need for high-dose vitamin B6 supplementation in many children and adults with autism.

In a later randomized, double-blind, placebo-controlled three month vitamin/mineral treatment study, 141 children and adults with autism, and pre and post symptoms of autism were assessed. None of the participants had taken a vitamin/mineral supplement in the two months prior to the start of the study. For a subset of the participants (53 children ages 5-16) pre and post measurements of nutritional and metabolic status were also conducted.



The results were that the vitamin/mineral supplement was generally well-tolerated, and individually titrated to optimum benefit. Levels of many vitamins, minerals, and biomarkers improved/increased showing good compliance and absorption. Statistically significant improvements in metabolic status were many including:

- Total sulfate (+17%, $p = 0.001$)
- S-adenosylmethionine (SAM; +6%, $p = 0.003$)
- Reduced glutathione (+17%, $p = 0.0008$)
- Ratio of oxidized glutathione to reduced glutathione (GSSG:GSH; -27%, $p = 0.002$)
- Nitrotyrosine (-29%, $p = 0.004$)
- ATP (+25%, $p = 0.000001$)
- NADH (+28%, $p = 0.0002$)
- NADPH (+30%, $p = 0.001$)

Most of these metabolic biomarkers improved to normal or near-normal levels.

The supplement group had significantly greater improvements than the placebo group on the Parental Global Impressions-Revised (PGI-R, Average Change, $p = 0.008$), and on the subscores for Hyperactivity ($p = 0.003$), Tantrumming ($p = 0.009$), Overall ($p = 0.02$), and Receptive Language ($p = 0.03$). Regression analysis revealed that the degree of improvement on the Average Change of the PGI-R was strongly associated with several biomarkers (adj. $R^2 = 0.61$, $p < 0.0005$) with the initial levels of biotin and vitamin K being the most significant ($p < 0.05$); both biotin and vitamin K are made by beneficial intestinal flora.

Oral vitamin/mineral supplementation is beneficial in improving the nutritional and metabolic status of children with autism, including improvements in methylation, glutathione, oxidative stress, sulfation, ATP, NADH, and NADPH.

The supplement group had significantly greater improvements than did the placebo group on the PGI-R Average Change. This suggests that a vitamin/mineral supplement is a reasonable adjunct therapy to consider for most children and adults with autism.

Personal experience with a multivitamin

One day when my son was in fourth grade, I ran out of the multivitamin that I gave him each day, and it was about a week before I picked up a new bottle. During that time his teacher contacted us to ask if there was some change in his medication, or some unusual stress at home. She asked because he had become more distracted in the classroom, and seemed unable to focus. His participation in the class had become somewhat chaotic. In assessing the situation, I wondered if the difficulty he was experiencing might be related to his not having the multivitamin. I immediately purchased the multivitamin and gave it to him the next morning. That evening I spoke to his teacher, and she reported that everything was back to normal. My wife and I were amazed at how quickly and how profoundly our son responded to multivitamin therapy.

Omega-3 fatty acids

Research examined the levels of fatty acids in a mainstream school-aged population and the relationship to learning and behavior. Cheek cell samples from 411 typically developing school children were collected and analyzed for polyunsaturated fatty acid (PUFA) content. In addition, measures of general classroom attention and behavior were assessed in these children by teachers and parents. Cognitive performance tests were also administered in order to explore whether an association between behavior and/or cognitive performance and PUFA levels exists.

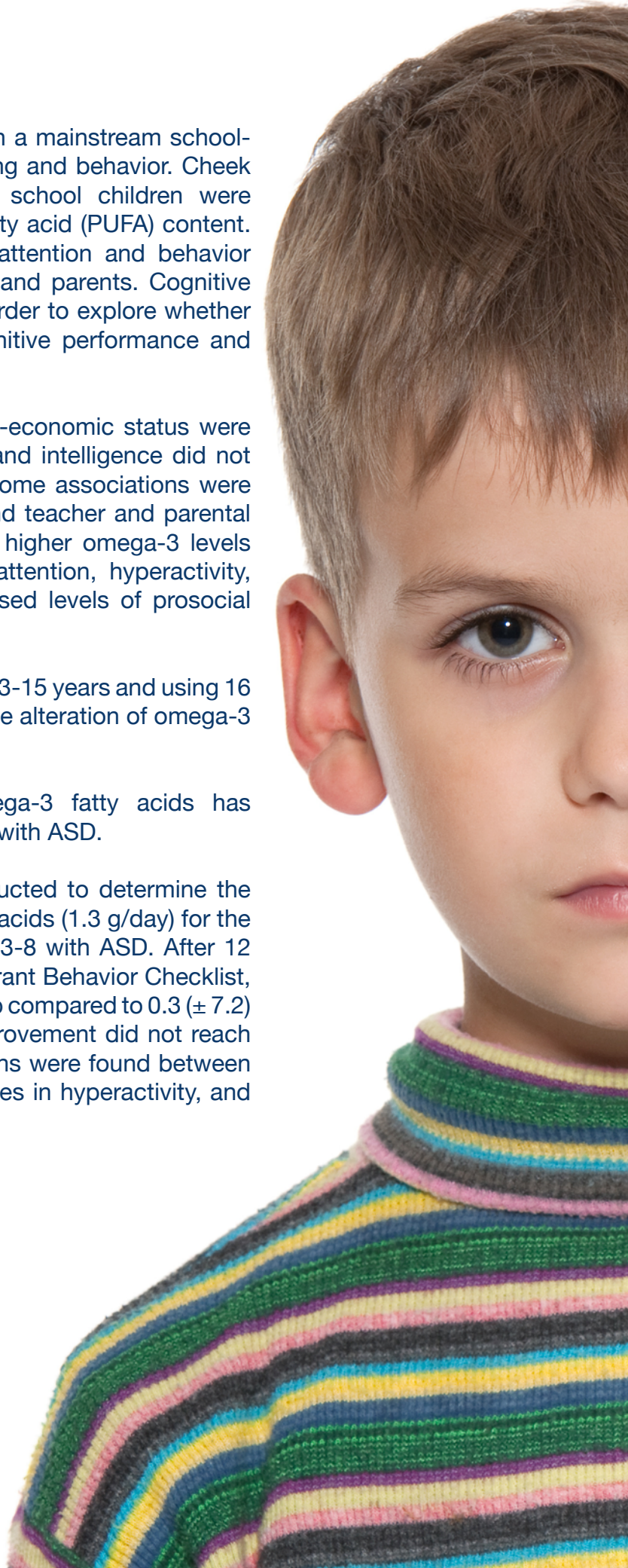
Relationships between PUFA levels and socio-economic status were also explored. Measures of reading, spelling and intelligence did not show any association with PUFA levels, but some associations were noted with the level of omega-3 fatty acids and teacher and parental reports of behavior, with some evidence that higher omega-3 levels were associated with decreased levels of inattention, hyperactivity, emotional and conduct difficulties and increased levels of prosocial behavior.


Likewise, in a study of 25 autistic children aged 3-15 years and using 16 healthy children in the control group, remarkable alteration of omega-3 fatty acids were reported.

Not surprisingly, supplementation with omega-3 fatty acids has demonstrated clinical improvement in patients with ASD.

A pilot randomized controlled trial was conducted to determine the feasibility, safety and efficacy of omega-3 fatty acids (1.3 g/day) for the treatment of hyperactivity in 27 children ages 3-8 with ASD. After 12 weeks, hyperactivity, as measured by the Aberrant Behavior Checklist, improved 2.7 (\pm 4.8) points in the omega-3 group compared to 0.3 (\pm 7.2) points in the placebo group (although the improvement did not reach statistical significance in this study). Correlations were found between decreases in five fatty acid levels and decreases in hyperactivity, and the treatment was well tolerated.

In an open-label pilot study to determine the efficacy and safety of omega-3 fatty acids for children with ASD, ten children aged 4-7 years old with ASD were given 1 gram daily of omega-3 fatty acids for 12 weeks.





The main outcome measure used was the Autism Treatment Evaluation Checklist (ATEC). The results were that, of the 9 subjects who completed the study, 8 showed improvement of about 33% on the Autism Treatment Evaluation Checklist (ATEC). None worsened and no side effects were reported. Omega-3 fatty acids appear to be safe and might be helpful for children suffering from ASD.

Another randomized, double-blind, placebo-controlled 6-week pilot trial investigated the effects of 1.5 g/d of omega-3 fatty acids (.84 g/d eicosapentaenoic acid, .7 g/d docosahexaenoic acid) supplementation in 13 children (aged 5 to 17 years) with autistic disorders accompanied by severe tantrums, aggression, or self-injurious behavior.

The outcome measure was the Aberrant Behavior Checklist (ABC) at 6 weeks. Researchers observed an advantage of omega-3 fatty acids compared with placebo for hyperactivity and stereotypy, each with a large effect size. A trend toward superiority of omega-3 fatty acids over placebo for hyperactivity was seen, and no clinically relevant adverse effects were elicited in either group. The results of this study provide additional evidence that omega-3 fatty acids may be an effective treatment for children with autism.

Personal experience with omega-3 fatty acids

One of the first supplements I gave my son was an omega-3 fatty acid supplement. After about a month of using it, I began to notice improvements in his hyperactivity. He has consistently taken an omega-3 supplement for over five years, and I am convinced that it has improved his ability to focus, probably as a result of reduced hyperactivity.

Iron

Research was undertaken to examine the prevalence of iron deficiency in 52 children with autism and 44 children with Asperger syndrome, and to examine whether this will influence guidelines and treatment. The results showed that six members of the autistic group had iron deficiency anemia, and, of the 23 autistic children who had serum ferritin (a marker for iron storage in the body) measured, 12 were iron deficient. Only two of the Asperger group had iron deficiency anemia, and, of the 22 children who had their serum ferritin measured, only three were iron deficient.

Iron deficiency, with or without anemia, can impair cognition and is associated with developmental slowing in infants, mood changes and poor concentration in children. This study showed a very high prevalence

of iron deficiency in children with autism, which could potentially further compromise their communication and behavioral impairments.

To determine if there is a relationship between low serum ferritin and sleep disturbance in children with autism spectrum disorder, an 8-week open-label treatment trial with oral iron supplementation was conducted as a pilot study.

Results were assessed using baseline and post treatment completion of a Sleep Disturbance Scale for Children and a Food Record by parents, and blood samples.

Thirty-three children completed the study. Seventy-seven percent had restless sleep at baseline, which improved significantly with iron therapy, suggesting a relationship between sleep disturbance and iron deficiency in children with autism spectrum disorder.

Sixty-nine percent of preschoolers and 35% of school-aged children had insufficient dietary iron intake.

Mean ferritin increased significantly (16 microg/L to 29 microg/L), as did mean corpuscular volume and hemoglobin, suggesting that low ferritin in this patient group resulted from insufficient iron intake.

Similar prevalence of low ferritin at school age as preschool age indicates that children with autism spectrum disorder require ongoing screening for iron deficiency.

Conclusion

While there are many dietary supplements that may offer benefit as part of a complementary strategy in the treatment of ASD, three that parents and clinicians should consider are multivitamins, omega-3 fatty acids and iron.

Research suggests that these supplements may help compensate for nutrients that ASD children aren't getting an adequate amount of, and that supplementation may help improve clinical symptoms of their disorder



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