

Autism Parenting Magazine

Issue 20 • July 2014

Magazine

SCIENCE OF SUPPLEMENTS



Social Skills

101

**Identifying
SENSORY OVERLOAD**

**Interview with
Dr. MARIA WYNNE**

Vitamin/Mineral Supplements for Children and Adults with Autism

INTRODUCTION:

The definition of a “vitamin” or “essential mineral” is that the lack of that vitamin or mineral results in disease or even death. The Recommended Daily Allowance (RDA) is the minimum amount required to prevent disease, but may be less than the amount needed for optimal mental and physical health. Most people in the US consume less than the RDA of one or more vitamins and minerals. For example, many women lack enough calcium and iron, leading to osteoporosis and anemia, respectively.

Vitamins and minerals are available in vegetables, fruits, meat, and other sources. However, the typical U.S. diet is lacking in key vitamins and minerals, so many people need to take a supplement. Children

with autism seem to have an increased need for certain vitamins and minerals.

The primary role of vitamins and minerals is to act as enzymatic co-factors for many important reactions in the body. For example, the production of serotonin (an important neurotransmitter) requires the conversion of 5-HTP to serotonin, and vitamin B6 is the co-factor for the enzyme for that reaction, meaning that it greatly accelerates the rate of the reaction. If you have too little vitamin B6, then the reaction is slow, and less serotonin is produced. Vitamin B6 is involved in over 100 enzymatic reactions in the body, including the production of several neurotransmitters. Some vitamins and minerals are involved in hundreds of enzymatic reactions, affecting most of the major metabolic pathways in the body. To put it simply, vitamins and minerals are essential for a healthy life.



RESEARCH ON INDIVIDUAL VITAMIN/MINERAL SUPPLEMENTS FOR CHILDREN AND ADULTS WITH AUTISM

According to a recent survey of 539 physicians, vitamin/mineral supplements are among the most widely recommended medical interventions for autism, and are recommended by 49% of physicians for children with autism [Golnick and Ireland 2009]. However, there have been relatively few treatment studies of vitamin/mineral supplements for children with autism. Three studies demonstrated that children with autism have impaired methylation (decreased SAM), decreased glutathione, and increased oxidative stress [James et al 2004, 2006, 2009] compared to neurotypical children. Two open-label studies demonstrated that nutritional supplementation - with vitamin methyl-B12, folinic acid (a special type of folic acid), and (in one of the studies) trimethylglycine - resulted in statistically significant improvements in methylation, glutathione, and oxidative stress. [James et al 2004, 2006]. A 30-week, double-blind, placebo-controlled study [Dolsek et al 1993] of high-dose vitamin C (110 mg/ kg) found a reduction in autism severity as measured by the Ritvo-Freeman scale. One small open-label study (Freeddenfeld et al 2011) found that two weeks of NADH (the active form of vitamin B3) was effective at improving methylation, glutathione, NADH, and ribose (Freeddenfeld et al . There have been 11 double-blind, placebo-controlled studies of very high dose vitamin B6 with magnesium, with almost all showing positive behavioral improvements. However, the studies were somewhat limited by methodological problems including small sample size and the use of assessment tools of limited validity [Adams et al 2006a].

RESEARCH ON MULTI-VITAMIN/MINERAL SUPPLEMENTS FOR CHILDREN AND ADULTS WITH AUTISM

2004 Study: In 2004 we published a small pilot study of a multi-vitamin/mineral supplement for children with ASD [Adams et al 2004], which used a randomized, double-blind, placebo-controlled design. None of the children in the study were on a vitamin/mineral supplement for two months prior to the study. They found that the treatment group generally improved more than the placebo group, with statistically significant greater improvements in sleep ($p=0.03$) and gastrointestinal problems ($p=0.03$), both of which are very common in autism.



2007/2008 Study: Due to the promising results of the 2004 study, in 2007/2008 we conducted a small open-label pilot study of a customized vitamin/mineral supplement with 10 children with ASD, which included extensive pre and post measurements of nutritional status (vitamins, minerals, amino acids) and metabolic functioning (oxidative stress, methylation, glutathione, sulfation, and neurotransmitters). The supplement was well-absorbed (as indicated by increases in blood levels and urinary excretion), and improved levels of glutathione and some neurotransmitters. The results of that pilot study were used to reformulate the supplement, adjusting the level of some ingredients slightly up or down based on the laboratory findings.

2008/2009 Study In 2008/2009 this revised “second generation” supplement was used to conduct a randomized, double-blind, placebo-controlled three-month treatment study. The study started with a detailed comparison study of the nutritional and metabolic status of the children with autism (N=55, recruited for the treatment study) vs. neurotypical children of similar age, gender and locale (Adams et al 2011a). The autism group had many statistically significant differences ($p<0.001$) in their average levels of biomarkers compared to the neurotypical group, including: Low levels of biotin, glutathione, S-adenosylmethionine (SAM), uridine, plasma adenosine-5'-triphosphate (ATP), reduced nicotinamide adenine dinucleotide (NADH), reduced nicotinamide adenine dinucleotide phosphate (NADPH), plasma sulfate (free and total), and plasma tryptophan; also high levels of oxidative stress markers and plasma

glutamate. A statistical analysis demonstrated significant associations between all three autism severity scales and several groups of biomarkers, including primarily vitamins, minerals, and amino acids.

The treatment part of the study involved a randomized, double-blind, placebo-controlled three month vitamin/mineral treatment study (Adams et al 2011b). The study involved 141 children and adults with autism. Biomarkers of nutritional and metabolic status were measured in a subset of the participants (53 children ages 5-16). 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. There were many statistically significant improvements in nutritional and metabolic status, including improvements in sulfate, methylation, glutathione, oxidative stress, ATP, and NADH. Most of these metabolic biomarkers improved to normal or near-normal levels.

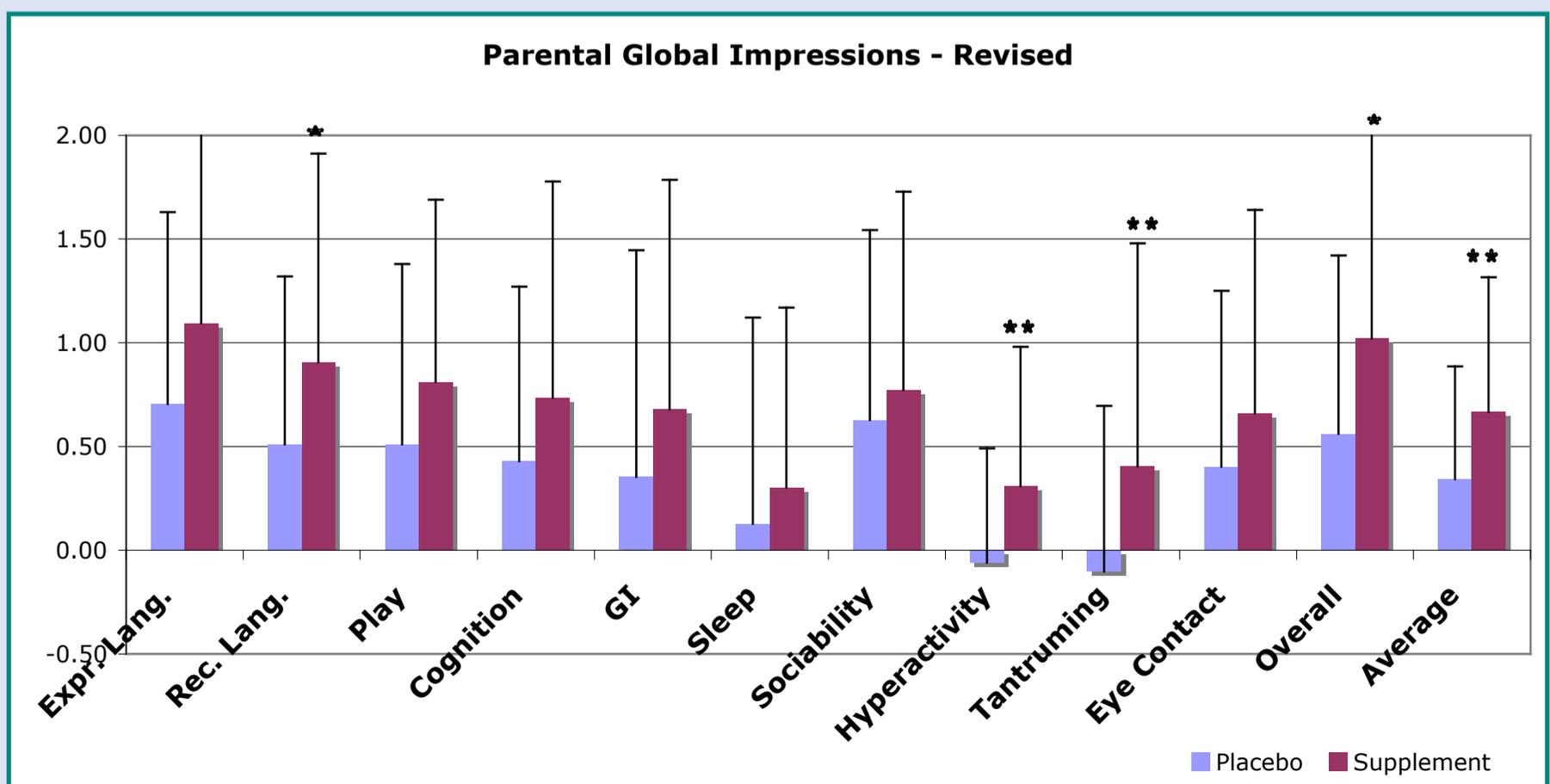
The supplement group had significantly greater improvements than the placebo group on the Parental Global Impressions-Revised (PGI-R, Average Change, $p=0.008$), and on the subscores for Hyperactivity

($p=0.003$), Tantrumming ($p=0.009$), Overall ($p=0.02$), and Receptive Language ($p=0.03$). Overall, it seemed that about 1/3 of the group had no improvement, 1/3 had some improvement, and 1/3 had substantial improvement. The improvements were greatest in the group under age 18, but there were some reported benefits in the adult group as well.

2011-2013 Study: From 2011 to 2013 we conducted a 12-month, randomized, single-blind, controlled study of treating children and adults with autism with a combination of 6 nutritional treatments, including an improved version of the vitamin/mineral supplement used in our 2008/2009 study. The vitamin/mineral supplement was rated by participants as one of the two most effective treatments, and the results of that study are now being written up for publication.

2014: Release of ANRC Essentials: In June 2014 we decided to release an improved version of the supplement used in our 2007/2008, 2008/2009, and 2011/2013 studies. To prevent any financial conflict of interest, we formed a non-profit, the Autism Nutrition Research Center (ANRC), which distributes the vitamin/mineral supplement, now known as ANRC

Figure 1 - Results for the Parent Global Impressions – Revised. The supplement group had greater improvements in the PGI-R Average score ($p=0.008$), and in the subscores for Receptive Language ($p=0.03$), Hyperactivity ($p=0.003$), Tantrumming ($p=0.009$), and Overall ($p=0.02$). The y-axis is from -3 (much worse) to 0 (no change) to +1 (slightly better) to +2 (better) to +3 (much better).



Essentials. ANRC also provides general nutritional recommendations to families at www.autismnrc.org

SUMMARY

Many research studies have demonstrated that children and adults with autism often have nutritional and metabolic problems, including problems with methylation, glutathione, oxidative stress, sulfation, lithium, and more. Our research has demonstrated that a vitamin/mineral supplement can substantially improve or even normalize those nutritional and metabolic problems, and result in significant improvements in symptoms based on a large, double-blind, placebo-controlled study.

RECOMMENDATION

We recommend that all children and adults with autism consider a 2-3 month trial of a vitamin/mineral supplement designed for individuals with autism that is similar to the one used in our studies. By starting at a low dose, and gradually increasing it, there is minimal risk of adverse effects, and many children and adults are likely to benefit, sometimes substantially.

FINANCIAL CONFLICT OF INTEREST: The author serves as President of the Autism Nutrition Research Center, a non-profit which produces a vitamin/mineral supplement (ANRC Essentials) for children and adults with autism. However, he works as a volunteer, and does not receive any royalties from the sales of ANRC Essentials or any nutritional supplement.

Bio: James B. Adams, Ph.D., is the Director of the Autism/Asperger's Research Program at Arizona State University. He is also the President of the Autism Nutrition Research Center, a new non-profit dedicated to providing autism families with science-based information and recommendations on nutrition. He is the co-leader of the Science Advisory Committee of the Autism Research Institute, and chair of the Scientific Advisory Committee of the Neurological Health Foundation. He is the President of the Autism Society of Greater Phoenix. He has published over 30 scientific articles on autism. He has an adult daughter with autism.

REFERENCES

Adams JB, Holloway C. **Pilot study of a moderate dose multivitamin/mineral supplement for children with autistic spectrum disorder.** *J Altern Complement Med.* 2004 Dec;10(6):1033-9.

Adams JB, George F, Audhya T. **Abnormally high plasma levels of vitamin B6 in children with autism not taking supplements compared to controls not taking supplements.** *J Altern Complement Med.* 2006a Jan-Feb;12(1):59-63.

Adams JB, Audhya T, McDonough-Means S, Rubin RA, Quig D, Geis E, Gehn E, Loresto M, Mitchell J, Atwood S, Barnhouse S, Lee W. **Nutritional and Metabolic Status of Children with Autism vs. Neurotypical Children, and the Association with Autism Severity,** *Nutr Metab (Lond).* 2011a Jun 8;8(1):34.

Adams JB, Audhya T, Mcdonough-Means S, Rubin RA, Quig D, Geis E, Gehn E, Loresto M, Mitchell J, Atwood S, Barnhouse S, Lee W **Effect of a Vitamin/Mineral Supplement on Children with Autism,** *BMC Pediatrics* 2011b, **11:111**

Dolske MC, Spollen J, McKay S, Lancashire E, Tolbert L. **A preliminary trial of ascorbic acid as supplemental therapy for autism.** *Prog Neuropsychopharmacol Biol Psychiatry.* 1993 Sep;17(5):765-74.

Freeddenfeld S, Hamada K, Audhya T, Adams JB. **Biochemical Effects of Ribose and NADH Therapy in Children with Autism,** *Autism Insights,* 2011:3 3-13; erratum *Autism Insights* 2011:3 15; Erratum - *Autism Insights* 2011:3 15

Golnik AE, Ireland M **Complementary alternative medicine for children with autism: a physician survey.** *J Autism Dev Disord.* 2009 Jul;39(7):996-1005. Epub 2009 Mar 11.

James SJ, Cutler P, Melnyk S, Jernigan S, Janak L, Gaylor DW, Neubrandner JA. **Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism.** *Am J Clin Nutr.* 2004 Dec;80(6):1611-7.

James SJ, Melnyk S, Jernigan S, Cleves MA, Halsted CH, Wong DH, Cutler P, Bock K, Boris M, Bradstreet JJ, Baker SM, Gaylor DW. **Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism.** *Am J Med Genet B Neuropsychiatr Genet.* 2006 141:947-956.

James SJ, Melnyk S, Fuchs G, Reid T, Jernigan S, Pavliv O, Hubanks A, Gaylor DW. **Efficacy of methylcobalamin and folic acid treatment on glutathione redox status in children with autism.** *Am J Clin Nutr.* 2009 Jan;89(1):425-30. Epub 2008 Dec 3.