Nutritional Considerations of Attention Deficit Hyperactivity Disorder and Autism

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ADHD Characteristics

- Problems paying attention
- Difficulty listening to instructions
- Difficulty completing tasks
- Fidget and squirm
- Hyperactive
- Blurt out answers
- Interrupt others
ADHD Statistics

- Roughly 20-25% of children with ADHD show one or more specific learning disabilities in math, reading or spelling.

- A conservative estimate is that 3-5% of the school-age population has ADHD.
Deficiency S/S

<table>
<thead>
<tr>
<th>N-6 Fatty Acids</th>
<th>ADHD Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Impaired growth</td>
<td>✓ Polydipsia</td>
</tr>
<tr>
<td>✓ Dry and scaly skin</td>
<td>✓ Eczema</td>
</tr>
<tr>
<td>✓ Polydipsia</td>
<td>✓ Asthma</td>
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<tr>
<td>✓ Polyuria</td>
<td>✓ Allergies</td>
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</table>
Nervous System and Fatty Acids

• The nervous system is the organ with the second largest concentration of lipids, exceeded only by adipose tissue.

• Approximately 35% of these lipids are long-chain polyunsaturated fatty acids (LC-PUFAs), such as arachidonic acid (AA; 20:4n–6) and docosahexaenoic acid (DHA; 22:6n–3), which are known to play an essential role in brain development and functions.

• AA and DHA could be either provided in diet or synthesized in the body from the essential fatty acid (EFA) linoleic acid (LA; 18:2n-6) and alpha linolenic acid (18:3n-3).

  Am J Clin Nutr (1993)
Zinc and Neurology

• Essential for brain development.
• Essential for Central Nervous System function.
• Very potent inhibitor of the NMDA (N-methyl-D-aspartate) receptor complex.
• Involved with Adenosine A_1 and A_2A receptors.
• Important for the production and modulation of Melatonin.
• May also influence the N2 wave in the frontal and parietal regions of the brain.
  ✓ Information processing and inhibitory processes.

Dopamine and Serotonin

- Both of these neurotransmitter systems appear to be involved in ADHD.

- Vitamin B6 required for serotonin synthesis.

- Melatonin regulates dopamine.

J Am Acad Child Adolesc Psychiatry (2001)
J Atten Disord (1999)
Zinc and Dopamine Connection

• Zinc is required for the conversion of dietary pyridoxine to its active form, pyridoxal 5’ phosphate, which is necessary for the conversion of tryptophan to serotonin.

Prog Neuropsychopharmacol Biol Psychiatry (2008)
Dopamine and Appetite

- Dopamine mediates the reinforcing value of food, and low concentrations of dopamine are related to increased feeding.

- Administering a drug that increases dopamine may reduce energy intake, possibly by reducing food reinforcement.

AJCN – 8/2007
Methylphenidate

- **Short-acting methylphenidate (MPH)**
  - Drug that increases the availability of dopamine by blocking its reuptake, reduces energy intake and alters macronutrient preference.

- Currently indicated for the treatment of childhood and adult attention-deficit hyperactivity disorder.

- Reduces overall energy intake with a selective reduction in dietary fat.

- Low brain dopamine predicts overeating and obesity, and administering agents that increase dopamine results in reduced feeding behavior.

AJCN – 8/2007
Dopamine and Obesity

• Human data suggest that low availability of circulating dopamine caused by rapid dopamine transport or reduced brain dopamine signaling may be related to the development of obesity.

• Ingesting foods high in sugar and simple carbohydrates, stimulates the release of dopamine in the accumbens shell.


Neuroscience (2005)
Zinc and ADHD

• Lower blood zinc concentrations have been found in children with ADHD than in control subjects in several countries.

Biol Psychiatry (1997)  
Int J Neurosci (1990)  
Long-chain PUFAs and the Human Brain

- The n–3 and n–6 PUFAs comprise 14% and 17% of the total FAs in the human brain and are predominantly DHA and arachidonic acid (AA; 20:4n–6), respectively.

AJCN – 1/2009
Essential Fatty Acids

- Essential fatty acids are required for optimal growth and development in children.

- In humans, alpha-linolenic acid (ALA) is converted into the long-chain n-3 (omega-3) fatty acid docosahexaenoic acid (DHA), a major constituent in membranes of the brain and retina and important for the maintenance of optimal brain function.

J Pediatr (1992)
DHA and Arachidonic Acid

- Both DHA and AA accumulate rapidly in neural tissues during the brain growth spurt that occurs during gestation and the first year of life.

AJCN – 1/2009
DHA and Brain Function

• DHA is important for both membrane fluidity and neurotransmitter function, especially synaptic signal transduction, particularly during the perinatal period.

Early Hum Dev (2007)
Lipids (2001)
J Am Acad Child Adolesc Psychiatry (2001)
DHA and Dopamine

• Deficits in frontal cortex dopamine neurotransmission seen in patients with ADHD could therefore be associated with lower brain DHA concentrations.

Prostaglandins Leukot Essent Fatty Acids (2006)
DHA and EFA Deficiency

- Children with ADHD have also been shown to have lower plasma or red blood cell DHA concentrations and symptoms such as increased thirst and urination that are characteristic of essential fatty acid deficiency, which suggests alterations in FA metabolism that may share a common genetic susceptibility.

Physiol Behav (1996)
Prostaglandins Leukot Essent Fatty Acids (2006)
DHA vs. EPA

- DHA and EPA can be synthesized from the parent n–3 FA -linolenic acid (ALA) in the liver through a series of elongation and desaturation steps.

- There have, however, been recent concerns that the efficiency of this process may be low (8%) because both n–6 and n–3 FAs share and compete for the same enzymes that are used for desaturation and elongation.

- n–6 FAs such as linoleic acid are widely present in vegetable oils, seeds, nuts, margarine, grains, eggs, and some meats.

- n–3 polyunsaturated FAs (PUFAs) are found primarily in canola and soybean oil, flaxseed, walnuts, eggs, some meats, and cold water fish.

- Intakes of n-6 FAs have increased, resulting in a high ratio of n-6:n-3 FA intakes in the diet that may be associated with increased risk of mental health disorders.

Biol Psychiatry (2005)

Iron and ADHD

- Serum ferritin levels <45 mcg/L might indicate a risk for sleep wake transition disorders, including abnormal sleep movements, in children with ADHD.
  
  *Eur Child Adolesc Psychiatry (2009)*

- Serum ferritin was found to be significantly lower in children with ADHD.
  
  *Indian Pediatr. (2010 Mar 15.)*
Nutritional Considerations of Autism

- The prevalence of nutritional intervention and complementary and alternative medicine (CAM) in children diagnosed with an autism spectrum disorder is estimated at 74%.

  Ann Neurol (2005)
**Autism Characteristics**

- Behavioral impairment
- High prevalence of gastrointestinal disease and dysbiosis
- Autoimmune disease
- Mental retardation
- Affects males more than females (4:1)


Research Studies and Autism

• Support the hypothesis that redox imbalance and oxidative stress may be a contributing factor to autism pathology.

Pathophysiology (2006)
Prostaglandins Leukot Essent Fatty Acids (2002)
Glutathione

- The complete transsulfuration of methionine to GSH occurs primarily in the liver, plasma concentrations of cysteine and GSH generally reflect hepatic synthesis and export.

- Approximately 80% of GSH synthesized in the liver is exported to the plasma where it is hydrolyzed to cysteinylglycine and cysteine for uptake by tissues, such as the brain, that lack or weakly express the complete transsulfuration pathway.

Factors that affect Glutathione

• Viral infection

• Nutritional deficiencies

• Impaired detoxification
  ✓ Negatively affect GSH synthesis in the liver and can indirectly affect peripheral redox status in brain and immune cells that require cyst(e)ine import from the liver to complete transsulfuration and GSH synthesis.

Methylation Capacity vs. Antioxidant Capacity

• Biochemical findings with Autistic Children

• Significant decrease in methylation capacity (↓SAM:SAH)
  ✓ S-adenosylmethionine (SAM)
  ✓ S-adenosylhomocysteine (SAH)

• Decrease antioxidant/detoxification capacity (↓GSH:GSSG)
  ✓ Reduced glutathione (GSH)
  ✓ Oxidized disulfide form of glutathione (GSSG)

• Increase in oxidative stress (GSSG)
Transmethylation and Autism

• Significant improvements observed in transmethylation metabolites and glutathione redox status after treatment suggest that targeted nutritional intervention with methylcobalamin and folinic acid may be of clinical benefit in some children who have autism.
Abnormal Pathways with Autistic Children

**Effects**

- DNA synthesis or repair and proliferation.
- Cellular methylation
- GSH redox homeostasis

*AJCN – 1/2009*
Magnesium and Dopamine

- Pharmacologic use of Mg can decrease neurologic deficit in experimental head trauma, possibly by blockade of N-methyl-D-aspartate receptors.

- In conjunction with high doses of pyridoxine, Mg salts benefit 40% of patients with autism, possibly by an effect on dopamine metabolism.

Magnes Trace Elem (1991-1992)
Ascorbate and Glutathione

- Ascorbate and glutathione compete for free radicals in cells, it is logical that an increase in the concentration of ascorbate will spare glutathione because ascorbate scavenges a greater percentage of free radicals.

- Ascorbate readily reacts with glutathione radicals arising from the reaction of glutathione and free radicals.

- Ascorbate spares glutathione first by competing with glutathione for free radicals and second by converting thiol radicals back to glutathione.

- Each 1-mol change in ascorbate is associated with a change of 0.5 mol in glutathione.

AJCN – (1/2003)
Inflammation and Autism

• A recent report documented the presence of chronic inflammation in the autistic brain that seems mediated by innate microglial activation and proinflammatory cytokines.

• The inflammatory response is augmented when GSH concentrations are low, and chronic inflammation depletes GSH further and promotes a self-perpetuating cycle that could exacerbate gastrointestinal and central nervous system inflammation associated with autism.

Int Rev Psychiatry (2005)
Ann Neurol (2005)
Gastrointestinal Inflammation and Autism

• Several clinical studies documented an increased prevalence of gastrointestinal inflammation and increased mucosal permeability in the upper and lower intestines in autistic children.

Micronutrient analysis

- Vitamin B2
- Vitamin B6
- Vitamin B12
- Folate
- Choline
- Zinc
- Glutathione
- Cysteine
- Magnesium
- Vitamin C

Homocysteine
- Gliadin antibodies
- Allergy
- Ferritin (serum)
Case Study

3 year old male
Dx. Autism

SpectraCell Results: (1/09)
- **Deficiencies:** B12, Pantothenate, G/Insulin, Chromium, Glutathione, Spectrox

SpectraCell Results: (6/09)
- **Deficiencies:** Glutathione and Spectrox
Case Study

10 year old male
Dx. ADHD

SpectraCell Results: (4/09)
- Deficiencies: B12, Carnitine, Glutathione, Vitamin D,
- Marginal: B6, Cysteine
- Spectrox 42%
Medication: Vyvance
Please join us next month, Thursday August 19th, for our webinar on, “Nutritional Considerations of Diabetes Mellitus.”

To register log on to www.spectracell.com/webinars