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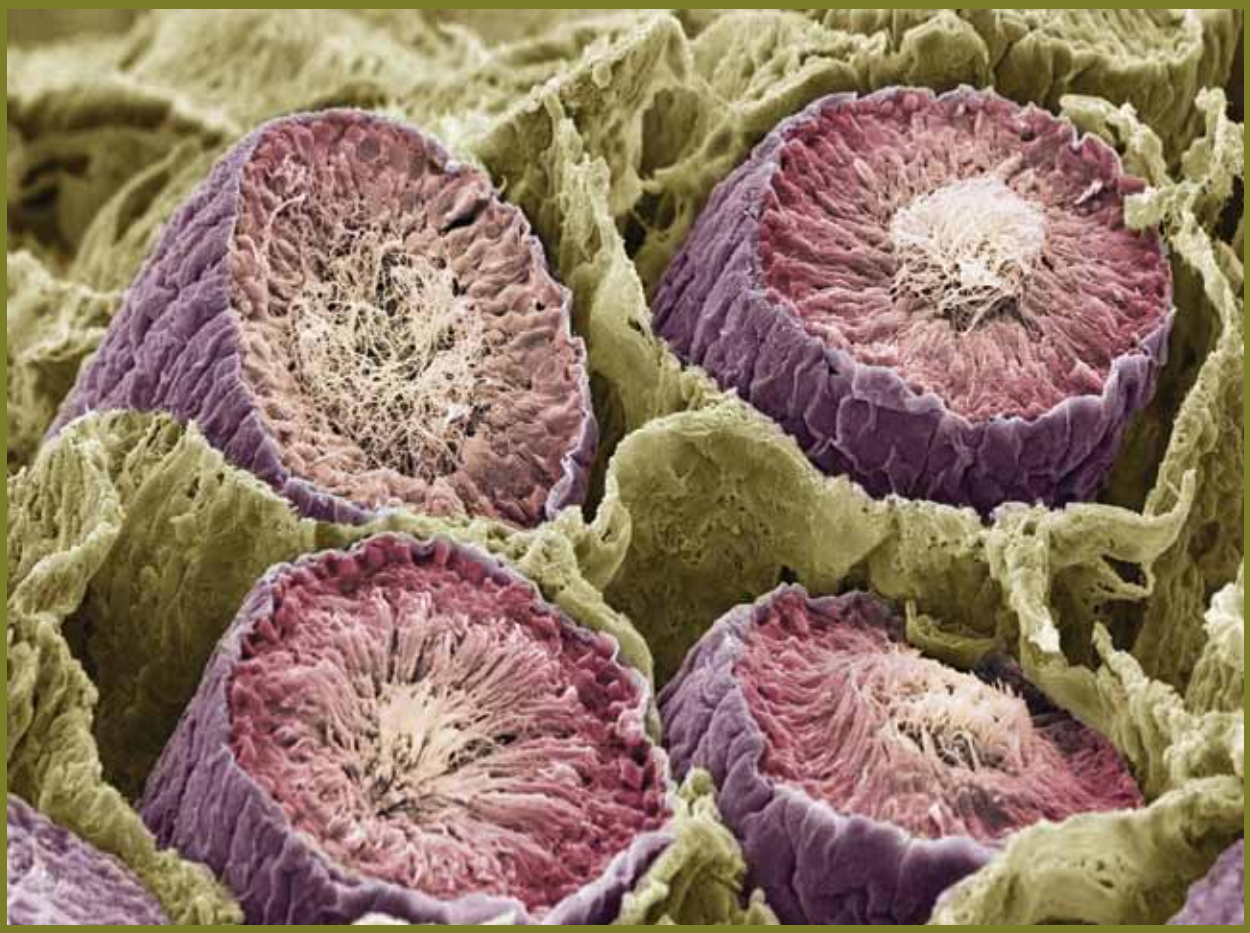

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Complementary and Alternative Medical Therapies for Children with Attention-Deficit/Hyperactivity Disorder (ADHD)

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) is a commonly diagnosed childhood disorder characterized by impulsivity, inattention, and hyperactivity. ADHD affects up to 1 in 20 children in the United States. The underlying etiologies of ADHD may be heterogeneous and diverse, and many possible risk factors in the development of ADHD have been identified. Conventional treatment usually consists of behavioral accommodations and medication, with stimulant medication most commonly being prescribed. Parents concerned about the side effects and long-term use of conventional medications are increasingly seeking alternatives to pharmacologic treatment. Complementary and alternative medicine (CAM) offers parents various treatment options for this condition, including dietary modifications, nutritional supplementation, herbal medicine, and homeopathy. CAM appears to be most effective when prescribed holistically and according to each individual's characteristic symptoms. Possible etiologies and risk factors for the condition also need to be considered when developing a treatment plan. This article serves to highlight the latest research regarding the most commonly used CAM for children with ADHD.

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a common childhood behavioral condition characterized by persistent symptoms of inattention, hyperactivity, and impulsivity.[1] ADHD is diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV),[2] which defines three types of ADHD: Predominantly Inattentive, Predominantly Hyperactive-Impulsive, and Combined.[3] The symptoms of ADHD affect cognitive, behavioral, emotional, and social functioning.[4] Its incidence is thought to range conservatively from 3-7 percent, with its diagnosis made 3-9 times more often in boys.[5,6] ADHD is a heterogeneous disorder that often continues from childhood and adolescence into adulthood and often carries a high risk of co-morbidity with learning disabilities and conduct disorder.[4] Around 25 percent of ADHD children also suffer from anxiety, and 15-75 percent have a co-morbid mood disorder.[7] Concerns about side effects and questions regarding the long-term safety of pharmacological treatment, as well as personal preference to avoid stimulant medication, has led many parents to seek complementary and alternative medical therapies.[4]

Pathogenesis

The underlying etiologies for ADHD are diverse.[8] Neurological and biochemical anomalies, as well as genetic influences, are discussed below.

Neurological Anomalies in ADHD

ADHD has been associated with conditions that cause neurological impairment, such as lead poisoning, chromosomal abnormalities, neurotransmitter deficits, oxygen deprivation at birth, smoking during pregnancy, and fetal alcohol syndrome.[9,10] A further non-genetic factor thought to contribute to ADHD is oxidative stress, which causes damage to DNA.[11] Most ADHD children, however, have no gross structural damage to the central nervous system (CNS). While certain neuro-imaging studies have shown anatomical

differences of certain areas of the brain in patients with ADHD, findings have been inconsistent, and it is now hypothesized that the brain in ADHD is altered in a more widespread manner.[12,13]

Biochemical Anomalies in ADHD

The biochemical etiology of ADHD has been postulated to be related to low levels of catecholamines (namely epinephrine, norepinephrine, and dopamine) and serotonin in certain areas of the brain. These neurotransmitters are responsible for activating the areas of the brain needed for focus and concentration.[12,14] Some recent studies have also shown evidence for abnormalities of glutamate/glutamine and creatine in the brain.[15,16] A disturbance in the interaction between the glutamatergic and dopaminergic systems has been proposed as a key pathogenetic factor in ADHD;[15] however, more research is needed in this area. While conventional ADHD medications attempt to restore neurotransmitter balance in the brain, there has been little discussion concerning the possible physiological causes of such low levels of neurotransmitters, e.g., dysfunction in the manufacture of these compounds, poor uptake into the brain, or increased transport out of the brain to the presynaptic terminal of the neuron.[8,14]

Genetic Effects

Numerous studies have shown evidence supporting genetic causes and associations with ADHD, with a five- to six-fold increase in occurrence among relatives of ADHD patients being noted.[13,14,17] Several genes are expected to be involved; however, ultimately the search is not for a specific ADHD gene but rather for genes that regulate brain growth and receptor development.[14]

Risk Factors

Numerous risk factors for ADHD have been proposed. The following potential etiological domains all appear to exacerbate existing ADHD symptoms and have a plausible neural mechanism of action,[18] as outlined in Table 1.

Key words: ADHD, attention-deficit hyperactivity disorder, ADD, inattention, hyperactivity, impulsivity, behavioral problems, anxiety, homeopathy

Dietary Influence and Nutritional Deficiencies

Poor diet and resultant deficiencies of various nutrients can contribute to oxidative stress and altered neuronal plasticity, both of which have an impact on children with ADHD. Deficiencies of zinc,

Table 1. Risk Factors for ADHD

Risk Factor	Mechanism
Dietary Factors and Nutrient Deficiencies	
Hypersensitivity to foods and/or additives	Increase in inflammatory mediators and neuropeptides in the blood
Phospholipid deficiencies	Possible impairments in neuronal structure and function, especially during early development
Omega-3 fatty acid deficiency	Impaired neurotransmitter reception in brain; altered neuronal plasticity
Amino acid deficiencies	Decreased production of amino acid-based neurotransmitters
Refined carbohydrates	Abnormal glucose metabolism, causing disruptions in hormone and neurotransmitter regulation
Mineral deficiencies	Impaired dopaminergic transmission
Antioxidant deficiencies	Oxidative damage to DNA
Exposure to Environmental Toxins	
Heavy metals, solvents, pesticides, neurotoxins	Disrupted neurotransmitter and neuromodulator function
Exposure to Electronic Media	
Television	Over-stimulation, sensory addiction, increased stimulus-seeking behavior
Cell phones	Pre-and post-natal exposure linked to increase in ADHD symptoms. Exact mechanism unknown.
Abnormal Lighting	
Natural light deficiency / Exposure to fluorescent lighting	Hyperactive behavior and decreased learning ability

magnesium, glutathione, and/or omega-3 fatty acids, for instance, have been linked to concentration, memory, and learning problems in children with ADHD.[19]

Hypersensitivity to Foods and/or Additives

A high proportion of children with ADHD tend to exhibit atopic symptoms, leading to a recent hypothesis by Pelsser et al that ADHD may comply with the criteria for hypersensitivity.[20] Exposure to sensitizing foods appears to increase inflammatory mediators and neuropeptides in the blood,[4] and hypersensitive children are likely to exhibit atopy, irritability, sleep disturbances and prominent hyperactive-impulsive symptoms.[18] Future research regarding a genetic atopic link is needed. Probiotic therapy has been shown to be beneficial in children with atopic conditions such as eczema,[21] thus may be useful for immune-mediated hypersensitivity reactions in ADHD.[20]

A potential link between ADHD and food additives (preservatives, artificial flavorings and colorings) has been debated for decades.[18,22] A study published in *Lancet* in 2007 put forward the findings that sodium benzoate and commonly used food colorings may exacerbate hyperactive behavior in 3-year- and 8/9-year-old children.[23] Dissimilarities in the behavioral responses of these children when consuming additives suggested a genetic influence.[22] Indeed, this was confirmed in a 2010 follow-up study of the same children, which showed adverse effects of food additives on ADHD symptoms to be moderated by polymorphisms in the genes controlling histamine degradation.[24] A relationship between food additives and behavior is concluded to be clinically relevant for individual children, particularly those with a tendency toward hyperactivity.[22]

Essential Fatty Acid and Phospholipid Deficiencies

Essential fatty acids (EFAs) and phospholipids are both essential for normal neuronal structure and function and must be supplied through the diet.[4,25,26] The myelin sheath, which insulates every neuron in the brain, is made up of roughly 75-percent phospholipids, with each molecule having an attached saturated and unsaturated fatty acid, the latter being either an omega-3 or an omega-6 fatty acid.[27] The brain and nervous system depend heavily on these essential nutrients, especially during critical periods of development such as childhood, and dietary deficiency during these periods may increase the risk of developing ADHD-type symptoms.[4]

Omega-3 fatty acids, specifically docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), appear to improve neurotransmitter reception in the brain. DHA, in particular, protects neurons and glia from death by maintaining brain-derived neurotrophic factor (BDNF), a protein formed within the brain that aids in maintaining neuronal plasticity.[19,27] The ratio between omega-3 and omega-6 fatty acids is especially important, and our modern Western diet has produced an imbalance in this ratio, with more foods rich in omega-6 (e.g., canola oil, sunflower oil) being consumed. This imbalance is considered to be a risk factor for ADHD.[28,29] ADHD children may also have an inability to metabolize EFAs correctly.[26] Children with ADHD frequently manifest EFA deficiency symptoms, which may include dry hair and skin, eczema, recurrent infections, increased thirst and behavioral problems.[30] Correcting underlying EFA deficiencies may improve ADHD symptoms in many individuals.

Low-Protein, High-Carbohydrate Diets

Amino acids are the building blocks of proteins, as well as precursors for most of the neurotransmitters in the brain (Figure 1). Certain amino acids are considered essential, as they need to be taken in through the diet; as a result, low protein diets may foster amino acid deficiency symptoms.[9] Many of the amino acids needed by the body to manufacture neurotransmitters, such as phenylalanine, tyrosine, and tryptophan, are found to be low in the blood of adults and children with ADHD.[19,31,32] Deficiencies of these neurotransmitter precursors, together with their vitamin and mineral cofactors, may result in ADHD-type symptoms.[8] Correcting underlying metabolic imbalances through amino acid supplementation may be an important treatment strategy in individual cases where a deficiency exists.

Excessive consumption of refined carbohydrates and sugar can negatively affect learning ability and increase aggressive and restless behavior in all children, although evidence for a direct link to ADHD is lacking. In one study, comparing 17 ADHD children with nine age-matched normal children, assessing the effects of sugar ingestion on behavior, the children with ADHD displayed more inattention.[33] It has been suggested that these results could be due to a relative glucose intolerance occurring in ADHD sufferers; however, evidence for this is contradictory. One study conducted by Langseth and Dowd on 261 hyperactive children found that after five-hour oral glucose

tolerance tests, 74 percent displayed abnormal glucose tolerance.[34] Other studies have failed to find differences in overall glucose metabolism between normal children and children with ADHD.[35,36] However, these studies did find significant differences in glucose metabolism within specific regions of the brain, such as the frontal lobe, where reduced metabolism was inversely correlated with symptom severity.[35] Reactive hypoglycemia after sugar ingestion typically causes a rise in plasma epinephrine and norepinephrine; however, the rise in ADHD children is nearly 50-percent lower than in normal children.[37] The data suggest that ADHD children have difficulty regulating hormones and neurotransmitters, which may be further aggravated by refined sugar consumption.

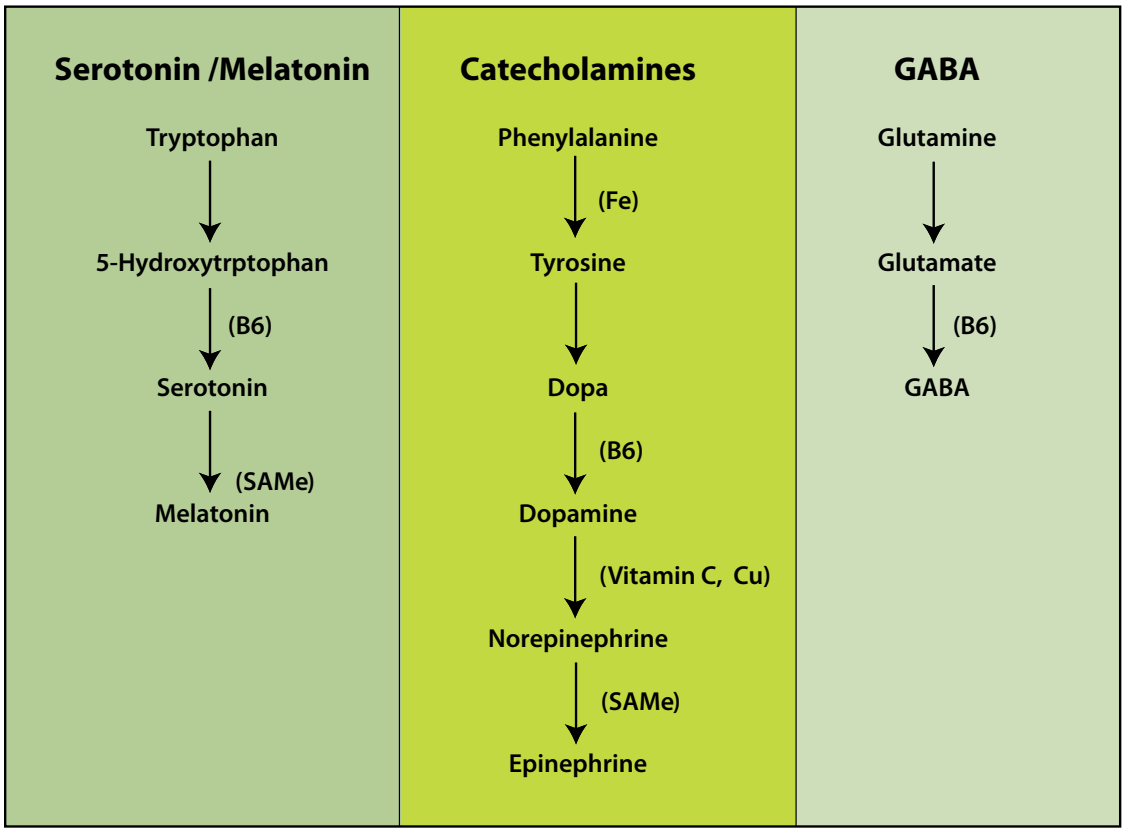
Mineral Deficiencies

Numerous studies have shown evidence of mineral deficiencies in children with ADHD, namely, zinc, iron, calcium, magnesium, and selenium.[19,38-41] As zinc and iron are associated with dopamine metabolism, a deficiency of either of these minerals might be associated with significant impairment in dopaminergic transmission.[42] Consumption of certain artificial food additives can lead to various nutrient deficiencies in some individuals, in particular zinc deficiency, which can exacerbate anxiety and conduct disorder problems.[19] A disturbance in the zinc:copper ratio is also evident, with high levels of copper being found in many ADHD children.[38]

Environmental Toxins and Contaminants

Exposure to metals (lead, cadmium, mercury, aluminum), solvents, pesticides, polychlorinated biphenyls, or other environmental toxins has been linked to ADHD.[43-45] Minerals such as zinc are needed to help metabolize and eliminate heavy metals; thus, a deficiency of such nutrients can exacerbate the problem.[19] The vast majority of toxicants released into the environment and their effects on a child's developing nervous system have, however, not been adequately researched. It has been proposed that prenatal and perinatal insults to the developing brain, including environmental

Figure 1. Key Neurotransmitters in ADHD and their Amino Acid Precursors



toxins, can disturb the timetable of expression of neurotransmitters and their receptors.[46] If so, this might have the effect of producing permanent changes in the brain that predispose to ADHD during childhood or adolescence. Although exact mechanisms were not clear, a literature review revealed a more than two-fold increased risk of ADHD among children whose mothers smoked during pregnancy.[47] Other studies suggest that these contaminants may disrupt two key sets of psychological mechanisms that are also disrupted in ADHD: higher-order executive functions and reinforcement responses.[18] Chelation therapy for binding heavy metals in the body may prove beneficial in cases of ADHD associated with toxic overload. In one small study conducted on children with both autism and ADHD, using chelation therapy in combination with other nutritional, behavioral, and educational approaches, all 10 children showed a significant improvement in social interaction, cognitive function, and behavior, as well as a significant reduction in urinary lead burden.[48]

Environment, Electronic Media, and Culture

It is a well-established theory that electronic media can influence children's development.[9] Research has shown that early television watching (ages 1-3) is associated with the development of attention problems in children by age seven.[49] Another study showed that children who watch two or more hours of television per day had increased attention problems in adolescence, suggesting that the adverse effects of television may be cumulative.[50] One possible explanation for these findings is that television watching replaces other activities that encourage concentration and attention, such as reading. Also, children's television programs may overstimulate the developing brain of a young child, leading to sensory addiction.[50] One result of sensory addiction is difficulty coping with slowness. In children, this can manifest as an inability to regulate their own behavior, motivating the need for more stimulus-seeking behavior. Restlessness, anxiety, and impulsivity may result from a perceived lack of stimulation.[51] Further studies are needed in this field for a fuller evaluation of the association between television and ADHD.[18]

According to a study published in the journal, *Epidemiology*, children exposed to mobile phones prenatally and, to a lesser extent, postnatally, were 80-percent more likely to exhibit ADHD-type symptoms, such as hyperactivity and behavioral problems, at school-going age.[52] Although this association has yet to be substantially proven, it does raise cause for concern due to the widespread use of this technology.

Natural light deficiency has been suggested as a risk factor for ADHD.[53] Exposure to cool-white fluorescent lights appears to affect learning ability in children, and research suggests that it may also be linked with the incidence of attention-deficit disorder and hyperactivity. One study showed that there was a 32-percent reduction in hyperactive behavior in children when fluorescent lighting was removed from their classrooms.[54] As a result, it has been suggested that radio-frequency (RF)-shielded full-spectrum lighting and/or natural unfiltered daylight preferably be used.[55] Spending time outdoors in "green" natural settings appears to improve ADHD symptoms.[56] Moreover, the greener and more natural the environment compared to indoor or relatively built up outdoor settings (e.g., parking lots, downtown areas), the less severe the ADHD symptoms.

Conventional Treatment

Conventional treatment for ADHD usually consists of medication, behavioral interventions, and educational accommodations to enhance learning.[57] The three major classes of drugs used include stimulant medications, non-stimulants, and antidepressant medications.[58] Stimulant drugs, such as methylphenidate (e.g., Ritalin® and Concerta®), are structurally similar to and mimic the action of norepinephrine and dopamine.[59] Stimulants improve ADHD symptoms in most children;[60] however, as many as 20-30 percent of children either do not respond to this class of drug or are unable to tolerate them due to the wide range of adverse effects they may produce.[59,61] Short-term side effects may include loss of appetite, insomnia, anxiety, mood swings, increased blood pressure and heart rate, tics, and "behavioral rebound." Higher doses may result in paranoid psychoses.[62,63] Long-term side effects may include suppression of growth and cardiovascular effects.[63] Stimulant drugs also may promote physical and/or psychological dependence.[62]

Atomoxetine (Strattera®), a non-stimulant drug that acts as a norepinephrine reuptake inhibitor, has been shown to improve ADHD symptoms.[62,64] However, side effects are possible, including cardiovascular symptoms, psychotic symptoms, or increased suicidal tendencies.[65]

Antidepressants are believed to increase serotonin and/or dopamine and norepinephrine in the brain by blocking their reabsorption in the brain, and are often beneficial in those individuals with a co-morbid mood disorder. There are numerous potential side effects associated with these drugs as well, such as dry mouth, fatigue, insomnia, decreased appetite, headaches, and nausea.[66]

Complementary and Alternative Medicine

Complementary and alternative medicine (CAM) is increasingly being used for children with ADHD.[4] CAM therapies focus on treating the patient holistically and individually, and aim to treat underlying etiologies.[67] Various commonly used CAM modalities will be discussed in the following section.

Diet

Parents who are troubled with medicating their children are often more comfortable with the initiative of dietary interventions.[18] Proper nutrition is essential for growing children, and children who eat a diet high in "junk food" in early childhood are more likely to exhibit hyperactivity by age seven; this may reflect a long-term nutritional imbalance.[68] Regular meals and snacks are advised, consisting of low-glycemic index carbohydrates, proteins, and essential fatty acids. Refined carbohydrates, sugars, and processed foods containing additives should be completely eliminated from the diet. When possible, organic fruits and vegetables and free-range meats should be consumed. Vegetable proteins, such as soy, quinoa, and beans are beneficial, in terms of blood sugar control and avoidance of chemical and hormonal additives in meat products. Foods rich in EFAs, especially omega-3 fats, include cold-water fish (e.g., salmon and sardines), walnuts, almonds, pumpkin seeds, and flax seeds.[43,62]

Evidence has shown the effectiveness of a restricted elimination diet (i.e., the "few foods" approach) in children with ADHD. According to parent ratings on both the Conners- and ADHD Rating Scales in one study, 62 percent of ADHD children showed at least 50-percent improvement in behavior.[69] The children who followed the dietary intervention no longer met the DSM-IV criteria for ADHD. This research further highlights that hypersensitivity to foods and additives may exacerbate ADHD symptoms.

Exercise Therapy

There is much evidence to show that physical exercise enhances brain activity and modulates neurotransmitter systems, thereby improving memory, concentration, learning, and mood. Regular exercise that is cognitively, socially, and aerobically challenging offers the most benefit, facilitating healthy cognitive development and alleviating the symptoms of ADHD.[70]

Supplementary Interventions

Essential Fatty Acids

Various studies have reported the benefits of EFA supplementation in varying dosages,[62,71] for reducing anxiety, attention difficulties, and behavioral problems in children.[27,72,73] In one clinical trial, high daily doses of fish oil (8-16 g), administered to ADHD children, produced a significant improvement in behavior and attention, as well as reduced hyperactivity and defiance.[72] Daily EFA supplementation or eating foods that are rich in EFAs is recommended.[4]

Vitamin B6 and Magnesium

Vitamin B6 facilitates the production of serotonin, and supplementation with vitamin B6 has been shown to increase serotonin levels and reduce hyperactivity in ADHD.[74] In one study, 40 children with ADHD were given magnesium (6 mg/kg/d) and vitamin B6 (0.6 mg/kg/d) for eight weeks. Almost all ADHD children showed an improvement in clinical symptoms, namely hyperactivity, hyperemotivity/aggressiveness, and inattention. Clinical symptoms returned a few weeks after treatment was stopped.[75]

Iron and Zinc

In a 12-week, double-blind study, children supplemented with 150 mg of zinc sulfate showed reductions in hyperactivity, impulsivity, and impaired socialization.[76] Supplementation with iron and zinc is only recommended in children who are deficient, and should preferably be in chelated form (i.e., complexed with picolinic acid, amino acids, or organic acids) for improved absorption.

Calcium/Magnesium

Calcium and magnesium work synergistically to relax the nervous system; deficiency symptoms include irritability, restlessness, fidgeting, muscle cramps, and twitches. Magnesium supplementation has been shown to reduce excitability and improve concentration in children with low serum- and RBC magnesium levels.[41,62]

Acetyl-L-Carnitine (ALC)

ALC is the acetyl ester of the amino acid, L-carnitine, and is responsible for transporting fatty acids into the mitochondria. While research has shown L-carnitine supplementation to be helpful in treating ADHD symptoms, particularly attention problems and aggression, ALC acts similarly and is more easily absorbed and utilized by the cells.[62,71] In an animal model of ADHD, ALC was shown to consistently reduce the impulsivity index; thus, it may be a viable treatment option for ADHD.[77]

Gamma-Aminobutyric Acid (GABA)

GABA is a neurotransmitter that has an inhibitory effect on the nervous system; its ability to reduce excitability of neurons accounts for its tranquilizing effects. GABA may be most useful to those children experiencing predominantly hyperactivity symptoms, as it calms the body and appears to be beneficial for anxiety and stress.[78]

Glycine

Glycine is another inhibitory neurotransmitter that produces post-synaptic inhibition and appears to calm aggression and anxiety in both children and adults.[78]

L-Theanine

L-theanine is an amino acid constituent of green tea that significantly increases the activity of alpha waves in the brain. Alpha waves play a critical role in attention. Thus, L-theanine can relax the mind without inducing drowsiness.[79] Further research is needed to investigate an association between L-theanine and attention.[80] A study on the effects of L-theanine on sleep quality in boys with ADHD is published in this journal.

L-Tyrosine

L-tyrosine, an essential precursor for dopamine and norepinephrine, has been shown to be beneficial for attention in adults with ADHD.[81] Around 5-10 percent of ADHD cases respond to L-tyrosine supplementation and are most likely those individuals who have impairments in neurotransmitter metabolism.[82] In one case study evaluating the effect of tyrosine supplements on a patient with ADHD and co-morbid phenylketonuria, tyrosine was found to reduce ADHD symptoms, possibly through the action of augmenting dopaminergic activity.[83]

Taurine

Taurine is considered essential for infants and children. The amino acid acts similarly to GABA and glycine as an inhibitory neurotransmitter with anti-anxiety properties.[78] While research has been conducted on its role in the management of seizure disorders, very little evidence exists regarding its use in children with ADHD.[84]

Table 2. Amino Acids and their Mechanisms of Action in ADHD

Amino acid	Proposed Mechanism of Action
Acetyl-L-Carnitine (ALC)	Reduces attention problems, impulsivity and aggression
Gamma-Aminobutyric Acid (GABA)	Tranquilizing effect; reduces hyperactivity and anxiety
Glycine	Tranquilizing effect; reduces anxiety and aggression
L-Theanine	Aids attention by increasing alpha waves in the brain; calms the mind
L-Tyrosine	Precursor for dopamine and norepinephrine
Taurine	Tranquilizing effect; reduces anxiety
5-Hydroxytryptophan (5-HTP)	Anti-depressant effect; increases serotonin synthesis
S-Adenosyl-L-Methionine (SAMe)	Essential for neurotransmitter synthesis; has anti-depressant activity

5-Hydroxytryptophan (5-HTP)

5-HTP, manufactured in the body from the amino acid L-tryptophan, readily crosses the blood-brain barrier and increases synthesis of serotonin. Supplemental 5-HTP is derived from the seeds of *Griffonia simplicifolia* and may offer an alternative to conventional antidepressants for ADHD children with co-morbid mood disorders. Use of 5-HTP in combination with serotonin-enhancing drugs should be under medical supervision.[62]

S-Adenosyl-L-Methionine (SAMe)

SAMe, the active form of methionine, has beta-adrenergic and dopamine receptor agonist activity.[85] SAMe is a major methyl donor in the brain and is required for the synthesis of norepinephrine, dopamine, and serotonin. SAMe appears to be a safe and effective treatment for depression[86] and shows promise in the treatment of ADHD. In a nine-week, double-blind, placebo-controlled, crossover trial, 75 percent of adult ADHD patients using SAMe showed improvement, with minimal and transient side effects.[85] SAMe does not appear to have toxic effects at the recommended dosages; however, it may increase anxiety and mania in patients with bipolar disorder.[86]

Table 2 summarizes the amino acids and their mechanisms of action in relation to ADHD.

Dimethylaminoethanol (DMAE)

DMAE is an acetylcholine precursor that is converted to choline inside the brain. Supplementation with DMAE is purported to increase acetylcholine in the brain, thus aiding with memory, learning, and improved mood. A double-blind study conducted in 1975 involving 74 children found that a daily dose of 500 mg of DMAE for three months was as effective as Ritalin.[87] DMAE itself is synthesized from phosphatidylethanolamine and phosphatidylserine, reactions that require other nutrients such as SAMe and magnesium in sufficient supply.[88] Side effects are rare but can include headaches, insomnia, and anxiety.[88]

Phosphatidylserine and Phosphatidylcholine

Phospholipids are essential components of all cell membranes and the functional ingredients of lecithin. Phosphatidylcholine supplementation has been found to support healthy brain function due to the essential nutrient, choline.[89] Phosphatidylserine (PS) is most concentrated in the brain, where it comprises 15 percent of the phospholipid pool.[89] PS appears to increase the output of acetylcholine, as well as dopamine. Several studies have been conducted showing its efficacy in improving cognitive functioning, mood, and memory.[90-93] In a 30-week, exploratory study evaluating the effect of PS combined with omega-3 fatty acids (PS-Omega-3) on 200 children with ADHD, an initial 15-week, double-blind, placebo-controlled trial was conducted, followed by a 15-week, open-label extension period. ADHD symptoms were assessed using both home and school rating scales, and a quality-of-life assessment was conducted. Significant reductions in ADHD symptoms were noted, particularly with regards to restless/impulsive behavior, and data suggested an improvement in emotional quality of life. PS-Omega 3 was well tolerated, with no major adverse events noted.[93]

Melatonin

Chronic sleep-onset insomnia (SOI) is common in children with ADHD and impacts academic performance and social well-being. SOI is a common side effect of stimulant medication. Melatonin, a hormone produced in the pineal gland that helps regulate sleep patterns, has been shown to be a well-tolerated and effective option for ADHD patients with SOI,[94] and may even improve insomnia in children using stimulant medications.[95]

Pycnogenol

Pycnogenol (Pyc), extracted from grape seeds or pine bark, consists of bioflavonoids, catechins, procyanidins, and phenolic acids. It has powerful antioxidant, chelating properties, and enzyme stimulating properties. It has been proposed that one of the risk factors for ADHD may be oxidative stress; studies have shown significantly increased oxidative damage to DNA in ADHD children when compared to controls.[96,97] In one study, Pyc was shown to significantly reduce hyperactivity, and improve attention, concentration, and visual-motoric coordination in children with ADHD over a four-week period.[98] Further studies showed Pyc to normalize urinary catecholamine concentrations,[11] plasma copper levels,[38] and total antioxidant status in ADHD children.[96] It also increased levels of the antioxidant, glutathione (GSH) and reduced levels of oxidized glutathione (GSSG).[96] Pyc supplementation has been shown to reduce oxidative damage to DNA, leading to less hyperactivity and improved attention in ADHD children.[97]

Probiotics

Probiotics are beneficial microorganisms normally found in the digestive tract. The most common organisms found in probiotics are various strains of Lactobacillus and Bifidobacteria.[9] Overgrowth of pathogenic organisms (bacteria, fungi) in the bowel can trigger the release of neurotoxic endotoxins. Some of these compounds have been identified in the urine of children with ADHD.[99] As a result, probiotics may be useful in ADHD children with atopic symptoms, parasites, and/or intestinal dysbiosis.[8,20]

Herbal Treatment

Certain herbal medicines, as shown in Table 3, show promise in the treatment of ADHD; however, very little research exists regarding their specific use for this condition in children. Those herbs that may be potentially beneficial for ADHD are discussed below.

Rhodiola (Rhodiola rosea)

Various studies have revealed that Rhodiola exhibits an adaptogenic effect, is neuroprotective, and has CNS-stimulating activity.[100] Rhodiola has been shown in rats to enhance the transport of serotonin precursors (tryptophan and 5-HTP) into the brain, thereby increasing serotonin levels.[101] Rhodiola also appears to inhibit acetylcholine esterase, the enzyme that degrades acetylcholine.[102] A number of clinical trials have demonstrated that Rhodiola extract has anti-fatigue and anti-anxiety effects that serve to increase mental performance and cognition (particularly the ability to concentrate) in adult subjects.[103,104] Rhodiola also appears to be useful for generalized anxiety disorder, as well as mild-to-moderate depression.[105,106] However, the use of Rhodiola in combination with conventional antidepressants should be medically supervised, as concurrent use may increase the risk of adverse effects.[107] General lack of side effects in the course of clinical trials makes it potentially attractive for use as a safe medication; however, no trials have been conducted on children with ADHD.[100]

Chamomile (Matricaria chamomilla)

This plant, belonging to the Compositae family, has known carminative and mild sedative properties and has traditionally been prescribed for restlessness and nervous irritability in children. While generally considered safe, allergies to plants of the Compositae family may predispose to atopic reactions and anaphylaxis. This is, however, extremely rare, and this risk is diminished if using an ethanolic tincture, as the alcohol in the extract denatures the proteins responsible for allergic reactions.[108,109]

St. John's Wort (Hypericum perforatum)

Experimental studies suggest that St. John's wort is capable of inhibiting the reuptake of serotonin, norepinephrine, and dopamine; many of its compounds appear to contribute to its antidepressant activity. As a result, St. John's wort offers an alternative option to conventional SSRI antidepressants for treating mild-to-moderate depression, even in children under the age of 12, and with few side effects.[108,109] The European Scientific Cooperative on Phytotherapy (ESCOP) recommends this herb for the treatment of restlessness, anxiety, and irritability.[108,109] In one small open trial, St. John's wort improved ADHD symptoms, according to the Conners Rating Scale.[110] The use of St. John's wort in combination with certain conventional medications is contraindicated and should therefore be used under medical supervision.[108,109]

Table 3. Botanical Agents and their Mechanisms of Action in ADHD

Botanical Agent	Proposed Mechanism of Action
Rhodiola *(Rhodiola rosea)*	Neuroprotective; anti-fatigue and anxiolytic; increases serotonin levels; has anti-depressant effects; CNS-stimulating; increases cognitive function
Chamomile *(Matricaria chamomilla)*	Anxiolytic and mildly sedative
St John's Wort *(Hypericum perforatum)*	Inhibits reuptake of serotonin, norepinephrine and dopamine; has anti-depressant activity; reduces anxiety, restlessness and irritability
Valerian *(Valeriana officinalis)*	Calmative and antispasmodic; reduces anxiety, restlessness and insomnia
Bacopa *(Bacopa monniera)*	Improves cognitive function: memory, learning, concentration; also has anxiolytic effects

Valerian (Valeriana officinalis)

Valerian acts primarily on the nervous system, with calmative and antispasmodic properties.[111] It has been used for the treatment of anxiety and insomnia,[112] and more recently for ADHD.[113,114] Valerenic acid, one of its key compounds, inhibits the breakdown of GABA in the CNS, making it an alternative option for disorders characterized by restlessness.[115,116] Although valerian is generally considered safe,[115] there are no studies specifically evaluating its safety in children, and, to date, no controlled trials evaluating its use in treating ADHD. ESCOP approves of the use of valerian for children ages 3-12 years, assuming medical supervision.[117]

Bacopa (Bacopa monniera)

Bacopa, an Ayurvedic herb, has been used for centuries as a brain tonic to promote higher cognitive functioning, with more recent research revealing its nootropic action (positive effects on memory, learning, and concentration).[118] In one study involving healthy subjects, the Bacopa (300 mg) group showed a significant improvement in speed of visual processing, learning rate, and memory consolidation, as well as reduced anxiety, when compared to the placebo group. Bacopa was most effective after a 12-week period of supplementation.[119] Another study conducted on children with ADHD revealed that Bacopa-treated patients (50 mg twice daily) showed significant improvements in memory and learning tasks over a 12-week period.[120] Bacopa appears to be well tolerated, with few adverse effects.[121]

Homeopathic Treatment

Homeopathy is increasingly becoming a sought-after treatment option for ADHD.[122] Homeopathy is a system of medicine which considers that each individual will both present and experience their illness characteristically and that there will be a specific medicine best suited to each individual.[123] This specific remedy is known as the similimum. Because not all children diagnosed with ADHD manifest symptoms of the condition in an identical manner,[124] the task of the homeopathic practitioner, in treating with the homeopathic similimum, is to find this remedy based on the individual and characteristic symptoms of the patient with ADHD.[125] The homeopath has to know all the patient's symptoms – mental, emotional, general, or local. All corresponding sensations, concomitants, alternating symptoms, as well as rare or peculiar characteristic manifestations of the patient and a personal medical history, are needed for the homeopathic prescription of the similimum remedy.[126] Mental and emotional symptoms are given priority in understanding the disease process of the sick, as well as symptoms that characterize the uniqueness of individual symptoms. The philosophy of homeopathy thus implies treating the patient, not the disease.[127]

Apart from the similimum remedy, many homeopaths make use of combination remedies, which are a complex of multiple, individual remedies that clinically relate to a particular condition. These combination remedies are sometimes used as a substitute for similimum, or "constitutional," prescribing. Various research studies on both similimum and combination homeopathic treatment of children with ADHD have been conducted, many of which have shown success in their treatment regimens.

Strauss, in a study to determine the efficacy of Selenium Homaccord®, a homeopathic complex, in the management of ADHD, observed overall improvement in children's symptoms.[128] A study conducted by Smith et al found that the homeopathic complexes, Cerebro® and Nerva 2®, reduced the symptoms of inattention and improved the scoring of the Conner's Abbreviated Teacher Rating Scale in children with ADHD, ages 7-12 years.[129] White et al studied the effects of *Valeriana officinalis* in mother tincture (MT) and 3X potency and observed a significant improvement in ADHD children's behavior while on the treatment, with no significant difference found between the MT and 3X potency.[130] Homeopathic complexes may provide symptomatic relief without any adverse effects; however, more research is required to verify these results.

Several studies have been conducted on similimum treatment. In 1997, Lamont conducted a double-blind, partial crossover study of 43 children with ADHD. Children were treated initially with either placebo or a similimum homeopathic remedy; after 10 days, the groups were switched. According to behavior rating scores by parents or caretakers, homeopathic treatment was found superior to placebo for reducing symptoms of hyperactivity.[131] A similimum research study by Barnard et al showed that 85 percent of the participants in the study group improved in symptoms of ADHD on their homeopathic similimum remedy over the 12-week treatment period.[132] Frei and Thurneysen carried out a study comparing similimum homeopathic treatment (using LM potencies, meaning a 1/50,000 dilution ratio) and

Ritalin treatment. Of the 115 participants, 75 percent responded sufficiently well to homeopathic treatment, 22 percent did not and needed Ritalin, and three children did not respond to either treatment.[133] A Swiss randomized, double-blind, placebo-controlled, crossover trial by Frei et al set out to obtain scientific evidence of the effectiveness of homeopathy in ADHD treatment. Each of the 83 children diagnosed with ADHD was individually prescribed homeopathic medication in LM potency. Sixty-two participants who responded well to the treatment were considered eligible for the study; these children were divided into two groups and received either their similimum remedy for six weeks, followed by placebo for six weeks, or vice versa. The results showed that the overall intensity of ADHD symptoms appeared lower during treatment compared to placebo and resulted in an improvement in the children's social, emotional, and scholastic behavior.[134]

Similimum therapy appears to offer benefits to ADHD sufferers. Efficacy of the treatment, however, depends on the accuracy of the prescription. Further research on the homeopathic treatment of ADHD is required in order to establish its efficacy and to develop future treatment protocols.

Conclusion

ADHD is a complex, chronic, and heterogeneous condition that affects up to 1 in 20 children in the United States. ADHD appears to have multiple possible etiologies and risk factors associated with its development, requiring long-term case management using various treatment modalities. CAM offers many alternatives to conventional medications. Treatment should be tailored to each individual. Dietary corrections, exercise therapy, and nutritional supplements all offer potential benefits to the ADHD child. Herbal remedies that are indicated for restlessness, anxiety, and depression may offer viable alternatives to pharmacotherapy, although further research related to children with ADHD is required. Homeopathy may provide a safe and gentle approach through both similimum and mixed homeopathic remedy treatment, with various research studies purporting its efficacy.

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