The Role of Nutrition in Mental Health: Attention Deficit Hyperactivity Disorder (ADHD)

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ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a mental illness that is on the rise. Every year, an increasing number of individuals (children and adults) are diagnosed with ADHD. The etiology of ADHD is complex, and conventional treatment is pharmacological intervention. A comprehensive search was conducted using various databases such as Pubmed, Medline (Ovid), and Google Scholar to investigate the relationship between nutrition and ADHD. The following report is an up-to-date review of a sample of epidemiological studies and intervention trials specifically focusing on the role of nutrition in children and adults clinically diagnosed with ADHD. The findings suggest a link between artificial food coloring and ADHD severity. In addition, the epidemiological studies showed that individuals diagnosed with ADHD were found to be deficient in several micronutrients including polyunsaturated fatty acids (PUFA), zinc, magnesium, and iron. Supplementation trials for these micronutrient deficiencies were very promising in reducing ADHD severity, especially following magnesium and iron supplementation. These results suggest that a change in diet consisting of foods free of artificial food colorings and high in these micronutrients may help to alleviate the severity of ADHD.

ATTENTION DEFICIT DISORDERS

Attention Deficit Hyperactivity Disorder (ADHD) is a mental disorder that affects both children and adults. Once believed to only occur in children, in up to 60% of sufferers ADHD persists into their adulthood (1). ADHD is also found to be more prevalent in males than in females (2). Both children and adults suffering from ADHD are inattentive, overly impulsive, hyperactive, and have problems listening to others and finishing tasks (3). Furthermore, children with ADHD suffer from social withdrawal, shyness, anxiety, lethargy, being poor at sports and show learning difficulties that include problems with reading and writing (4). The etiology of ADHD is complex and is associated with genetic, environmental, neurological, and biological factors (5). However, there is substantial amount of research that has focused on the nutritional influences on ADHD (i.e. artificial food colorings and micronutrients).

Artificial Food Coloring and ADHD

Following Dr. Feingold's investigation of the effects of food colorings and preservatives on individuals with ADHD (6), several other studies have continued to investigate this association. A quarter century review by Jacobson and Schardt (1999) reported that in 1976, 10% of children

between the ages of 1 and 5 y consumed more than 121 mg/d of dyes/food colorings and that 10% of children between the ages of 6 and 11 y consumed 146 mg/d or more, with the average being 76 mg/d for all children (7). Although maximum recommended consumption has not been established, dye production has been steadily increasing. In 1955, production per capita amounted to 12 mg/d, increasing to 32 mg/d in 1975 and 47 mg/d in 1998 (7). In 2007, production per capita was reported to be 59 mg/d (8), representing a fivefold increase over the past five decades. With the production of food colorings continuing to increase and with ADHD diagnoses on the rise, an increased consumption of food colorings may be associated with behavioral disturbances.

Following a double blind, placebo-controlled study, Schmidt et al (1997) examined the effectiveness of an oligoantigenic diet in children diagnosed with ADHD (n = 49; age 6-12 y) (9). They were provided with either an oligoantigenic diet followed by a control diet or the reverse order. The oligoantigenic diet consisted of 2 meats (lamb and turkey), 2 carbohydrate sources (rice and potatoes), 2 types of vegetables (cabbage and carrots), 2 fruits (apples and bananas), and either apple juice or mineral water, whereas the control diet consisted of the same foodstuffs but included common food ingredients, specifically, artificial colorants and other additives and substances such as cereal proteins and citrus fruits. The drinks that were provided during the control diet also included artificial colorants (tartrazine, quinoline yellow, new coccine and carmoisine). The following behavioral tests were conducted: how the children played with others, performed in tests (Paired Associated Tasks-PAT, and Continuous Performance Task-CPT), and behaved in the classroom (Connors Abbreviated Parent Teacher Questionnaire-CAPTQ). The oligoantigenic diet improved most tested behavioral ratings (playing with others, 26%, $P = 0.0002$; PAT and CPT, 29%, $P = 0.0006$), except classroom behavior (CAPTQ), as compared with the control diet (9).

Micronutrients and ADHD

a) Polyunsaturated Fatty Acids (PUFA)

As previously mentioned, the etiology of ADHD is very complex and involves a variety of influencing factors including neurological brain functioning. Long chain polyunsaturated fatty acids (LC-PUFA) are essential in normal brain and nervous system development and function (10). Not only is the dietary intake of omega-3 (n-3) fatty acids declining in western societies, but the consumption of other micronutrients responsible for PUFA metabolism is also declining (11).

In 1981, Colquhoun and Bunday (1981) hypothesized that a deficiency of essential fatty acids (EFA) could be a possible cause of hyperactivity in children (12). Since then, more research has focused on the connection between EFA deficiencies in both children and adults and ADHD/ADHD like symptoms (13).

In an epidemiological study conducted by Stevens et al (1995), ADHD children (n = 53; age 9.1 ± 2.0 y) had significantly lower plasma (arachidonic acid-AA, $P < 0.02$; eicosapentaenoic acid-EPA, $P < 0.02$; docosahexaenoic acid-DHA, $P < 0.03$) and red blood cell (RBC) (AA, $P < 0.02$; and DHA, $P < 0.06$) EFA than control subjects (n = 43; age 9.1 ± 2.3 y) (14). In another study, Stevens et al (1996) found that children (n = 96; age 6-12 y) with lower plasma n-3 fatty acids scored higher (implicating impaired ADHD) on the many different behavior indices of the

Conners Parent Rating Scale (CPRS) (Conduct, P = 0.002; Anxiety, P = 0.008; Hyperactivity/Impulsivity, P = 0.01; Hyperactivity Index, P = 0.002), as well as showed more frequent and excessive temper tantrums (P = 0.002), problems getting to sleep (P = 0.02), problems getting up in the morning (P = 0.006), and even significantly worse learning problems and overall academic abilities (P = 0.005 and P = 0.03, respectively), as compared to children with higher plasma n-3 fatty acids (14). Furthermore, children with ADHD (n = 79; age 6-13 y) consume half the amount of fish/seafood, meat and eggs (all excellent sources of EFA) when compared to the Australian National Nutrition Survey (P = 0.021) (10).

Young et al (2004) found that adults diagnosed with ADHD (n = 37; age 18-65 y) had 7% less PUFA in serum phospholipids (P = 0.001) and 3% less PUFA in RBC (P = 0.02) as compared to adults not diagnosed with ADHD (n = 35). More specifically, adults diagnosed with ADHD had 17% less DHA (an n-3 fatty acid) in serum phospholipids (P = 0.009) and 19% less in RBC (P < 0.001) as compared to adults not diagnosed with ADHD (1). Also, low DHA levels in serum phospholipids (r = 0.15) and RBC (r = 0.27) correlated with increased ADHD scores (implicating impaired ADHD) as measured by the Amen questionnaire, but were not considered significant (P = 0.11) (1).

An intervention study examined the effectiveness of PUFA supplementation in children with ADHD symptoms (11). In the first phase (15 weeks; double blind and placebo-controlled) of this three-phased study, non-medicated children (n = 167; age 7-12 y; scoring at least 2 standard deviations above the population mean on the Conners abbreviated ADHD Index) received either PUFA (EPA, 558 mg/d; DHA, 174 mg/d; GLA, 60 mg/d) or 6 palm oil capsules/d. PUFA supplementation improved all outcome measures (Conners ADHD index, Cognitive problems/inattention, DSM-IV inattention, and DSM-IV hyperactive/impulsive; P < 0.01 for all) as compared to the placebo group (11).

Raz and Gabis (2009) provide a very comprehensive review of intervention studies focusing on the association of EFA deficiencies and individuals suffering from ADHD/ADHD like symptoms (13). This review presents contradicting results, as some (11, 16-18), but not other (19-22), interventions show significant improvements in ADHD/ADHD-like symptoms following EFA supplementation (13). There are several factors that may potentially contribute to the conflicting results. With the exception of the studies by Richardson and Montgomery (2005) (18) and by Sinn and Bryan (2007) (11) (both showing significant improvements in ADHD severity following EFA supplementation), studies reviewed by Raz and Gabis (2009) differed in the following aspects: the amount of EFA supplemented, the type of EFA supplement administered and the duration of the intervention. Studies showing significant improvement had an average period of supplementation of 14 wk as compared to 11.5 wk for those studies that did not show significant improvement. The review confirms that EFA deficiency is associated with ADHD/ADHD like symptoms, however more interventions are needed to establish the optimal amounts of EFA and the specific fatty acids that could help improve ADHD/ADHD like symptoms.

b) Zinc

Several studies investigated the relationship between zinc and ADHD, since zinc plays a very important role in proper brain function and development (5). A comprehensive review by Arnold and DiSilvestro (2005) ascertained that individuals diagnosed with ADHD had lower zinc tissue levels (serum, RBC, hair, urine, and nails) as compared to individuals not diagnosed with ADHD

(23). In addition, Arnold et al (2005) found a negative correlation between serum zinc concentrations and the severity of inattention in children (n = 48; age 5-10 y) clinically diagnosed with ADHD (r = -0.45, P = 0.004; as measured by the Conners Parent/Teacher Rating scale for inattention) (24).

Bilici et al (2004) examined the effectiveness of zinc supplementation in the treatment of ADHD (25). In a double blind, placebo-controlled study, children (n = 400; 72 girls, 328 boys; age 9.6 ± 1.7 y) with a primary DSM-IV diagnosis of ADHD were randomly assigned to receive either an oral dose of 150 mg/d of zinc sulfate (equivalent to 40 mg Zn/d) or placebo (sucrose). Efficacy of the intervention was assessed over the duration of the 12 wk study using the Attention Deficit Hyperactivity Disorder Scale (ADHDS), Attention Deficit Subscale (ADHDS-A), Hyperactivity Subscale (ADHDS-H), Impulsivity Subscale (ADHDS-I), Impaired Socialization Subscale (ADHDS-S), Ankara Conners Teacher Questionnaire Subscales (Attention Deficit, ACTQ-A; Hyperactivity, ACTQ-H; Conduct, ACTQ-C) and the DuPaul Parent Ratings. Zinc supplementation significantly reduced (implicating improvement) ADHDS (34%, P = 0.002), ACTQ-H (30%, P = 0.03) and ACTQ-C (25%, P = 0.04), but not ADHDS-A (P = 0.78), ADHDS-H (P = 0.84), ADHDS-I (P = 0.88), ADHDS-S (P = 0.89), ACTQ-A (P = 0.88) and DuPaul Parent Ratings (P = 0.52), as compared with the placebo. Furthermore, full therapeutic response rates (defined as having less than 20 points on the ADHDS-A, less than 16 points on the ADHDS-H, and less than 12 points on the ADHDS-I and ADHDS) were significantly higher in the zinc versus the placebo group (P = 0.04) (25).

c) Magnesium

Individuals with ADHD have been found to be deficient in magnesium. Magnesium is involved in energy metabolism, synaptic nerve cell signaling, and cerebral blood flow, and hence may impact proper brain function (5). In an epidemiological study conducted by Kozielec et al (1997), 95% of children diagnosed with ADHD (n = 116; age 9-12 y) had lower serum, RBC and hair magnesium levels as compared to healthy children (n = 304; age 5-11 y) (26). These findings were further supported by Mousain-Bosc et al (2004) who found that out of 52 children diagnosed with ADHD (age 1-15 y), 30 had 17- 25% less intracellular magnesium as compared to typical magnesium values for normal subjects (2.46-2.72 mmol/L) (27). In addition, Mousain-Bosc (2006) found that decreased magnesium levels were associated with increased hyperactivity, poorer school attention and sleep disturbances (28).

Starobrat-Hermelin and Kozielec (1997) examined the effectiveness of magnesium supplementation in the treatment of ADHD (29). In this study, children with a DSM-IV diagnosis of ADHD (n = 75; age 7-12 y) were randomly assigned to receive either 200 mg/d of magnesium or the “standard” treatment which consisted of a variety of pharmacological medications. Efficacy of the intervention was assessed at baseline and at conclusion using the CPRS, Conners Teacher Rating Scale (CTRS), Wender’s Behavior Scale (WBS) and Quotient Development to Freedom from Distractibility (QDFFD). After the 6 mo intervention, the children in the magnesium supplementation group (n = 50) significantly improved in all outcome measures (CPRS, 36%, P < 0.001; CTRS, 37%, P < 0.001; WBS, 21%, P < 0.01; QDFFD, 10%, P < 0.001) as compared to the “standard” treatment group (n = 25) (29).

d) Iron

Iron deficiency has also been reported in individuals diagnosed with ADHD. According to Black (2003) and Konofol et al (2004), iron deficiency may play a significant role in ADHD, because it

affects cognition and behavior in individuals, as iron serves as a co-factor for tyrosine hydroxylase, the rate limiting enzyme that is involved in dopamine synthesis (30, 31).

An epidemiological study conducted by Konofol et al (2004) found serum ferritin levels (protein that stores and releases iron) to be 47% lower in non-anemic children with ADHD (n = 53; age 9.2 ± 2.2 y) as compared with control children (n = 27; age 9.5 ± 2.8 y) ($P < 0.001$) (31). More specifically, serum ferritin levels were abnormally low (< 30 ng/mL**)** in 84% of children diagnosed with ADHD as compared to only 18% of the control children ($P < 0.001$). Furthermore, low serum ferritin levels were correlated with increased cognitive deficits ($r = -0.38$, $P < 0.01$) and increased ADHD symptom severity ($r = -0.34$, $P < 0.02$) as measured by the CPRS (31).

In the first double blind, placebo-controlled study to examine the effects of iron supplementation on ADHD in children, non-anemic children (n = 23; age 5-8 y) with low serum ferritin levels (< 30 ng/mL) meeting the DSM-IV criteria for ADHD were randomized to receive either 80 mg/d of iron or placebo tablets (32). The ADHD ratings were measured over the duration of the 12 wk study using the CPRS, Attention Deficit Hyperactivity Disorder Rating Scale (ADHD RS) and CTRS. The iron supplemented group significantly reduced their ADHD RS scores (27%, $P = 0.008$) as compared to the placebo group. In addition, a trend was observed whereby the iron supplemented group reduced their CPRS (12%, $P = 0.055$) and CTRS ($P = 0.076$) scores as compared to the placebo group (32).

Discussion

As seen from the studies presented in this report, it is evident that nutrition plays a significant role in ADHD. Artificial food coloring is an issue of growing concern. The production of artificial food coloring per capita has increased 5 fold in the last decade (7), and this increased production coincides with the increase in ADHD diagnoses, thus emphasizing the relationship between the two. Children and adults suffering from ADHD were also found to be significantly deficient in several micronutrients (PUFA, zinc, magnesium and iron) as a result of genetic predisposition and/or diet. Currently, pharmacological intervention is believed to be the conventional treatment of ADHD, however intervention trials clearly showed that micronutrient supplementation significantly ameliorates ADHD severity. In light of these findings, the impact and effectiveness of nutritional intervention in ADHD can no longer be overlooked. These findings provide valuable information for clinicians, dietitians and nutritionists to develop diets for individuals diagnosed with ADHD that consist of foods free of artificial food coloring and foods high in omega-3, zinc, magnesium and iron. Although dietary supplementation was successful in reducing ADHD severity, these findings by no means suggests the cessation of treating ADHD with pharmacological medication, but rather nutrition-based strategies should be used in conjunction with pharmacotherapy to help treat ADHD. More randomized control trials in micronutrient supplementation need to be conducted to determine the optimal amounts of micronutrients recommended to mitigate ADHD severity.

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