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Role of Vitamins and Nutrients in the Management of Attention-Deficit Hyperactivity Disorder (ADHD): A Narrative Review

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ABSTRACT

Attention-deficit hyperactivity disorder (ADHD) is a common psychiatric disorder that affects individuals across all age groups, including children, adolescents, and adults. The ADHD etiology encompasses a lack of several nutrients and food compositions. Some applied strategies, such as increased intake of specific nutrients, were proposed as additional therapy for this condition. In our narrative review, we explored the relationship between dietary patterns and ADHD by searching through "Google Scholar, Scopus, and PubMed" for relevant studies. This review sheds light on the connection between dietary patterns and ADHD and provides a concise summary about practicing these dietary therapies. Several studies reported that unhealthy eating habits were positively correlated with ADHD, while healthy eating habits showed a negative correlation. Furthermore, there is a potential association between ADHD and deficiency in certain nutrients, including magnesium, iron, zinc, polyunsaturated fatty acids, and vitamin D. However, despite the promising nature of the dietary modifications as strategies for managing ADHD, the need for more robust scientific evidence to validate their effectiveness is highly recommended.

KEYWORDS

ADHD, minerals, nutrients, polyunsaturated fatty acids, vitamins

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a developmental disease manifested by excessive hyperactivity and/or inattention (Vahia, 2013). The patient appears clinically to have a lack of focus, impulsivity, and hyperactivity in a variety of spectrum levels. According to the latest statistics, the incidence of ADHD differs between regions, in adults, ranging from 1.2% to 7.3%, and in children, from 5.9% to 7.1% (Huss et al., 2017; Danielson et al., 2018).

It is common for ADHD to coexist with other mental health problems involving personality disorders and substance abuse (Jensen and Steinhausen, 2015). The etiology of ADHD is thought to involve a combination of genetic predisposition and social/environmental variables. There is an absence of biological diagnostic indicators that support the reliability of the ADHD theory, and there is no consistent evidence of structural or functional brain alterations in patients with ADHD (Wankerl et al., 2014). Although short-term treatments with behavior therapy, psychostimulants, and parent training can alleviate impulsivity, hyperactivity, and poor attention in ADHD children and adolescents, the long-term effectiveness of these treatments is still up for discussion (Lange, 2017b).

Hence, substantial improvements in the primary ADHD symptoms, as measured by clinical rating scales, have been demonstrated in multiple trials when medication is given for multiple weeks in comparison to a placebo (Coghill et al., 2017; Faraone et al., 2022). Nevertheless, how little of a change in ratings would be needed to have an ecologically significant impact is anybody's guess. So, even modest changes in symptom scores that are statistically significant could not translate into improvements in everyday challenges that are clinically relevant (Lange, 2017b).

On the other hand, pharmacotherapeutic approaches involving stimulant agents (amphetamine and methylphenidate) and non-stimulant agents (e.g., guanfacine, clonidine, selective norepinephrine reuptake inhibitor, atomoxetine) are known to alleviate ADHD symptoms in children and adolescents, at least temporarily (Wolraich et al., 2019; Pinto et al., 2022). The inadequate quality of outcome measures in previous studies complicates the assessment of therapeutic efficacy (Shellenberg et al., 2020; Carolan, 2021). Consequently, there is a surge in scientific interest in utilizing nutritional interventions for managing ADHD. Nonetheless, randomized controlled studies indicate that psychostimulants provide enduring benefits in the long term (Storebø et al., 2018; Martins et al., 2024).

Longitudinal studies revealed that children with ADHD who used psychostimulants into adulthood may show a short stature without continuing to ameliorate their symptoms (Swanson et al., 2017), and a few of the short-term side effects of stimulants include anxiety, sleeplessness, headaches, nausea, vomiting, and lack of appetite (Jerome and Jerome, 2020). An example comes from atomoxetine which, like other non-stimulants, may induce adverse effects such as nausea, xerostomia, insomnia, and reduced appetite in adults, as well as somnolence, abdominal pain, and headaches in children (Childress, 2015). Moreover, it appears that atomoxetine can lead some children to contemplate suicide (Davies et al., 2017).

Even though the research above suggests that ADHD is mainly inherited, environmental pollutants have a substantial effect on developing ADHD throughout pregnancy and the early years of childhood. Heavy metal and chemical exposure, dietary deficits, and prenatal exposure to other toxins are among these (Barkley, 2002). Many hypothesized lifestyle variables, such as food and nutrition, contribute to the etiology of ADHD (Lange, 2017a, 2018). Many mental diseases, including schizophrenia, depression, ADHD, and autism spectrum disorder, may have dietary defects as a contributing factor in their development or treatment (Sarris et al., 2015; Lange, 2020).

Therefore, scientific interest should have an explosion in the implementation of nutritional interventions for managing ADHD. In this narrative review, the current scientific literature on ADHD and nutritional determinants will be presented to assess various dietary components that have demonstrated the potential to either exacerbate or alleviate symptoms of ADHD. By conducting a comprehensive search, this review aims to provide valuable insights for researchers and healthcare professionals looking to recommend certain dietary modifications for children with ADHD to improve the quality of life and mitigate their symptoms.

MATERIALS AND METHODS

We searched scientific literature to identify papers examining the association between ADHD and specific eating habits. The databases "Google Scholar, Scopus, and PubMed" were queried from October 2023 till August 2024, using a range of search terms, involving "ADHD," "attention deficit hyperactivity disorder," "diet," "heavy metal," and "vitamins," among others. The selection of relevant studies was based on the screening of abstracts by coauthors with appropriate experience. Also, the reference list of the selected studies was revised to ensure that all relevant literature was included.

Inclusion criteria

- Participants/animals: Studies involving human ADHD patients or rodent models of ADHD were included.
- Interventions: Studies evaluating the effects of nutrients, such as vitamins and minerals, on patients or rodents were considered.
- Outcome indicators: Studies demonstrating improvements in ADHD symptoms in patients or rodents were included.
- Language: Only studies published in English were included.
- Research type: Original research articles were exclusively included.

Exclusion criteria

- Studies categorized as abstracts, reports, or editorials were excluded.
- Duplicate publications or studies with incomplete data were excluded.
- Studies lacking validated statistical analysis or failing to provide reliable conclusions were excluded.

Bias control

Bias in included studies was addressed through critical appraisal based on the established criteria and the authors' expertise, considering potential biases and assessing the quality of the literature included.

Correlation analysis

This review elaborates on the argument concerning the correlation between ADHD and nutrients, highlighting key insights into the relationship between symptoms of ADHD and specific nutrient deficiencies based on the reviewed literature.

RESULTS

Eating habits and worsening of ADHD

The health of many individuals has been adversely affected following increased consumption of processed foods, takeaways, oily foods, and sugary drinks (Popkin et al., 2012). A recent systematic review demonstrated that the risk of

ADHD is influenced by the specific type of diet consumed (Shareghfarid et al., 2020). Consuming an appropriate amount of docosahexaenoic acid (DHA), a category of polyunsaturated fatty acid (PUFA), during pregnancy supports the growth and differentiation of brain progenitor cells. Reduced DHA consumption through brain development has been linked to ADHD and further neurodevelopmental problems (Gharami et al., 2015).

Exposing pregnant mothers to pesticides is a specific environmental factor linked to ADHD. Exposing children to polychlorinated biphenyl and p,p′-dichlorodiphenyldichloroethylene during pregnancy showed a significantly higher incidence of ADHD, according to findings from a prospective cohort study (Sagiv et al., 2010).

Children coming from a region contaminated with lead showed high blood levels of lead, cadmium, and manganese in a positive association with ADHD, as indicated previously (Liu et al., 2014). Another study, previously published, found that ADHD children have higher urine amounts of molybdenum, chromium, tin, barium, cobalt, manganese, nickel, copper, and lead (Li et al., 2020b), as shown in Table 1.

On the other hand, multiple research studies have demonstrated that ADHD children exhibit decreased amounts of elements, involving zinc, iron, copper, magnesium, and selenium, in their plasma (Effatpanah et al., 2019; Wang et al., 2019; Luo et al., 2020; Robberecht et al., 2020; Skalny et al., 2020a). These elements are crucial in brain development and functioning (Bourre, 2006; Gómez-Pinilla, 2008). Iron is a necessary cofactor for various processes, encompassing the metabolism of neurotransmitters, particularly dopamine, a key component in ADHD. Additionally, zinc plays a vital role in cell processes, like melatonin metabolism, prostaglandins, and neurotransmitters. The development and exacerbation of ADHD have been associated with fluctuations in iron and zinc levels, as demonstrated in Table 2 (Granero et al., 2021).

At the level of individual items, both Western and junk food diets are associated with ADHD due to their high sugar, processed food, and refined grain content (Del-Ponte

Table 1: Studies of heavy metal exposure in ADHD.

Heavy metal	Sample	Results	References
Lead	164 children aged 3-15 were enrolled in 2014-2015	(+) hyperactivity/impulsivity scores and oppositional defiant disorder (ODD) behavior of the children in the high blood lead group	Lin et al. (2019)
	71 children diagnosed with ADHD aged 5-8 and 9-12 years	(+) clinical development of ADHD in lead-exposed children after birth but (−) association in cadmium or mercury	Kim et al. (2013)
Lead, cadmium, and antimony	29 ADHD patients have inattentive type (ADHD-I), 47 ADHD patients have hyperactivity/impulsivity type (ADHD-H/I), 46 healthy control children	(+) severity of ADHD symptoms in patients with high levels of lead, cadmium, and antimony in urine	Lee et al. (2018)
Chromium, molybdenum, barium, cobalt, nickel, copper, manganese, tin, and lead	178 ADHD children aged 6-11 years and 106 healthy children aged 6-14 years	(+) ODD ratio in ADHD in children with increasing urine concentrations of cobalt, chromium, nickel, copper, molybdenum, manganese, tin, barium, and lead	Li et al. (2020b)

Abbreviation: ADHD, attention-deficit hyperactivity disorder.

Table 2: Studies of nutrient deficiencies in ADHD.

Nutrient deficiencies	Sample	Relation to ADHD	References
Iron	116 ADHD children/adolescents	Positive relation Negative relation to methylphenidate and iron supplements	Pongpitakdamrong et al. (2022)
	1565 ADHD, 1694 tic disorder (TD), and 1997 healthy children aged 5-12 years	Positive relation	Tang et al. (2022)
	51 ADHD and 51 TD patients aged 6-14 years	Positive relation	Chen et al. (2022)
Iron and ferritin	119 ADHD children	Positive relation	Islam et al. (2018)
Iron and zinc	42 children, aged 4-14 years, whose parents reported concerns over inattention ADHD	Positive relation	El-Saadany et al. (2022)
Vitamin D, ferritin, and serum iron	630 ADHD children and 630 controls aged 5-18 years	Positive relation	Berner et al. (2014)
Vitamin D	1331 ADHD children and adolescents aged 5-18 years	Positive relation	Kamal et al. (2014)
Retinol and vitamin D	82 ADHD children	Positive relation	Li et al. (2020a)

Abbreviation: ADHD, attention-deficit hyperactivity disorder.

Table 3: Possible association with dietary pattern in children with ADHD.

Dietary pattern	Sample	Relation to ADHD	References
Abundant vegetables and dairy products	507 boys, 479 girls aged 9-10 years	Negative relation	Park et al. (2012)
Healthy pattern and snack pattern	192 children aged 7-12 years	Negative relation with healthy pattern Positive relation with snack pattern	Woo et al. (2014)
Foods rich in saturated fat and sugar	390 children aged 6-17 years, 169 with ADHD and 221 healthy	Positive relation	Akin et al. (2022)
A lot of sugar and fast food	375 school-age children	Positive relation	Azadbakht and Esmaillzadeh (2012)
Sugar-sweetened beverages	25,945 individuals (meta-analysis)	Positive relation to its symptoms	Farsad-Naeimi et al. (2020)
Sugar-sweetened beverages	173 ADHD and 159 non-ADHD children aged 4-15 years	Not significant	Yu et al. (2016)
Sucrose consumption	3799 children aged 6 years 3566 children aged 11 years	Not significant	Del-Ponte et al. (2019)

Abbreviation: ADHD, attention-deficit hyperactivity disorder.

et al., 2019). Furthermore, the results of a Korean study involving 986 school-aged ADHD children and its association with the observed learning disabilities revealed that consuming excessive amounts of sugary desserts and salt was linked to attention, behavioral, and learning difficulties. Conversely, following a well-balanced diet that includes regular meals, abundant vegetables, and dairy products was found to have a negative correlation with these problems (Park et al., 2012). One previous study documented that children older than 7 years old who consumed more sugary beverages were 40% highly susceptible to present symptoms of ADHD compared to those whose intake was lower (Farsad-Naeimi et al., 2020). Nevertheless, the researchers also discovered that consuming sweets through food alone did not elevate the likelihood of acquiring symptoms linked to ADHD. The relation between sugar consumption and ADHD is still inconclusive in the scientific evidence, as some researchers have reported positive associations while others have found no significant connections (Yu et al., 2016; Del-Ponte et al., 2019; Farsad-Naeimi et al., 2020), as shown in Table 3.

This disorder was associated with serum retinol concentrations and 25(OH)D, even after controlling for age, body mass index, blood collection period, and solar exposure. There exists a correlation between symptom severity and this co-deficiency, and in recent times, vitamins A and D have become recognized as micronutrients that are pertinent to ADHD (Li et al., 2020a).

A meta-analysis of five case–control studies revealed a strong correlation between low vitamin D status and a higher ADHD incidence. Additionally, inadequate vitamin D levels during neonatal stages are closely linked to an elevated risk of developing ADHD later in life. This finding received support from a meta-analysis of prospective studies involving 4137 participants, as outlined in Table 2 (Khoshbakht et al., 2018).

Additionally, infants whose mothers consume insufficient amounts of ω-3 PUFAs during pregnancy are likely to have difficulties in areas including social development, communication, and fine motor skills more than those having normal levels. There is some evidence that ω-3 insufficiency contributes to ADHD; however, pharmacotherapies such as methylphenidate and atomoxetine are ineffective for 20-40% of individuals. Prosocial conduct, fine motor coordination, linguistic communication, and social development are all negatively influenced in children whose moms eat much seafood while pregnant (Wolford et al., 2017).

Furthermore, PUFAs are essential for the most efficient release of neurotransmitters, and according to specific research, ADHD children and adolescent patients have reduced levels of total PUFA series ω-3, (DHA-C20:5), and eicosapentaenoic acid (EPA-C20:5) in their buccal tissues and blood (Chang et al., 2018).

Dietary and nutritional interventions in the management of ADHD

Dietary supplements containing minerals, vitamins, PUFAs, and other alternatives, including microbiome-targeted strategies involving probiotics, are a vital component of dietary interventions for helping manage ADHD.

Minerals

Minerals and essential trace elements are important in neurodevelopment (Skalny et al., 2023). Although the currently available information on the impairment of micronutrients and minerals in children with ADHD is insufficient, hypotheses have been advanced regarding the influence of minerals on symptoms of ADHD, explicitly concerning zinc, copper, magnesium, iron, and selenium (Robberecht et al., 2020). Nevertheless, research investigating these correlations has produced inconclusive results (Robberecht et al., 2020). In accordance with this, evidence exists regarding the correlation between magnesium concentrations in the serum and ADHD diagnosis. In a systematic review and meta-analysis, the existing experimental data about the topic were assessed (Effatpanah et al., 2019).

Individuals with ADHD have been attributed to magnesium deficiency on the grounds of either inadequate ingestion or an increased need. As a case study, the magnesium content in the hair of 44 ADHD boys aged 4-9 years was observed to be 11% lower in comparison to a 32-boy control group who were continuing normally (Skalny et al., 2020b).

According to previous reviews and meta-analyses, ADHD children have lower serum magnesium levels than normal children (Effatpanah et al., 2019; Huang et al., 2019). Moreover, Kiddie et al. (2010) reported that ADHD children show lower copper levels. Another study found that a little selenium intake was detected in ADHD groups in comparison to controls (Dura et al., 2014).

A prior systematic review displayed that zinc and iron supplementation for a duration of 6-10 weeks was combined with ameliorations in the severity of ADHD after the treatments when compared to the use of a placebo. While the effect sizes of the outcome measures were generally small and/or concentrated on a particular symptom of ADHD, zinc appeared to have the most consistent results (Granero et al., 2021).

Furthermore, iron and zinc act as dopamine reuptake inhibitors, targeting the same mechanism as the stimulant drugs used in combination therapeutic approaches for the disease. This may account for the relationship between zinc–iron levels and the diverse manifestations of ADHD (Granero et al., 2021). Moreover, zinc supplementation significantly improved overall ADHD scores compared to controls but did not affect hyperactivity or inattention scores (Talebi et al., 2022). However, a different systematic analysis did not declare improvement in ADHD symptoms associated with zinc supplementation, either alone or in conjunction with stimulants, after adjusting for initial zinc levels (Ghanizadeh and Berk, 2013). Researchers looked at the possibility that iron contents in the blood or brain are lower in children with ADHD than in normal children in a comprehensive literature analysis. Twenty case–control studies comparing ADHD patients with healthy controls found variations in iron levels. Statistically significant alterations were reported among these groups in 2 out of 10 reports examining blood iron concentrations and 10 out of 18 studies evaluating serum ferritin levels. Despite contradictory findings about systemic iron levels, three studies that looked at brain iron concentration found that the thalamus of ADHD children had far lower amounts (Degremont et al., 2021).

In 959 children from Chile, a relation between infantile iron deficiency (in 12-18-month infants) and symptoms of ADHD or lethargic cognitive tempo, as rated by the mothers of these children, during childhood and adolescence (ages 5, 10, and 16 years) was investigated. Higher severity of children with iron deficiency was linked with frequently noticed symptoms of ADHD and lethargic cognitive tempo in the studied ages after adjusting for various confounding variables (East et al., 2023). Potentially helpful interventions with minerals include those that enhance neurological growth after early malnutrition. The effectiveness of supplementation with iron–zinc in handling ADHD in children and adolescents was investigated in a qualitative comprehensive evaluation of nine randomized clinical trials. This meta-analysis found that both the severity of ADHD at baseline and treatment outcomes were worse in patients having low levels of zinc and iron. When compared to a placebo group, those whose diets included zinc and iron supplements had less severe ADHD symptoms (Granero et al., 2021). The beneficial effects of zinc and iron supplements in ADHD can only be proven by future large-scale, well-designed, randomized controlled studies, as shown in Table 4.

Vitamins

Dietary patterns provide new insights into different undiscovered aspects of metabolic diseases (Maghsoudi and Azadbakht, 2012) and behavior disorders (Bakhtiyari et al., 2013).

ADHD patients were characterized by low levels of specific vitamins, which could indicate deficient dietary consumption of these micronutrients in these patients (Landaas et al., 2016). It is crucial to introduce dietary intervention trials for these ADHD patients. People with ADHD encounter a variety of symptoms due to the substantial changes in brain processes that may be attributed to the deficiency of vitamins (Landaas et al., 2016).

Vitamin D is recognized for its significant and varied functions within the neuronal system, including inhibiting calcium signaling and facilitating the synthesis of serotonin and glutathione (Patrick and Ames, 2015). Vitamin D functions as a neuroactive steroid. Vitamin D receptors and related enzymes are found in the prefrontal cortex, substantia nigra, hippocampus, and hypothalamus. Insufficiency of vitamin D during the brain's development phase has been shown to impact the dopamine pathways negatively. Vitamin D is involved in brain cell (axonal growth) differentiation and proliferation, as well as in the enhancement of antioxidative capability, which provides a protective effect against oxidation and regulates neurotrophic factors (Lepping and Huber, 2010; Villagomez and Ramtekkar, 2014). A recent study reported that vitamin D functions as a potent antioxidant and immunological modulator, and it may possess a critical role in normal brain growth and both prenatal and childhood development. Thus, the fetus' neuropsychological functions are negatively impacted by vitamin D deficiency during the pregnancy stage (Tahir et al., 2023).

Mohammadpour et al. (2018) investigated the impact of vitamin D supplementation in conjunction with methylphenidate on the manifestation of ADHD symptoms in children aged 5 and 12 years. It was reported that the intervention group experienced a substantial reduction in ADHD symptoms, and the authors did not highlight significant differences in the symptoms evaluated utilizing the ADHD rating scale-IV or Conner's Parent Rating Scale-Revised. Moreover, Bener and Kamal (2014) inspected the connection between ADHD and low vitamin D levels in a case–control study. This study examined the serum levels of 25(OH) vitamin D in 60 hospitalized and 30 healthy participants. They specifically stated that the serum levels of 25(OH) vitamin D in the diseased cases were lower than those of the healthy people. Their findings were noteworthy ($P = 0.001$) (Bener and Kamal, 2014). Kamal et al. (2014) carried out an epidemiological investigation involving 5-18-year-olds, wherein they assessed and quantified the 25(OH) vitamin D serum level in a couple of distinct groups—diseased and normal. The findings highlighted a strong correlation between vitamin D and ADHD ($P = 0.0001$) (Kamal et al., 2014). Supplemental vitamin D, when used in conjunction with methylphenidate,

Table 4: Investigations on the effects of dietary supplements on ADHD.

Dietary supplements	Sample	Relation to ADHD	References
Zinc supplementation 10 mg/d for 6 weeks	40 ADHD children, aged 7-14 years	Negative relation, as indicated by the Conner's global index	Zamora et al. (2011)
Iron supplement 80 mg/d for 12 weeks	23 ADHD children aged 5-8 years with serum ferritin levels <30 ng/ml	Negative relation	Konofal et al. (2008)
	50 ADHD children	Negative relation	Tohidi et al. (2021)
Iron–zinc supplementation	ADHD children and adolescents	Negative relation	Granero et al. (2021)
Vitamin D (50,000 IU per week) and magnesium (6 mg/kg daily) for 8 weeks	66 ADHD children	Negative relation	Hemamy et al. (2021)
Vitamin D (50,000 IU per week) for 6 weeks	96 ADHD children aged 2-18 years	Negative relation	Dehbokri et al. (2019)
2000 IU vitamin D for 8 weeks	62 ADHD children aged 5-12 years	Negative relation	Mohammadpour et al. (2018)
ω-3/6 fatty acids for 12 months	90 ADHD children	Negative relation	Barragán et al. (2017)
PUFAs for 15 weeks	132 Australian ADHD children aged 7-12 years	Negative relation	Sinn and Bryan (2007)
ω-3/6 fatty acids for 3 and 6 months	75 ADHD children and adolescents aged 8-18 years	Negative relation	Johnson et al. (2012)
ω-3/6 fatty acids for 16 weeks	40 ADHD children, aged 8-14 years	Negative relation	Bos et al. (2015)
Probiotics (*Lactobacillus acidophilus* LB) for 3 months	80 ADHD children aged 6-16 years	Negative relation	Elhossiny et al. (2023)
Probiotic strain *Lactobacillus rhamnosus* GG ATCC53103	32 ADHD children and adolescents aged 4-17 years	Negative relation	Kumperscak et al. (2020)
Probiotics (*Lactobacillus reuteri*, *L. acidophilus*, *Lactobacillus fermentum*, and *Bifidobacterium bifidum*)	17 ADHD children	Negative relation	Sepehrmanesh et al. (2021)
Probiotic (*B. bifidum*)	30 ADHD children aged 4-16 years	Negative relation	Wang et al. (2022)

Abbreviations: ADHD, attention-deficit hyperactivity disorder; PUFA, polyunsaturated fatty acid.

alleviated ADHD symptoms without significant side effects (Evatt et al., 2008; Bener and Kamal, 2014; Mohammadpour et al., 2018; Gan et al., 2019). Supplementation with vitamin D seems to be an efficient treatment for impulsive behavior. The potential efficacy of this supplement has been enhanced through the augmentation of both the supplement dosage as well as the sample size (Naeini et al., 2019), as shown in Table 4.

Vitamin A, known for its antioxidant properties, significantly contributes to neuroplasticity through its active metabolite retinoic acid (RA) (Oades, 2008). RA regulates dopamine metabolism in the corpus striatum by acting as a transcriptional regulator (McCaffery and Dräger, 1994). Vitamin A impacts the concentration of 5-hydroxytryptamine, an element that, along with dopamine, is implicated in the mechanism of ADHD and is similarly affected by vitamin A (Guo et al., 2018).

Polyunsaturated fatty acids

As mentioned above, PUFAs include two fatty acid pathways, ω-3 and ω-6, both of which are recognized for their significant biological contributions as structural and functional constituents of cellular membranes, as well as their profound impact on central nervous system development (Tesei et al., 2017). ω-3 PUFAs, in particular, are widely acknowledged as essential nutrients for appropriate brain development (Königs and Kiliaan, 2016; Macaron et al., 2021; Yap et al., 2023). Clinical investigations have demonstrated that ω-3 PUFAs can alleviate depression symptoms (Su et al., 2003; Chang et al., 2020) and memory loss in patients with mild impairment in cognitive function (Chiu et al., 2008). Interestingly, recent studies show that ADHD is associated with changes in the functions and levels of PUFAs in the brain (Gao et al., 2022; Sengottuvel et al., 2023).

In the past decade, several systematic reviews and meta-analyses have examined the potential of ω-6 and ω-3 PUFAs as supplementary treatments for ADHD (Puri and Martins, 2014; Derbyshire, 2017; Gillies et al., 2023). Additionally, blood long-chain PUFA levels in erythrocyte membranes and plasma are lower in ADHD children versus the healthy control groups, per previous studies (Stevens et al., 1995; Burgess et al., 2000; Antalis et al., 2006). Furthermore, supplementing the children with doses of long-chain PUFAs improved the parental assessments of ADHD symptoms reported by a couple of meta-analyses of randomized controlled intervention trials (Bloch and Qawasmi, 2011; Sonuga-Barke et al., 2013). Also, another study showed that after 8 weeks of administration, 1 mg/kg/day of methylphenidate combined with ω-3 PUFA supplementation (EPA 180 mg/day and DHA 120 mg/day) improved ADHD symptoms versus the *per se* pharmacological treatment in an Iranian double-blinded, randomized clinical trial (Moghaddam et al., 2017). Similarly, a systematic review including 16 randomized controlled trials was conducted (Derbyshire, 2017) and found that 4 studies used supplements of EPA/DHA/gamma-linolenic acid (GLA) in a 9:3:1 ratio that amended erythrocyte levels and were considered promising adjunctive therapy to old medical treatments, reducing the dose and leading to enhancement in compliance with medical treatments like methylphenidate (Johnson et al., 2012; Matsudaira et al., 2015; Barragán et al., 2017).

ω-3 PUFAs have been evaluated for their potential therapeutic benefit in the management of symptoms associated with ADHD (Bonvicini et al., 2016; Chang et al., 2018). ω-6 PUFAs and ω-3 PUFAs are implicated in the neurotransmitter synthesis, release, and reuptake. Following this, a deficiency in ω-3 PUFAs or the absence of the balance between ω-6 and ω-3 PUFAs may result in compromised neurological functionality and behavioral disruptions that resemble the symptoms of ADHD (Schuchardt et al., 2010). Recently, Döpfner et al. (2021) discovered that children at risk of ADHD displayed symptomatic improvements after a 4-month therapeutic period with ω-6/ω-3 fatty acids. Interestingly, a study conducted by Döpfner et al. (2021) indicated that ADHD children who were prescribed methylphenidate needed less of the medication and had fewer side effects when given ω-3/ω-6 PUFAs supplements for 12 months. This suggests that ω-3/ω-6 PUFAs could be a helpful supplement to methylphenidate, enhancing tolerability, dosage, and adherence. The dosage of the supplements was 174 mg DHA, 558 mg EPA, and 60 mg GLA, in a 9:3:1 ratio (Döpfner et al., 2021). In another study, 75 children (8-18 years) were casually allocated to take a placebo or ω-3/ω-6 for 3 months (Johnson et al., 2012). On the other hand, dietary consumption of fatty fish and shellfish was shown to be lower in children with ADHD compared to control patients in a previous cohort study (Fuentes-Albero et al., 2019).

Furthermore, the participants who showed a successful reduction in their ADHD symptoms by more than 25% were found to have a significantly higher increase in the plasma level of ω-3 and a lower ω-6:ω-3 ratio at the two study time points (3 months and 6 months) of follow-up, as shown in Table 4.

Interestingly, the understanding of nutrient interactions between ω-3 and ω-6 PUFAs and infant brain development and mental health may be crucial for the advancement strategy aiming for upregulation of the serum levels of PUFAs that may aid in the management of ADHD, which is attributed to ω-3 and ω-6 PUFAs that had an essential role in the physiological function of cells, particularly in the brain where there are substrates for the creation of various signaling molecules (Bazinet and Layé, 2014).

Probiotics

A human being's mental health, behavior, and brain activity may be impacted by their intestinal flora and probiotics (Lange et al., 2020a,b). The gut microbiota, which includes about 100 trillion microbes, can directly regulate and produce chemicals with neuroactive properties and neurotransmitters (Martin et al., 2018; Strandwitz, 2018). ADHD symptoms, including changes in behavior, emotions, and cognition, originate in the dopaminergic system that is affected by nutrients (Cortese, 2012; de Araujo et al., 2012). For this reason, the gut–brain axis and the microbiota of the digestive tract have recently attracted much attention in the study of ADHD's etiology (Cenit et al., 2017). Probiotic supplementation could have an indirect or direct effect on the gastrointestinal severity index; children with ADHD score higher than healthy children, and they also report more frequent symptoms of flatulence and constipation (Ming et al., 2018).

Previous evidence has suggested that alterations in tight junctions, mucin synthesis, and antigen-specific immunoglobulin are probable processes by which *Lactobacillus rhamnosus* GG stabilizes the gut permeability barrier (Isolauri et al., 2008). As well, certain neuropsychiatric disorders are attributed to the effects of *L. rhamnosus* on the vagus nerve and the central GABAergic system, which regulate emotional behavior (Enticott et al., 2010; Bravo et al., 2011). Additionally, some bacterial taxa are more prevalent in ADHD patients than in healthy persons (Pärtty et al., 2015; Bull-Larsen and Mohajeri, 2019). Adolescents and children with ADHD who took *L. rhamnosus* supplements for 3 months had far improved health-associated quality of life and physical, academic, emotional, and social functions than those who took a placebo. This supports the idea that *L. rhamnosus* could have positive effects when given orally. Nevertheless, there were no discernible advantages to taking probiotic supplements, according to the psychometric findings of parent and teacher surveys (Kumperscak et al., 2020), as shown in Table 4.

Probiotics may be an effective preventive and treatment measure for ADHD, according to preliminary interventional data (Pärtty et al., 2015).

Likewise, the correlation between *Bifidobacterium* and ADHD was observed in the study by Aarts et al. (2017), which illustrated that a lower future risk of ADHD would be associated with higher levels of *Bifidobacterium longum* in younger children.

This means that a variety of bacterial species may have a role in the development of ADHD, and the gut microbiome is considered as a factor contributing to its etiology.

Further investigations ought to be prolonged in duration, involve a more significant number of participants, and incorporate minors who are not susceptible to drugs. Unquestionably, further investigation is required in this field. Furthermore, it appears imperative to undertake intervention research aimed at ameliorating the symptoms associated with ADHD while minimizing adverse effects.

DISCUSSION

Results from observational research point to food habits as a possible risk factor for ADHD. While these studies generally demonstrate evidence that mineral deficiencies and environmental pollutants are associated with the pathophysiology of ADHD and support the beneficial effects of dietary supplementation regimens such as PUFAs, minerals, probiotics, and vitamins in improving behavior in children with ADHD, the outcomes were limited by the concise data of nutrients investigated across these studies. Herein, we provide a more detailed examination of the lack of various types of nutrients in the pathogenesis of ADHD in addition to the role of feeding or supplementation.

Consistently with recent studies, there is considerable evidence correlating mineral deficiencies and environmental pollutants to ADHD (Aschner et al., 2024; Robinson et al., 2024), but it should be noted that the correlation between adhering to a healthy diet and a low prevalence of ADHD does not necessarily mean that good foods consumed as children have a preventive impact as demonstrated in recent evidence (Robinette et al., 2023; Jakobi et al., 2024), but it could help in identifying targets for dietary interventions as therapeutic support for ADHD patients.

Although several pieces of evidence demonstrate that a junk diet could have an association with ADHD (Rawan, 2020; Khazdouz et al., 2024), on the other hand, another study evaluated the effects of sugar intake on behavior and learning skills in ADHD school children and demonstrated that sugar intake does not affect them (Kim and Chang, 2011). Hence, further research for investigating the relationship between junk diet and ADHD should be conducted.

The neurotransmitters norepinephrine and dopamine are affected by iron, zinc, and magnesium deficiency, originating in ADHD. Also, the downregulation of serum ferritin levels is associated with severe symptoms of ADHD (Kiddie et al., 2010; Zhou et al., 2016; Khan, 2017; Salvat et al., 2022). Moreover, some studies found that dietary supplements helped those trials that had severe methodological flaws like very brief intervention durations, no randomization, and no placebo or prospective monitoring of the supplement's long-term effects. The growing body of research indicates that more research on the impact of dietary therapies on ADHD is required, but they may be beneficial for specific subgroups of children and adolescents. Even though there are several nutritional deficiencies associated with ADHD, orthomolecular treatment approaches continue to depend on biochemical uniqueness to personalize remedies for each patient. It would be helpful for future research to try to figure out which subsets of people with ADHD would benefit from these dietary strategies.

The authors believe that this review is helpful as it discusses the lack of various nutrients in the pathogenesis of ADHD and the role of feeding or supplementation with these nutrients in overcoming the symptoms of ADHD. This can open avenues for comprehensive studies and meta-analyses that aim to determine and judge the role of different types of nutrients in ADHD. However, several limitations should be considered. First, the review's reliance on existing literature may introduce potential bias based on the quality and scope of the studies included. The variability in study designs, methodologies, and participant characteristics across the selected literature may impact the generalizability of the findings. Second, the limitations inherent in the search strategy, despite utilizing several well-known databases, may have constrained the inclusion of all relevant studies on the topic. The exclusion of non-English language studies and the absence of unpublished or gray literature may have restricted the comprehensiveness of the review. Furthermore, the narrative nature of this review may limit the ability to quantitatively analyze and synthesize the data, potentially affecting the depth of insight into the relationship between dietary patterns and ADHD management. The absence of a systematic review methodology may influence the reproducibility and rigor of the review process. Lastly, the evaluation of dietary strategies and nutrients' impact on ADHD management is influenced by a range of confounding factors, such as individual differences in response, compliance with dietary interventions, and the presence of comorbid conditions. These factors could introduce complexities in interpreting the efficacy/applicability of dietary therapies for ADHD.

IMPLICATIONS AND FUTURE PERSPECTIVES

In light of the findings presented in this review, it is essential to consider several implications for clinical practice and future research. The identified associations between dietary patterns, specific nutrients, and ADHD symptoms underscore the potential significance of nutritional interventions in managing ADHD. Clinicians and healthcare providers may benefit from considering dietary modifications as complementary strategies in the comprehensive treatment of individuals with ADHD. Furthermore, public health initiatives aimed at promoting healthy eating habits and nutritional awareness may help mitigate the risk factors associated with ADHD.

Future research efforts could explore the effectiveness of specific dietary interventions, such as supplementation regimens or tailored nutritional plans, in addressing ADHD symptoms. Longitudinal studies tracking the impact of dietary modifications on ADHD outcomes over extended periods may provide valuable insights into the sustainability and long-term benefits of nutritional interventions. In addition, exploring the mechanistic pathways through which nutrients impact ADHD pathophysiology could deepen our understanding and inform targeted nutritional strategies for personalized treatment approaches.

CONCLUSIONS

Collectively, nutrient imbalances, including low vitamin D, iron, zinc, and PUFA levels, have also been associated with the worsening and advancement of ADHD, but nutritional supplements improve its symptoms. There appears to be a strong correlation between ADHD and eating habits, with poor eating habits being negatively related to the disorder and the possibility of getting or worsening symptoms of ADHD being highest for those with ADHD. Consequently, dietary changes have come up as a potential remedy for ADHD. However, in order to incorporate these dietary modifications into ADHD treatment, several lines of scientific evidence are needed.

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DATA AVAILABILITY STATEMENT

All data were sourced from publicly available scientific literature and databases.

DECLARATION OF GENERATIVE AI IN SCIENTIFIC WRITING

The authors did not use generative artificial intelligence (AI) and AI-assisted technologies in the writing process.

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