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Review Article

The Omega-3 Benefits on Treatment of People with Attention Deficit/Hyperactivity Disorder: A State of Art

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Abstract

The Attention Deficit and Hyperactivity Disorder [ADHD] is a more common disorder in the majority of the world population, could be present in any age. It is easily diagnosticated in children, always, in scholar phase. The individual that has these disorders could present injuries like low self-esteem relationships difficulties and problems on school or work. The treatment is done by the use of psychostimulants as methylphenidate that acts in dopamine/norepinephrine neurotransmitter systems, and is the substance prescribed all over the world. Because the collateral effects of this medicine, and in some cases, low efficacy, the omega-3 is presented as an alternative to the treatment, and some studies pointed his efficiency, to meliorate the quality of life in individuals with the referred disorder. This work aims to present the data from literature that support the use of omega-3 and to discuss the disease.

Keywords: ADHD, Treatment, Omega-3, Effects, Benefits

INTRODUCTION

The ADHD or Hyperkinetic Syndrome **(Figure 1)** is characterized by a pattern of behavior persistent as loss attention, hyperactivity and impulsivity. People that have this disorder present difficulties of learn, autoregulation, and inconsequent attitudes. The genetic predisposition is a preponderant factor in the diagnosis, generally, the grade of heredity stays between 55-92%. There are three subtypes of ADHD, mentioned below: ADHD with impulsive-hyperactive type predominance, where the difficult of autoregulation prevails; ADHD with attention deficit prevails, where there is a difficulty to sustain the attention; and the ADHD of combined type, with hyperactivity, impulsivity and attention difficult prevails. Factors as premature born, encephalic lesions, maternal smoke prenatal exposition, plumber exposition, vitamin D perinatal deficiency and severe institutional privation in first infancy, also could be related to the ADHD. People with this disorder could present a gene abnormality linked to the dopaminergic neuron's function. The dopaminergic transmission has a very important role in the behavior. It is a neurobiological disorder, that reaches about 5% of children and teenagers in all the world. Could the symptoms be partially reduced in adult life [1-4].

The consumption of a diet rich in protein foods diminished the levels of sugar, that contribute to the hyperactivity, in the blood. Some foods could bring great benefits, in special, the cold-water fishes, as: salmon, sardine, and other fishes that contribute to the melioration of brain functions and reduction of aggressive behavior. These deep and cold-water fishes are rich in fatty acids, in special the omega-3, because present a significative reduction in the ADHD symptoms. It is a polyunsaturated fatty acid of essential long chain, that not is produced by the human organism, which family is formed by alpha-linoleic acid [ALA], eicosapentaenoic acid [EPA], and docosahexaenoic acid [DHA]. In the last decade many researches about the action mechanism and the potential therapeutic effects of these fatty acids, including their action in the ADHD were performed. Besides of the cardiovascular and anti-inflammatory effects, also identified neurologic benefits. The omega-3, in the form of DHA, is present in rich concentrations in neuron and synaptic vesicle plasma membrane phospholipids [5,6].

The omega-3 fatty acid **(Figure 2)** acts in central nervous system, modulating the cell signalization, affecting the dopaminergic and serotonergic pathways. Beyond of the omega-3 benefit, in ADHD, studies also pointed efficiency in psychiatric disorders as in the treatment of serious depression symptoms and bipolarity, also as in the initial phases of schizophrenia. The ADHD manifests as a comorbid mental illness. As demonstrated, the ADHD is a

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condition persistent of inattention and hyperactivity or impulsivity that affects the mental function or development. Experiments conducted in rats with DHA deficiency, showed behavior change, increase motor activity and diminish of the learn capability. In the fetal human brain, the deficit of this fatty acid could affect it normal development and contribute to the referred disorder. In the present study it is considered that the omega-3 performs fundamental role in the infancy formation, growing and development, beyond that, contribute to the cognitive function performance, and could it present as an alternative treatment, that not produce collateral effects, in ADHD [7,8].

Figure 1. Types of ADHD manifestations in subjects.

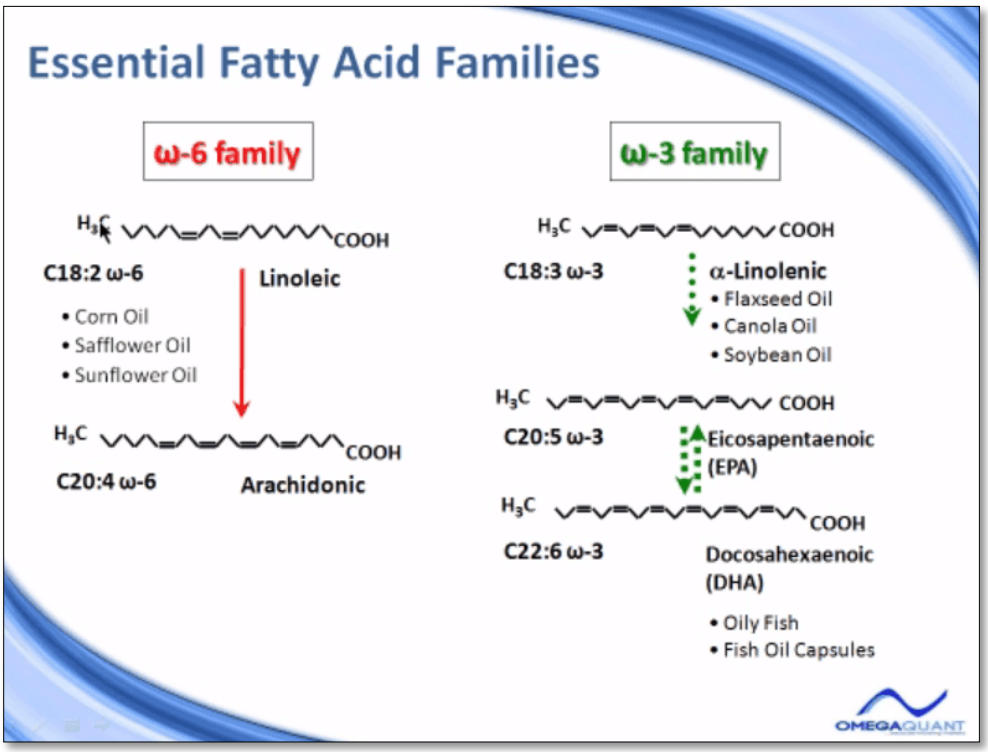

Figure 2. Types of omegas 3 substances in the fatty acid families.

This work has the objective of demonstrating the actuation of omega-3 and its benefits for people with ADHD besides explaining the concept, and types e physiopathology of ADHD. Furthermore, here we define the concept and discuss the benefits of omega-3, demonstrating its use in other psychiatric diseases and pointing out the contribution of omega-3 in the treatment of ADHD, in terms of its effectiveness.

CONCEPT, CHARACTERISTICS AND PHYSIOPATHOLOGY OF ADHD

For years scientists have been trying to understand how is the manifestation process of ADHD, and make it analyzing by various aspects, from the genetic causes to the environmental, to search the better treatment. It was known that the ADHD presents DNA variants, which by occult mechanisms, cause inattention, impulsivity and hyperactivity and need to be present in various environments of the child life, as, for example, in school and home. In the matter of infant neurodevelopment and growth, omega-3, in DHA form, plays an important role [4,8].

The first detailed medical description of ADHD was presented in 1902, published in the Lancet, by the pediatrician George Frederick Still, being a work that approached the psychic and abnormal conditions in children. In this, are listed observations about of children that presented a "permanent or temporary defect of moral control". Dr Still, made an association this "defect" with some type of cerebral disturb. It was in the end of de decade of 1930, that have begun the treatment of ADHD, by Bradley, to describe the therapeutic effect of the amphetamines in the control of behavior anomalies in children [9-11].

Nowadays, it can affirm that ADHD is a neurodevelopment disturb with genetic causes, or, it is a neurocompartmental impairment, characterized by abnormal levels of inattention, hyperactivity and impulsivity, causing substantial functional loss, with a correlation between cerebral lesion and behavior characteristics, such as: Impulsivity and restlessness, that are the scope of what is understood by ADHD. The neurobiological mechanisms that involve ADHD are much complexes, including the dopaminergic, noradrenergic and serotonergic pathways, its diagnostic is based in the behavioral clinical features. The hexogen factors, such as socioeconomic, psych affective, familiar and emotional, could also contribute to the disorder. Some research pointed to rare variants, expressed in the study of chromosomic syndrome anomalies, which contribute to the disturb appearance, they are, to know, the velocardiofacial syndrome, fragile X syndrome, Turner syndrome, tuberous sclerosis, Klinefelter syndrome, neurofibromatosis, Williams syndrome, which the ADHD symptoms are seen in the bearers of the cited diseases [4,9,12,13].

With the great changes occurring in the learn class, especially in the scholar curriculum, there was a triggering of the use of psychostimulants, as in the case, the methylphenidate substance, that is a medicine of first line, used in the treatment of ADHD, that presents some acute and chronic effects, including yet its pharmacodynamic characteristic [relation of drug concentration effect] and the long-term treatment effect in patients during their lives. As alternative therapy, some studies pointed that the supplementation with essential fatty acid, plus precisely, the omega-3, it shows effective and well-tolerate in some patients [13,14].

The prevalence of ADHD is high in the population **(Figure 3)**, mainly in children, and the symptoms are an irrelevant public health problem. The ADHD is the comorbid with higher prevalence and it is correlated with other disorders as bipolar disorder and food intake disorders. It is important to have the diagnose done because the disorder involves problems as accidents risk, suicide risk, exposition to violence, internet and sexual abuse besides prior cited disturbance. It is necessary to do the diagnostic with urgency to initiate the adequate treatment. Some studies, analyzed the food intake patterns and ADHD, when was verified is there is an association between high sugar and fat levels, as well as, the low vegetable, fruits and Mediterranean diet consume, with the ADHD diagnosis. Other associated point to diagnosis is the absence of morning coffee and the fast-food consume. In this way there is a high interest in dietetic consume of omega-3, as pharmacological therapy to the ADHD [15-17].

DEFINITION AND BENEFITS OF OMEGA-3

The fat acids are carboxylic acids with hydrocarbon chains having of 4 to 36 carbons, that are founded mainly esterified to triglycerides, cholesterol and phospholipids constituents of cellular membranes. In case of omega-3, it is a fat acid classified as poli-unsaturated n-3, with benefic effects. These acids are considered essentials because they not be produced in human organism, it is present only in human diet. The omega-3 family is constituted by docosahexaenoic acid form [DHA] and eicosapentaenoic acid [EPA], of sea origin and alpha linolenic acid [ALA]. These acids produce uncountable effects, under different physiological and metabolic aspects, that could prevent the chance of developing cardiovascular and neurological diseases. The majority of world population has omega-3 deficiency, mainly in the form of DHA, that displays high importance to the development of the brain and eyes. The DHA has fundamental role during the first infancy, acting in the mental health, and even in adulthood [17-19].

The omega-3 is present in our ancestral for millions of years, the ingestion of DHA and EPA acids happens since the Paleolithic era, it does. DHA and EPA are founded in frozen water fishes, as the sardine, salmon, cod, herring, etc. The source of these fishes is the salt, frozen and profound water,

which is important because of the absence of mercury that has neurotoxic potential. Between the food's rich in ALA, there are the chia seeds, linseeds, nuts, hemp seeds, perilla oil etc. It is important to say that, the only fruit that has a low concentration of ALA, is the avocado, with a concentration of 40 mg in 100 g of fruit. The DHA acts in cellular membrane fluid, function and neurotransmitters delivery. Some evidences pointed that a low ingestion of omega-3 can increase the risks to mental health, including here, the ADHD, autism, bipolar disorder, depression and suicide ideation [19,20].

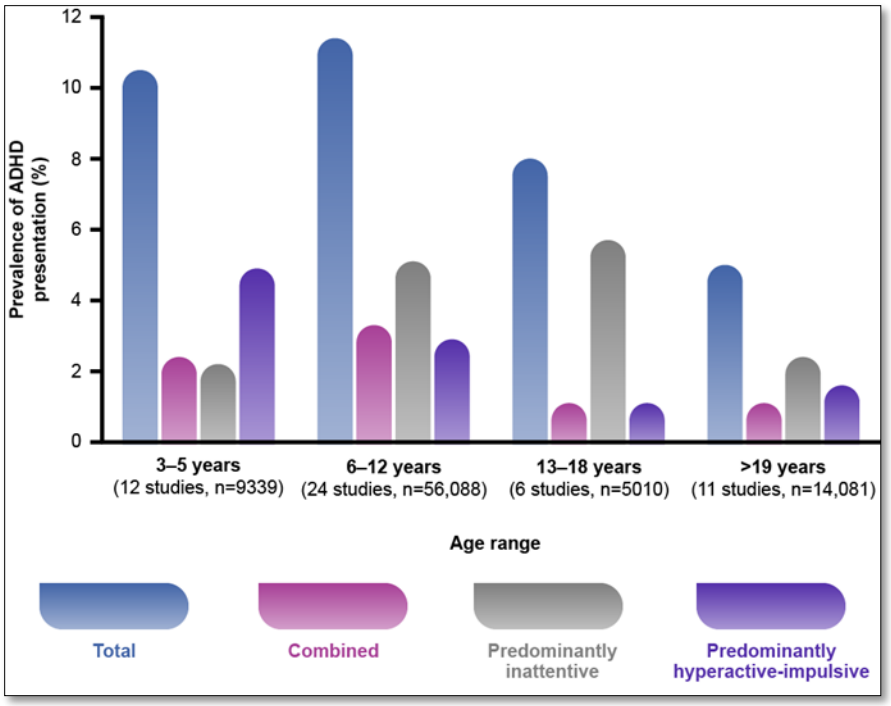

Figure 3. Prevalence of ADHD along the years [modified from ADHD Institute] [https://adhd-institute.com].

Studies indicate that a supplementation with omega-3, could meliorate the condition of mental health of the individuals, and that pregnant woman and nursing mothers consume about of 60-80 mg/day of DHA, when the recommendation by International Society for the Study of Fat Acids and Lipids that the woman must consume 300 mg/day, in this condition. Before born, these fat acids [n-3] cumulated by fetus are prevenient of the blood circulation, by placenta transfer, which has the major part of DHA, and after born are prevenient of mother milk, when the lactation is exclusive. Blood fetal concentrations more elevated, by various weeks before child is born is beneficial for the premature baby and to the development of nervous system. Some studies also suggested that supplementary premature babies with DHA, meliorate the intelligence, speed the visual process of information and promote a better attention. Babies from mothers that had few months of pre-natal supplementation with DHA and the AA [arachidonic acid], could present a good cognitive development, showing better abilities in problems resolution, in comparation with babies form mothers that didn´t have supplementation with these acids [18,19,21].

UTILIZATION OF OMEGA-3 IN OTHER PSYCHIATRIC DISEASES

There are various studies that suggested the association of psychiatric disorders with the excessive consume of high levels of fat and food with high content of sugar, as well as an inadequate ingestion of nutrients. Yet that the collateral effects of the psychotropic medicines can affect food intake, an inadequate nutritional ingestion, is a factor that is present before of psychiatric diagnostic. In the case of depression, as well as, in the psychotic disorders, inadequate diet is a factor that precedes symptoms, contributing as risk factor to the appearance of these mental disorders. The importance of diet to the health is notorious since it is observed its benefits in cardiometabolic diseases, cancer and premature death. In the same way, their impact in mental disorders also is strongly accept. A lot of psychiatric diseases, including the schizophrenia, DAHD and also the depression, encompass the dysregulation of the dopamine systems in the brain. Studies pointed that a rich diet with omega-3 can protect people of cognitive decline and of insanity [22-24].

The bigger consumers of omega-3 present smaller risk of suffer of anxiety, in comparation to people with low ingestion. This acid, object of study, is an important tool to the treatment of neuropsychiatric diseases, principally the related to the humor. Evidences pointed that the omega-3 consume benefits the production of resolves [mediators

which specialty is the resolution of problems due of omega-3 fat acids] and contribute to diminish the cytokines quantity, meliorate the communication between the neurons. Similarly, studies in China, involve the omega-3, concluded that the fat acid would be capable of attenuate the anxiety effects. All of this because the omega-3 modulates neurobiological process, as systems of neurotransmission and neuroplasticity, essential processes to the mental health manutention. French scientists observed that the DHA and the EPA, seems to interfere in hypothalamus-hypophysis-adrenal axle, contributing in a cortisol diminution. Au contrary, the low ingestion of DHA can predisposal individuals to anxiety and also to depression [24-26].

It appears that the ADHD share risk factors with a lot of psychiatric diseases. In schizophrenia, a chronic and incapacitating mental disease, of unknown origin yet, with symptoms like, hallucinations, delirious, disorganized behavior and thought and as negative symptoms, there is a great number of evidences which pointed that the omega-3 can prevent the disease or to soften their curse and symptoms. Equally it was observed in the major depressive disorder, disease characterized by evident alteration of humor and significant disturbance of cognitive and neurovegetative abilities, the high consume of fish could be related to the reduction of the risk to develop this disorder, as well as meliorate in the white substance integrity [4,7,26,27].

CONTRIBUTION AND EFFICACY OF OMEGA-3 IN TREATMENT OF ADHD

The ADHD is one of the more common psychiatric diseases. Beside of its principal cause being unknown yet, it is known that many factors contribute to the development, between them, the nutritional factor that is associated to hyperactivity in the children. The lack of omega-3 fat acid contributed to the development of this, because it plays an important role in the nervous cell's communication. It is understood that the essential fat acids affect the function of cell membranes and of neurotransmitters. Controlled assays with omega-3, combined with micronutrients [vitamins and minerals], showed considerable reductions in antisocial, violent and aggressive behaviors in the youth and in young adult prisoners. Reports pointed it´s efficacy as anti-depressive substance in adults and preliminary data suggested proprieties of suicide prevention [19,28,29].

Animals' studies showed that an insufficiency of DHA in the pre- and post-natal, is associated to great structural changes, as retarded neuronal migration, interrupted dendritic arborization, an abnormal neuronal development in the hippocampus, and abnormalities as apoptosis. Some neurochemistry studies showed alterations in various neurotransmitters systems, between them the dopaminergic and serotonergic systems. This impaired connectivity can occasion results as permanent disturbs. It can say that, the injuries of cognitive order will be the memory and learning, and the of emotional and behavior order, the depression, anxiety and animal aggression [19,29,30].

Again, about the pregnancy, it can be said that the major vulnerability index to damage caused by nutritional deficiencies occur in this moment, because is when the central nervous system is initiating its development. These deficiencies are prompt of occasional problems in the neurodevelopment, behavior, as well as problems of visual acuity and cognitive in premature babies. A good maternal diet will depend of the ingestion of micronutrients [vitamins], elements as iron, iodol, zinc and especially of omega-3 fat acids [DHA]. This last one, object of study, is fundamental, to rapid cerebral development by the fetus development. The mother milk, besides of bringing the essential nutrients to prole, also brings growing factors, cytokines and immunomodulator that affects newborn receptors. The fetus is totally dependent of DHA, through mother milk, as cited previously [19,29,30].

In the United States, almost of 4 to 15% of the children in scholar age, present the ADHD. Children and adults, with ADHD, have lower levels of omega-3, and this has direct effect in behavior, learning, conduct, hyperactivity-impulsivity, anxiety, tantrums and sleep problems. In Japan, were done controlled double-blind studies, with 40 children that presented the ADHD, and was found that food rich in omega-3 [having about of 510 mg of DHA and 100 mg of EPA/day] intake reduces the disorder symptoms. Other control randomized double-blind study showed that children between 7 to 9 years, that presented low lecture development, when making use of 600 mg of DHA [seaweed oil], had improvement in ADHD symptoms, according their parents. Other studies with associations of omega-3, including the omega-6, controlled double-blind test, in 50 children, also with ADHD, using oil of primula/night using [480 mg DHA, 80 mg EPA, 96 mg GLA e 40 mg of arachidonic acid plus 24 mg alfa-tocopherol acetate], have considerable improvement in attention, and in opposite challenge behavior [19,28,31].

CONCLUSION

The DAHD is a common reality, that happens in various age, principally the child age, can bring loss, will in the individual self-esteem, social convivence, familiar, and in his work relations. It not knows the cause precisely, perhaps, it knows that there are factors that contribute to it arise, as example, the genetic factors, which individuals carried DNA variants that, through unknown mechanisms, present inattention, hyperactivity and impulsivity. By owning a DNA variation increase the risk to the disorder. The ambiental causes also are factors that can inside as cause, as well as the tobacco use in pregnancy, because provoke complications during the born, could reduce the weight of the baby. This factor is associated to the disorder, also as nutritional's factors, between them, the high sugar and fat

consume and, the low ingestion of vegetables, fruits and Mediterranean foods, that are rich in omega-3.

There is medicine of first line, to the treatment of DAHD, that is the substance known as methylphenidate, but its effects are not prolonged and produce collateral effects. The omega-3, an essential fat acid, which can be encountered in diverse foods, include the DHA, found in the fish oil, has effects in nervous cells, principally those of the brain, that present alterations in it function, and with more benefit effects, can be part of the diet, until the gestational phase, lactate, infant, adult and to the longevity. To produce the wish effects the fishes, need specific habitats, cold and profonds water, free of heavy metals.

Besides the contribution of omega-3 in the diverse phases of an individual' life, studies also shown that the ingestion of DHA contribute to reduction of psychiatric diseases, as the humor bipolar disorder, anxiety, depression, schizophrenia, behavior problems, opposite challenge disorder, and also the DAHD development risk. In DAHD the ingestion of DHA contributes to the reduction of the hyperactivity, as well as it can diminish behavioral, learning, conduct, hyperactivity-impulsivity, anxiety, angry access and sleep problems. The ingestion of the essential fat acid DHA is practically fundamental to individual health.

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