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Effects of Polyunsaturated Fatty Acids on Mental Health

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Abstract

Depression, bipolar disorder, Alzheimer's disease, and Parkinson's Disease may be associated with dietary imbalances currently seen in the average Western diet. The increase in intake of omega-6 fatty acids is a point of concern, as evidence links disproportionate intake with inhibited neural membrane function and increased inflammation. This paper reviews evidence related to problems associated with decreased omega-3 fatty acid intake in the average Western diet. Evidence connects omega-3 supplementation with alleviation of symptoms of depression, bipolar disorder, and defiant behavior. Further research may be warranted regarding the degree of omega-3 deficiency in given populations of interest, such as the University of Northern Iowa. Further research using the Diet History Questionnaire (DHQ) from the National Institutes of Health to measure dietary intake is planned.

Effects of Polyunsaturated Fatty Acids on Mental Health

Omega-3 and Omega-6 Fatty Acids

Fatty acids are compounds composed of carbon chains which vary in length and contain both a carboxylic acid group and a methyl group in their chemical composition. They can be categorized as saturated, monounsaturated, or polyunsaturated, based on the number of hydrogen atoms the compound contains. Polyunsaturated fatty acids, categorized into either omega-3s or omega-6s, have divergent effects on the body despite differing only in the location of one double bond (Ander et al., 2003). Due to the complementary role these molecules play in the human body, their optimal ratio is 1:1. However, the average individual consuming a Western diet has an omega-6 to omega-3 ratio of nearly 16:1 (Ilardi, 2009).

It is important to recognize the distinctions between variations of omega-3s due to their varying effects on the body. Docosahexaenoic acid (DHA)—found most abundantly in the brain— prevents phospholipid membranes in brain cells from becoming inflexible (Ilardi, 2009). Eicosopentaenoic acid (EPA) is necessary in the production of anti-inflammatory hormones and increases the reactivity of neurotransmitters (Ilardi, 2009). Alpha linolenic acid (ALA)—which serves as a precursor for both DHA and EPA (Brenna et al., 2009)—has beneficial effects on coronary artery disease and other cardiovascular diseases (Ander et al., 2003). In regard to chemical composition, these three molecules differ only in their shape and number of double bonds (Khan et al., 2015).

Effects of Omega-3 and Omega-6 Fatty Acid Intake

Neural Membranes

Polyunsaturated fatty acids have the ability to change the fluidity of neural membranes by changing phospholipid structure, therefore impacting the processes within the cell such as neurotransmitter binding, receptor activity, protein function, and affecting membrane enzymes (Horrobin, 1998). This change in structure occurs due to folding and bending of the membrane as the number of double bonds increases. DHA and EPA, composing 15-30% of neuronal and retinal tissue dry weight, are seen to increase membrane fluidity more so than other polyunsaturated fatty acids due to their high number of double bonds (6 and 5, respectively) (Husted & Bouzinova, 2016; Horrobin, 1998). DHA is also necessary in the cell membrane for production and breakdown of necessary phospholipids, axon and dendrite growth, and forming synaptic connections (Tanaka et al., 2012; Horrobin, 1998). Increasing omega-3 polyunsaturated fatty acids also increase fluidity by dislodging cholesterol from the membranes. The change in structure of the neural membranes affects vital cellular functions (Husted & Bouzinova, 2016).

Neurotransmitters, along with calcium, are located within vesicles, surrounded by a phospholipid bilayer (Horrobin, 1998). The contents of these vesicles aim to be released and re-uptaken, depending on the realignment of the phospholipids. When dietary intake of omega-6 exceeds intake of omega-3 to an extreme, membrane fluidity decreases, decreasing the binding of neurotransmitters to their receptors (Horrobin, 1998). Genetic factors strongly influence the synthesis and breakdown of phospholipids, however, a lack of intake of essential fatty acids will cause the phospholipids to uptake less effective fatty acids. This causes a change in the phospholipid function and interaction with its environment (Horrobin, 1998).

Inflammation

Omega-3 polyunsaturated fatty acids are seen to decrease inflammation within the body. Microglial cells are cells within the central nervous system which respond to infection. These responses include release of proinflammatory and anti-inflammatory cytokines. An inflammatory response is a beneficial response to infection, however, when excess proinflammatory cytokines are produced, they become toxic to the neurons (Layé, 2018). This excess production leads to cell damage. Omega-3 polyunsaturated fatty acids limit the amount of proinflammatory cytokines produced in two ways: restricting the inflammatory gene expression and inducing anti-inflammatory lipids (Layé, 2018).

Increase in Dietary Intake

Omega-6s, synthesized in nuts, grains, and other plant seeds, saw a drastic increase in dietary intake in the Western diet immediately following a revolution in farming. This revolution, referred to as The Green Revolution, originated in Mexico due to increased investment in crop improvement (Pingali, 2012). More health focus was placed on crop genetics in order to increase plant yield and resistance, contributing to an increase in grain-based diets due to the accessibility and ease of harvesting of grains (Pingali, 2012; Ilardi, 2009). Negative health outcomes such as diabetes and metabolic conditions are related to the increased intake of omega-6 rich diets, which may be reversed by returning the omega-3 to omega-6 ratio to 1:1 (Ilardi, 2009).

Links to Mental Health

Mechanisms Proposed

The omega-3 to omega-6 ratio is important to keep in balance because in excess, omega-6 polyunsaturated fatty acids are associated with negative health outcomes. Omega-6 polyunsaturated fatty acids are seen to cause inflammation because linoleic acid, a particular omega-6 fatty acid, is a building block for arachidonic acid, which is a building block for proinflammatory leukotrienes and prostaglandins. These compounds, as well as several others, are often referred to as AA-derived eicosanoids and excess buildup is often associated with inflammatory diseases (Marion-Letellier et al., 2015).

Given the physical effects of polyunsaturated fatty acids on phospholipids and inflammation, it is not surprising that consuming omega-3 fatty acids in an improper balance may have important negative effects on mood and mental health. The Membrane Phospholipid Concept of Schizophrenia attributes schizophrenic behaviors to an abnormal rate of loss of EPA and DHA, leading to changes in cell signaling and membrane protein function (Horrobin, 1998). Evidence for this concept includes reduced levels of DHA in red blood cells of schizophrenia, an increased rate of phospholipid breakdown in the brain of unmedicated schizophrenics, and a reduced maximal electro-retinogram response to light, likely due to decreased DHA availability for cell signaling (Horrobin, 1998). The rate at which these essential fatty acids are synthesized and incorporated into the brain decreases with stress, old age, male sex, and viral infections (Horrobin, 1998). This explains the trends in the age of onset of schizophrenia as well as the population who is most at risk. Despite providing great evidence, this concept fails to explain the delay between decreased levels of DHA and increased levels of sex hormones around puberty and the onset of symptoms in adult life (Horrobin, 1998).

Similar mechanisms are seen to cause depressive symptoms. The monoamine hypothesis suggests that neurotransmitter function is altered, causing depression. This could further be explained by the evidence associating low levels of omega-3 to depression and the impact that omega-3 polyunsaturated fatty acids have on neural membrane fluidity. Depressive symptoms are also caused by proinflammatory cytokines, as seen in both rats and humans. This may explain the increase in prevalence of depression associated with the increase of omega-6 polyunsaturated fatty acids, which are building blocks for proinflammatory compounds.

Research is beginning to suggest that certain neurological disorders such as Alzheimer's disease and Parkinson's disease, which are related to high levels of brain inflammation, may be prevented by an increase of polyunsaturated fatty acids in an individual's diet (Layé et al, 2018). Increased amounts of omega-3 polyunsaturated fatty acids in the blood are associated with decreased proinflammatory cytokine production which increased amounts of omega-6 is considered proinflammatory (Layé et al, 2018; Marion-Letellier et al., 2015). Animal research, using well controlled experimental designs, also points to this effect. As seen in perinatal mice and rats, decreased dietary intake of omega-3s caused microglial alteration as well as increased amounts of proinflammatory cytokines (Layé et al, 2018).

Non-Experimental Human Research

Many studies suggest that decreased levels of omega-3s are associated with mood disorders such as depression. Peet et al. (1997) measured amounts of fatty acids in red blood cell membranes in fifteen patients suffering with major depressive episodes, as defined by DSM-IV, and fifteen patients with no history of psychiatric or medical illness. Their study found that red blood cell membranes of depressive patients have decreased levels of fatty acids when compared to healthy patients. Reduced levels of omega-3 polyunsaturated fatty acids are also seen in red blood cells of patients diagnosed with bipolar disorders (Bozzatello et al., 2016).

Controlled experiments with participants randomly assigned to treatment conditions are the gold standard for determining cause and effect relationships regarding mental health outcomes. It is important to appreciate that the experimental control and random participant assignment prevents selection bias and minimizes confounding factors as explanation for effects. The effects of fatty acids on mental health have also been investigated using the experimental method.

Experimental Human Research

Multiple studies supplemented individuals diagnosed with bipolar disorder with EPA, DHA, ALA, or unspecified omega-3 fatty acids. Stoll et al. (1999) completed a 16 week study providing 14 participants with 6.2g of EPA and 3.4g of DHA and 16 participants with a placebo each day. This study is one of three which found improvement of depressive symptoms, but not mania. Other studies which saw improvements of the depressive side of bipolar disorder symptoms include studies by Frangou et al. (2006) and Gracious et al. (2010). Frangous et al. (2006) administered 1 or 2g per day of EPA to 75 patients, each of which continuing their regularly prescribed psychotropic medications. Findings were similar to that of Stoll et al. (1999), as depressive symptoms of bipolar disorder were improved. Gracious et al. (2010) also found an improvement of symptoms when ALA was administered to adolescents in tandem with psychotropic medications, compared to the medications alone.

Nonetheless, the effect of omega-3 fatty acids on bipolar disorder are mixed; three other studies did not find significant improvement of symptoms as compared to control groups (Bozzatello et al., 2016). Studies which did not find any significant improvement of bipolar symptoms were conducted by Chiu et al. (2003), Keck et al. (2006), and Murphy et al. (2012).

For example, Chiu et al (2003) treated 15 participants with acute mania for four weeks with supplementation of 4.4g of EPA and 2.4g of DHA. The placebo group received 20mg/kg/day of valproate, a mood stabilizer and did not report significant improvements of manic symptoms. Despite mixed results between the six studies, it was seen that EPA or ALA supplementation is more beneficial than DHA supplementation. Finally, findings suggest that EPA should be administered in doses of at least 1mg in order for improvement of depressive symptoms to be seen (Bozzatello et al., 2016).

Similar findings have also been demonstrated in a randomized clinical trial studying depression. For example, 20 children (10 experimental and 10 control) ranging from eight to twelve years of age, were given sixteen weeks of omega-3 treatment or placebo. Their depression was rated by the Children's Depression Rating Scale (CDRS) before and after receiving treatment. Their results indicate that omega-3 is a successful treatment for depression in children. Seven out of ten children receiving the omega-3 treatment saw at least a fifty percent reduction in their CDRS score at the end of the sixteen weeks and three of these ten met remission criteria (Nemets et al., 2006).

Young adult prisoners have also participated in randomized clinical trials which measure the impact of fatty acids, as well as other vitamins and minerals, on behavior. Gesch et al. (2002) provided 231 young adult inmates with nutritional supplements to determine the impact that intake of vitamins and minerals has on behavior. Antisocial behavior was measured by the number of infractions an inmate received. These infractions typically comprised rule violations. Dietary intake was measured by food diaries completed by inmates and portion weights were provided by those which served the meal. Several tests were used to measure verbal ability, cognition, emotional control, health status, and levels of anxiety and depression. Findings show that the group receiving true supplements reduced the number of minor reports received by 35.1% while the placebo group reduced their minor reports by 6.7%. This suggests that dietary intake of vitamins, mineral, and essential fatty acids improves antisocial and defiant behaviors (Gesch et al., 2002).

Conclusions and Future Research

Though there is no definite answer for the causal mechanism between dietary intake of polyunsaturated fatty acids and mental health outcomes, animal research and studies of blood levels indicate that omega-3 fatty acids increase neural membrane fluidity and production of anti-inflammatory cytokines. Placebo controlled clinical trials point to the importance of maintaining a proper omega 3 to omega 6 ratios, as imbalances are related to negative mental health outcomes (Stoll et al., 1999; Nemets et al., 2006). Thus, it is not altogether surprising that decreasing symptoms of psychological disorders such as bipolar disorder, depression, and schizophrenia, as well as Parkinson's Disease and Alzheimer's Disease may all be linked to these substances (Bozzatello et al., 2016; Ilardi, 2009; Nemets et al., 2006; Layé et al., 2018; Horrobin, 1998; Dyall, 2015). An imbalance in intake of fatty acids in the average Western diet has become extreme, resulting from the Green Revolution providing increased reliance upon seeds and grains (Pingali, 2012; Ilardi, 2009). Recognizing the importance of increasing dietary intake of omega-3 fatty acids and returning the omega-6 to omega-3 ratio back to 1:1 may aid in alleviation of negative mental health outcomes.

Future research may benefit society by increasing awareness of this issue, such as by quantifying actual dietary intake of populations. Using the DHQ, I plan to further this project by determining if students at the University of Northern Iowa may be at risk for mental health issues based on imbalances in dietary intake of omega-3 and omega-6 fatty acids.

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