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2734 17 Avenue SW,
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+15878858911
editorial-office@sciformat.ca

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THE ROLE OF OMEGA-3 FATTY ACIDS IN SLEEP DEPRIVATION AND MEN-TAL HEALT: A NARRATIVE REVIEW

Dominika Galińska (Corresponding Author, Email: dominika.galinska260@gmail.com)

University Clinical Centre, Gdansk, Poland

ORCID ID: 0009-0004-8037-2679

Natalia Domańska

University Clinical Centre, Gdansk, Poland

ORCID ID: 0009-0008-6378-8903

Anna Roman

Faculty of Medicine, Medical University of Gdansk, Poland

ORCID ID: 0009-0008-7152-9880

Joanna Zajęczkowska

University Clinical Centre, Gdansk, Poland

ORCID ID: 0009-0003-4912-9809

Natalia Marzec

St. Adalbert's Hospital, Gdańsk, Poland

ORCID ID: 0009-0008-4722-7321

Natalia Krupa

Specialist Hospital in Kościerzyna, Kościerzyna, Poland

ORCID ID: 0009-0007-6691-0073

Aleksandra Marzec

St. Adalbert's Hospital, Gdańsk, Poland

ORCID ID: 0009-0007-7885-948X

Małgorzata Cherek

St. Vincent de Paul Hospital in Gdynia, Poland

ORCID ID: 0009-0007-4116-1854

Weronika Praska

Polish Red Cross Maritime Hospital, Gdynia, Poland

ORCID ID: 0009-0004-1544-1404

Stanisław Maria Wardecki

Polish Red Cross Maritime Hospital, Gdynia, Poland

ORCID ID: 0009-0008-7703-490X

ABSTRACT

Objectives: The influence of omega-3 fatty acids on sleep disorders and mental health functioning constitutes a complex research problem, necessitating a clear distinction between their therapeutic potential and alleged prophylactic properties. Unrecognized neurochemical imbalances and neuroinflammatory states may contribute to the development of depression, anxiety, and insomnia, making a rigorous assessment of supplementation efficacy essential for safe and accurate therapeutic decisions. Our objective is to present a comprehensive synthesis of current evidence regarding the mechanisms of action, clinical effectiveness, and limitations of omega-3 fatty acid use in the context of sleep quality and mental health.

Methods: Based on the available sources, a narrative literature review was conducted, focusing on studies analyzing the influence of polyunsaturated fatty acids (primarily EPA and DHA) on the nervous system. The evidence was synthesized based on observational and experimental studies, meta-analyses of randomized clinical trials, and current clinical guidelines (including those regarding the use of nutraceuticals in the treatment of psychiatric disorders).

Key findings: Omega-3 fatty acids, specifically DHA and EPA, constitute key modulators of cell membrane structure, neurotransmission (dopaminergic and serotonergic systems), and the melatonin secretion rhythm. Current evidence strongly supports their use as adjunctive therapy in the treatment of depressive disorders and the alleviation of anxiety, particularly in patients with elevated inflammation and oxidative stress. However, they are not recommended as monotherapy. There is also a lack of evidence confirming their efficacy in the primary prevention of depression in healthy individuals. Accumulated data indicate that improvement in objective sleep parameters and mood stabilization require an individualized approach, and the therapeutic effect depends largely on the patient's baseline metabolic status.

Conclusion: Omega-3 fatty acids may perform a significant corrective and supportive function in the treatment of mental disorders and sleep problems, acting as a stabilizer of pathological neurobiological changes rather than a universal mood enhancer. Integrated with appropriate clinical diagnostics, they allow for the safe support of standard pharmacotherapy. Future research should focus on determining optimal doses and EPA/DHA ratios, standardizing research protocols, and long-term evaluation in strictly selected clinical populations.

KEYWORDS

Omega-3 Fatty Acids; Circadian Rhythm; Sleep Disturbances; Mental Health; Depression; Anxiety; EPA; DHA

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Introduction

Contemporary times have seen a dynamic increase in the prevalence of sleep disorders, including insomnia, which represent a significant public health issue. (Miller et al., 2014) Numerous studies indicate that insufficient sleep quality and quantity exert a direct, negative impact on psychological well-being, increasing the risk of developing mood disorders, including depression and anxiety. This relationship is, however, bidirectional- deterioration of mental health promotes the occurrence of sleep difficulties and circadian rhythm disruptions. (Baglioni et al., 2011)

Therapeutic approaches to sleep disorders encompass both non-pharmacological interventions, such as lifestyle modification and the implementation of sleep hygiene principles, and pharmacological treatment. (Wichniak et al., 2017) Increasingly, however, attention is being turned toward the role of nutritional factors as a potentially safe and supportive element of therapy. In recent years, a growing body of scientific reports has pointed to the significant impact of a balanced diet on the regulation of physiological processes, including the circadian rhythm and the functioning of the nervous system. (Freund Levi et al., 2014; Ayee et al., 2020; Deacon et al., 2017; Patan et al., 2021)

Particular research interest focuses on omega-3 polyunsaturated fatty acids, which play a crucial role in brain function, neuroinflammatory processes, and neurotransmission. (Freund Levi et al., 2014; Deacon et al., 2017) Preliminary research results suggest that they may influence mechanisms regulating the sleep-wake

rhythm (Jackson, 2024), as well as alleviate symptoms of mental disorders.(Aucoin et al., 2021; Smith et al., 2019; Wang et al., 2025) Despite the increasing number of publications in this field, there remains a lack of comprehensive studies synthesizing the current state of knowledge.

The aim of this narrative review is to analyze available data regarding the role of omega-3 fatty acids in the regulation of the circadian rhythm and their potential impact on mental health, with particular emphasis on biological mechanisms and clinical implications.

Methodology

Database Search Strategy

A narrative literature review was conducted by searching databases such as MEDLINE (PubMed) for publications released between January 1, 2000, and May 1, 2026. Controlled vocabulary (MeSH) and free-text keywords related to omega-3 fatty acids, sleep, and mental health were combined using Boolean operators: "Omega-3 fatty acids", "Docosahexaenoic Acid" (DHA), "Eicosapentaenoic Acid" (EPA), "Circadian Rhythm", "Sleep", "Insomnia", "Mental Health", "Depression", "Anxiety", "Blood-Brain Barrier", and "Bioavailability".

Inclusion and Exclusion Criteria

Eligible studies included meta-analyses, systematic reviews, randomized controlled trials (RCTs), observational studies, as well as relevant in vitro studies, animal model studies, and clinical guidelines that: (I) assessed the impact of omega-3 polyunsaturated fatty acid intake or supplementation on sleep parameters, circadian rhythm regulation, or mental health (including depressive and anxiety disorders); and (II) investigated physiological mechanisms, such as blood-brain barrier penetration or membrane receptor modulation. Case reports, articles published in languages other than English, and abstracts without access to the full text were excluded from the review.

Study Selection and Data Extraction

Initial selection was conducted based on a review of titles and abstracts, followed by an assessment of the full texts of potentially relevant publications. The data review focused on the study design, characteristics of the study populations (including healthy adults, patients with depression, insomnia, or comorbidities), details of the intervention (dose and type of omega-3 fatty acids), measured outcomes (sleep quality, severity of psychiatric symptoms, biological markers), and their clinical significance.

Results

Biological characteristics of omega-3 fatty acids

Omega-3 fatty acids are a group of polyunsaturated fatty acids (PUFAs) in which the first double bond (counting from the methyl end of the chain, denoted as ω or η) is located at the third carbon atom. They are among the essential components of the human diet. The most important omega-3 acids include α -linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). They are primarily supplied through food, although limited conversion of ALA to EPA and DHA is also possible within the body.(The Nutrition Source, 2023)

Sources of ALA are primarily plant products, such as flaxseed, soybean and rapeseed oils, as well as walnuts and chia seeds. In turn, EPA and DHA occur in larger quantities in fish, such as salmon, mackerel, tuna, herring, and sardines. Some food products are additionally fortified with DHA and other omega-3 acids. These include selected yogurts, eggs, milk, juices, soy beverages, and marine algae oils.(Patted et al., 2024; Abete et al., 2009; Cholewski et al., 2018)

Omega-3 fatty acids perform many vital physiological functions in the human body. They are components of cell membrane phospholipids, where they modulate the organization of the lipid bilayer, leading to increased fluidity due to the presence of polyunsaturated double bonds in the acyl chains.(Ayee et al., 2020)

A significant mechanism of action for omega-3 acids is also their anti-inflammatory effect. Eicosapentaenoic acid (EPA) and DHA compete with arachidonic acid (AA) for incorporation into cell membrane phospholipids, which leads to a reduction in the production of pro-inflammatory eicosanoids derived from AA. Consequently, these acids increase the synthesis of mediators with anti-inflammatory effects. As demonstrated in studies, EPA and DHA reduce the production of pro-inflammatory eicosanoids, and eicosanoids derived from EPA exhibit mainly anti-inflammatory activities. Additionally, omega-3s inhibit the secretion of pro-inflammatory cytokines, such as interleukin-1 beta interleukin-6, or TNF-alpha, which are associated with inflammatory processes in the central nervous system and may play a role in the development of depressive disorders.(Deacon et al., 2017)

The relevant literature also indicates their potential anticancer effects.(di Blasio et al., 2026) Furthermore, omega-3 fatty acids demonstrate the ability to lower blood triglyceride levels (Zhang et al., 2025) and moderately reduce arterial blood pressure, which has been confirmed in meta-analyses of randomized clinical trials.(Shen et al., 2022; Zhang et al., 2022) These effects may be significant in the prevention and supportive treatment of lifestyle diseases such as hypertension, obesity, and type 2 diabetes.(Shen et al., 2022; Huang et al., 2023) Research is also being conducted on the use of omega-3 fatty acids in the prevention and treatment of dermatological conditions. Particular attention is paid to their anti-inflammatory properties and beneficial impact on skin function and appearance.(Thomsen et al., 2020)

Omega-3 fatty acids and brain function

Omega-3 polyunsaturated fatty acids, particularly docosahexaenoic acid (DHA), constitute key structural components of neuronal cell membranes and are found in high concentrations in the brain, retina, and cardiac tissue.(Schuchardt et al., 2013) They are incorporated into the phospholipid bilayer, where they influence membrane fluidity, receptor functioning, and processes essential for proper neuronal activity.(Guixà-González et al., 2016) It has been demonstrated that omega-3 acids play a significant role in the modulation of monoamine systems, specifically serotonergic and dopaminergic transmission, which are crucial for mood regulation and cognitive function. Deficiencies in their supply are associated with abnormalities in these functions. The relevant literature emphasizes that "profound n-3 PUFA deficiency disrupts the functioning of the dopaminergic and serotonergic systems," highlighting their importance in maintaining the proper neurochemical balance of the brain.(Deacon et al., 2017)

Dietary supplementation with omega-3 fatty acids can increase their concentration in the cerebrospinal fluid, indicating that exogenous supply affects the lipid composition of the central nervous system.(Freund Levi et al., 2014) However, the transport of DHA across the blood-brain barrier does not occur in an entirely passive manner and requires the involvement of specific carrier mechanisms. One such mechanism involves DHA bound to lysophosphatidylcholine (LysoPC-DHA), which serves as an efficient transport form, increasing the delivery of DHA to the brain by approximately tenfold compared to free DHA. Significantly, this mechanism exhibits specific selectivity for nervous tissue, as LysoPC-DHA does not significantly increase DHA transport to other organs, such as the heart, liver, or kidneys. This suggests the existence of a specialized physiological system that preferentially directs DHA to the brain.(Hachem et al., 2016a; Hachem et al., 2016b)

Relationship between sleep and mental health

Sleep disorders, including insomnia, are a frequent comorbid symptom accompanying depression. On the other hand, it has also been observed that prolonged insomnia constitutes a risk factor for the development of a depressive episode.(Baglioni et al., 2011) The development of insomnia and depression is determined by both environmental and genetic factors. Among environmental factors, stressful life events are of particular importance, as they increase susceptibility to the development of both disorders. The genetic component also plays a significant role, which is confirmed by their familial occurrence and the increased risk of depression in the offspring of individuals affected by these conditions.(Bastien et al., 2000; Klein et al., 2005) Genome-wide association studies (GWAS) indicate the presence of numerous genetic loci associated with both insomnia and depression. It is observed that there is also a partial overlap of genetic variants that increase the risk of these disorders.(Jansen et al., 2019; Stein et al., 2018; O'Connell et al., 2021) This suggests the existence of common underlying biological mechanisms and a close link between insomnia and depression at the genetic level. Various hypotheses regarding the biological mechanisms underlying the occurrence of depression are mentioned in the relevant literature. One of them is the cholinergic-monoaminergic hypothesis. It assumes that depression is rooted in, among other things, an imbalance in the production of cholinergic and monoaminergic neurotransmitters. In patients with depression, the level of serotonin metabolites is decreased, while the level of acetylcholine is increased.(Perez-Caballero et al., 2019) Animal studies show that monoamines (serotonin, noradrenaline) decrease their activity during the transition to REM sleep, while the cholinergic system increases it.(Takahashi et al., 2010; Sakai, Crochet, 2001) This suggests that the same systems associated with depression also regulate REM sleep and may mutually influence each other.

Similar to the case of depression, sleep disorders show a close relationship with anxiety disorders. Insomnia is recognized as a significant risk factor for their development, while at the same time, intensified anxiety leads to a deterioration in sleep quality and continuity.(Hertenstein et al., 2023; Baglioni et al., 2016) A common mechanism underlying both phenomena is a state of hyperarousal, involving increased activity of the stress axis and neurotransmitter systems responsible for arousal.(Xie et al., 2024) Particular significance is attributed to REM sleep disturbances, which may play a key role in emotional regulation. Normal REM sleep promotes the adaptive processing of emotional experiences, whereas its fragmentation and the presence of

micro-arousals may lead to sustained arousal and improper processing of emotional stimuli. Consequently, this results in increased reactivity to stress and difficulty in extinguishing negative emotions, which favors the development and maintenance of anxiety symptoms. (Wassing et al., 2016; Wassing et al., 2019) Additionally, individuals with insomnia tend toward negative information processing, which may reinforce the vicious cycle of sleep disorders and anxiety. (McCrae et al., 2008; Scott et al., 2008)

In the context of the presented relationships between sleep and mental health, factors that modulate both the sleep rhythm and the functioning of neurobiological systems involved in emotion regulation—including, among others, omega-3 fatty acids—take on particular importance.

Omega-3 fatty acids and sleep quality

Omega-3 fatty acids, particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), may play a significant role in the regulation of physiological processes related to sleep. As Philippa Jackson notes, recent years have seen an increase in the number of studies analyzing their impact on the quality, duration, and efficiency of nightly rest, as well as the biological mechanisms underlying these relationships. Although earlier systematic reviews suggested a limited impact of supplementation in adults, recent data point to a much more complex and multifaceted picture. (Jackson et al., 2024)

Some contemporary randomized controlled trials suggest that omega-3 acids may improve objective sleep parameters, especially sleep efficiency and sleep onset latency (the time needed to fall asleep). These benefits appear to be more closely linked to the intake of DHA than EPA. Interventions using DHA-rich oil led to a reduction in sleep onset latency in healthy adults. In contrast, EPA-rich interventions showed less definitive results—observing only a trend toward improved sleep efficiency and, compared to DHA interventions, also a reduction in total sleep time and time spent in bed. (Patan et al., 2021) These differences may indicate distinct functional roles for individual fatty acids in the regulation of sleep-wake processes.

Furthermore, research findings suggest that the effects of supplementation may depend on the characteristics of the study population, including age, sex, and baseline sleep quality. (Liu et al., 2024) Beneficial changes were observed both in healthy individuals with low omega-3 intake (Patan et al., 2021) and in older adults with sleep disorders, who showed improved sleep efficiency following fish oil supplementation. (Yokoi-Shimizu et al., 2022) Simultaneously, in some studies involving clinical populations, such as postmenopausal women or patients with chronic diseases, no significant improvement in subjective sleep quality compared to placebo was demonstrated (Iqbal et al., 2023; Savard et al., 2023; Wang et al., 2024), particularly in the case of interventions based primarily on EPA.

Currently available data do not allow for a definitive determination of the optimal dose or the ratio of DHA to EPA. (Patan et al., 2021; Yokoi-Shimizu et al., 2022) Discrepancies in results may stem from both participant characteristics and lifestyle factors, such as sleep-related habits. (Yang et al., 2020)

One of the key mechanisms linking omega-3 fatty acids to sleep is their involvement in the regulation of melatonin secretion. It has been shown that the synthesis of this hormone is dependent on the DHA status in tissues, and high concentrations of DHA are observed in the pineal gland (Catalá, 2010). Animal model studies indicate that omega-3 fatty acid deficiency leads to changes in the phospholipid composition of cell membranes, including the replacement of DHA with omega-6 acids, which is associated with a decrease in nocturnal melatonin secretion. (Checa-Ros et al., 2022)

Moreover, omega-3 fatty acids, especially DHA, may function as synchronizers of the circadian rhythm by influencing the molecular mechanisms of the biological clock. (Checa-Ros et al., 2022) The relationship between sleep and lipid metabolism is bidirectional—sleep disturbances lead to changes in lipid metabolism, further emphasizing the importance of an adequate supply of fatty acids. (Depner et al., 2020)

Omega-3 fatty acids and mental health

It is believed that omega-3 fatty acids may exhibit anxiolytic effects. Studies have shown a correlation between increased omega-3 supplementation and a reduction in anxiety levels, primarily concerning ALA and EPA. (Aucoin et al., 2021) In 22 experimental human trials evaluating the impact of omega-3 fatty acid supplementation on the severity of anxiety symptoms, improvement was observed in eleven, while the remainder yielded inconclusive results. Two out of three conducted meta-analyses also indicated a beneficial effect of omega-3 supplementation on anxiety reduction. (Smith et al., 2019; Deane et al., 2021; Su et al., 2018) Most studies involved individuals with various mental disorders, such as eating disorders, addictions, or ADHD; however, only one study included individuals specifically with anxiety disorders. (Yehuda et al., 2005) In that study, 126 individuals struggling with exam anxiety received polyunsaturated fatty acids (omega-3 and omega-6), which was associated with a reduction in symptom severity after three weeks. The results suggest that omega-3 supplementation may have a beneficial effect on reducing anxiety symptoms, yet the available

data are not entirely conclusive. Further research, particularly involving individuals with diagnosed anxiety disorders, is necessary to confirm the effectiveness of these methods. According to clinical guidelines for the treatment of psychiatric disorders using nutraceuticals and phytochemicals (Sarris et al., 2022): "Omega-3 fatty acids at doses standardised to 1 g to 2 g of eicosapentaenoic acid (EPA) are Recommended for Adjunctive use in MDD; and Not Currently Recommended for Monotherapy use [although it may be still effective as a monotherapy in people with raised inflammation and/or obesity]". (Sarris et al., 2022) These recommendations demonstrate that, despite growing interest in nutraceuticals, their role in treating depression remains adjunctive rather than primary. In practice, this implies a degree of caution-omega-3s are promising, but the evidence is not strong enough for them to replace standard pharmacotherapy. At the same time, the indication of greater efficacy in specific patient groups suggests that the future of their application may lie in a more personalized approach to treatment. In a study involving adolescents with depression, in which EPA and DHA were used as adjunctive therapy to paroxetine treatment, significant modifications in the lipid profile were demonstrated, particularly regarding phospholipid metabolism. (Wang et al., 2025) An increase in EPA and DHA content in cell membranes and a decrease in the $\omega 6/\omega 3$ ratio were observed, indicating a remodeling of the membrane lipid composition. (Wang et al., 2025) Simultaneously, a decrease in lipid peroxidation markers and an increase in antioxidant activity were noted, signifying a reduction in oxidative stress and improved cell membrane stability. (Wang et al., 2025) These changes co-occurred with a reduction in depressive symptoms and improved cognitive functions, with these correlations being more pronounced for EPA than for DHA. (Wang et al., 2025) In subgroup analyses, greater improvement was observed in patients with higher baseline levels of oxidative stress. Additionally, supplementation was associated with an increase in plasma serotonin levels. (Wang et al., 2025) The influence of omega-3 fatty acids was also observed at the level of brain functioning. A study conducted in older adults with late-life depression showed changes in brain activity assessed by resting-state functional magnetic resonance imaging (rs-fMRI). (Lin et al., 2024) Omega-3 supplementation was associated with a decrease in signal entropy in selected areas, including the posterior cingulate gyrus, inferior frontal gyrus, occipital cortex, and the Rolandic operculum. (Lin et al., 2024) Changes in the posterior cingulate gyrus co-occurred with improved language functions and a reduction in interleukin-6 (IL-6) levels. (Lin et al., 2024) A trend toward improved information processing speed was also observed, despite the absence of significant changes in global cognitive functions. (Lin et al., 2024) Modifications in activity within the brain's default mode network (DMN) included structures involved in the integration of cognitive and emotional processes. (Lin et al., 2024) However, it should be noted that the effectiveness of omega-3 fatty acids may depend on the patient's baseline mental health status. A multi-year study conducted on a group of individuals over 50 years of age, who initially did not show clinically significant symptoms of depression, yielded inconclusive results. During a follow-up lasting an average of 5.3 years, no differences in mood scores were recorded between the supplement group and the placebo group. Furthermore, a small but statistically significant increase in the risk of developing depressive symptoms was observed in the omega-3 supplement group. The study authors state that the data: "do not support the use of omega-3 supplements in adults to prevent depression". (Okereke et al., 2021) This suggests that while omega-3s may be effective support in treating existing disorders, they are not justified as a prophylactic measure to prevent depression in healthy individuals. The above data point to a key distinction between the therapeutic and prophylactic actions of omega-3 fatty acids. While they show potential in alleviating existing anxiety and depressive states through the modulation of neuroinflammation and stabilization of cell membranes, their role in healthy individuals appears negligible. These results suggest that omega-3 fatty acids act more as a "corrector" of pathological changes in the body (e.g., oxidative stress or inflammatory states) rather than a universal mood enhancer. Consequently, their supplementation should be preceded by a clinical diagnosis or an assessment of inflammatory marker levels.

Discussion

The presented data indicate that omega-3 fatty acids play a supportive role in body functioning, encompassing neurobiological processes, the promotion of sleep regulation, and mental health. Their action appears to stem from, among other things, their influence on cell membrane structure, modulation of neurotransmission, and anti-inflammatory properties. (Ayee et al., 2020; Deacon et al., 2017) These mechanisms may constitute a common basis for the observed correlations between omega-3 supply and the functioning of the central nervous system.

In the context of brain function, particular importance is attributed to DHA, which influences the fluidity of neuronal membranes and the activity of the serotonergic and dopaminergic systems. (Schuchardt et al., 2013;

Guixà et al., 2016; Deacon et al., 2017) Simultaneously, it is pointed out that its transport to the brain is a selective process dependent on specific transport forms, such as LysoPC-DHA.(Hachem et al., 2024; Hachem et al., 2016) This highlights the significance of omega-3 acid supply and the mechanisms determining their bioavailability in nervous tissue.

The collected results also indicate complex relationships between sleep and mental health. Insomnia may act as a risk factor and also represent one of the symptoms of depressive and anxiety disorders.(Baglioni et al., 2011; Hertenstein et al., 2023; Baglioni et al., 2016) In this context, omega-3 fatty acids may serve as a modulating factor that directly influences the regulation of emotions and the sleep rhythm.

Analysis of studies regarding sleep quality points to inconclusive results. Some research suggests a beneficial effect of supplementation, especially DHA, on sleep parameters such as sleep onset latency and sleep efficiency.(Patan et al., 2021) However, the findings are inconsistent, and the effects depend on the characteristics of the study population and the type of intervention applied.(Liu et al., 2024; Yokoi-Shimizu et al., 2022; Iqbal et al., 2023; Savard et al., 2023; Wang et al., 2024) The lack of definitive data regarding the optimal dose and the EPA-to-DHA ratio further complicates the interpretation of results.(Patan et al., 2021; Yokoi-Shimizu et al., 2022) Mechanisms potentially underlying these relationships include the regulation of melatonin secretion and influence on the circadian rhythm (Catalá, 2010; Checa-Ros et al., 2022), though their significance requires further clarification.

A similar inconsistency is observed regarding mental health. Some studies indicate a beneficial effect of omega-3 supplementation on reducing anxiety symptoms (Aucoin et al., 2021; Smith et al., 2019; Deane et al., 2021; Su et al., 2018); however, results are not unequivocal, and the number of studies involving individuals with diagnosed anxiety disorders is limited.(Yehuda et al., 2005) In the case of depression, data suggest that omega-3s may be effective as an adjunctive therapy, particularly in specific patient groups.(Sarris et al., 2022; Wang et al., 2025) Simultaneously, there is a lack of evidence confirming their efficacy in preventing depression in healthy individuals.(Okereke et al., 2021)

A significant aspect is also the dependence of supplementation effects on the baseline state of the organism. More favorable results were observed in individuals with elevated levels of oxidative stress.(Wang et al., 2025) This points to the need for a more personalized approach to supplementation, taking into account individual patient characteristics and their health status.

Limitations of the presented data include the heterogeneity of the study populations, differences in study designs, and the interventions used, which makes direct comparison of results difficult. Additionally, many studies do not allow for a definitive determination of cause-and-effect relationships, and available results are often ambiguous in nature.

Conclusions

Omega-3 fatty acids demonstrate significant potential in modulating brain function, sleep quality, and mental health; however, their effects are complex and dependent on numerous factors. The most consistent data indicate their supportive role in the treatment of mental disorders, especially depression, while their efficacy in prevention and their impact on sleep remain inconclusive.(Patan et al., 2021; Sarris et al., 2022; Okereke et al., 2021)

Available results suggest that the benefits of supplementation are more prominent in individuals with existing disorders or metabolic abnormalities, pointing to their potential application in an approach targeted at specific patient groups.(Wang et al., 2025) Simultaneously, the lack of definitive recommendations regarding the dosage and composition of supplementation highlights the need for further research in this area.(Patan et al., 2021; Yokoi-Shimizu et al., 2022)

In light of current data, omega-3 fatty acids should not be treated as a standalone treatment method or a universal prophylactic measure, but rather as a supportive element whose application should be tailored to the individual clinical context.

Conflict of Interest: The author declares no conflict of interest.

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