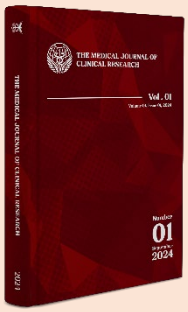
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Association of Use of Omega-3 Polyunsaturated Fatty Acids With Changes in Severity of Anxiety Symptoms

[1] Bayu, [1] Rahayu

[1] Faculty of Medicine, Sebelas Maret University, Surakarta City, Central Java, Indonesia

Correspondence : dr.bayu281739@gmail.com

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ABSTRACT

Background: The exploration of omega-3 polyunsaturated fatty acids (PUFAs) and their potential association with anxiety symptoms has garnered increasing attention in the scientific community, as reflected in the literature spanning from 2007 to 2021. **Literature Review:** The review by (Bozzatello et al., 2019) provided a deeper understanding of the biochemical pathways involved in the anxiolytic effects of omega-3s, particularly focusing on interleukin-6, BDNF, and cortisol modulation. Their findings indicated a modest anxiolytic effect, particularly in neuropsychiatric disorders, while also acknowledging the need for more rigorous research specifically targeting anxiety disorders. (Fatemi et al., 2020) examined the dietary quality of fats and their relationship with anxiety, suggesting that a lower intake of omega-3s correlates with increased anxiety symptoms. This observation aligns with the findings of (Aucoin et al., 2021), who emphasized the role of inflammation and dietary composition in anxiety management. Their review underscored the protective benefits of omega-3-rich diets compared to other dietary fats, reinforcing the importance of nutritional strategies in addressing anxiety symptoms. **Conclusion:** In conclusion, the collective body of literature indicates that omega-3 PUFAs may have a beneficial role in managing anxiety symptoms, primarily through their anti-inflammatory effects and influence on neurotransmitter function. However, the limitations of current research, including small sample sizes and methodological inconsistencies, highlight the necessity for more rigorous and targeted studies. Future research should focus on well-defined clinical populations to better understand the efficacy and mechanisms of omega-3 supplementation in anxiety disorders.

Keyword: Omega-3 Polyunsaturated Fatty Acids, Severity of Anxiety Symptoms

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INTRODUCTION

The exploration of omega-3 polyunsaturated fatty acids (PUFAs) and their potential association with anxiety symptoms has garnered increasing attention in the scientific community, as reflected in the literature spanning from 2007 to 2021. The foundational work by (M Ross et al., 2007) highlights the nascent stage of research in this area, noting that only two placebo-controlled trials had been conducted on the efficacy of omega-3 PUFAs in anxiety disorders at that time. Their findings suggested that while omega-3 supplementation showed some promise, particularly in patients with substance use disorders, the limitations of small sample sizes and short durations necessitated further investigation into well-defined anxiety populations.

Building upon this foundation, (Santos et al., 2018) provided a comprehensive review of the anxiolytic properties of omega-3 fatty acids, emphasizing their role in counteracting oxidative stress and neuroinflammation. The authors articulated that omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are crucial for neuronal health and can modulate inflammatory responses that influence anxiety. This perspective paved the way for understanding the biochemical mechanisms through which omega-3s might exert their effects on anxiety symptoms.

In 2019, (R. Polokowski, 2019) expanded on these insights by systematically reviewing the mechanisms linking omega-3 fatty acids to anxiety disorders, suggesting that these fatty acids play a critical role in regulating behavior and gut microbiota, which are increasingly recognized as influential in mental health. This review highlighted the inverse relationship between adipose DHA levels and depression, further reinforcing the potential of omega-3s in addressing anxiety-related symptoms.

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(Nasir & H. Bloch, 2019) contributed to the discourse by presenting evidence of lower levels of EPA and DHA in individuals with social anxiety, suggesting that deficiencies in these fatty acids could be linked to heightened anxiety symptoms. They noted that while some randomized controlled trials indicated a reduction in anxiety symptoms with omega-3 supplementation, the overall literature remains cautious, advocating for a critical examination of the existing studies due to methodological limitations.

Further exploring the therapeutic potential of omega-3 PUFAs, (Bozzatello et al., 2019) elucidated the mechanisms by which these fatty acids influence anxiety, including their effects on interleukin-6, brain-derived neurotrophic factor (BDNF), and cortisol modulation. Their findings underscored a modest anxiolytic effect of omega-3s in various neuropsychiatric disorders, although they also acknowledged the scarcity of robust randomized controlled trials specifically targeting anxiety disorders.

(Fatemi et al., 2020) examined the relationship between dietary fat quality and anxiety, highlighting the importance of omega-3 fatty acids in maintaining membrane fluidity and neurotransmitter function. Their work indicated that lower levels of omega-3s and higher ratios of omega-6 fatty acids were associated with increased anxiety symptoms, providing further evidence for the dietary influence on mental health.

Finally, (Aucoin et al., 2021) synthesized the existing evidence on diet and anxiety, concluding that omega-3 fatty acids may possess anti-anxiety effects through their impact on inflammation and neuroplasticity. They emphasized the need for more nuanced investigations into dietary fats, particularly as high-fat diets have shown varying effects on anxiety symptoms, depending on the composition of fatty acids.

Collectively, these articles illustrate a complex interplay between omega-3 fatty acids and anxiety symptoms, highlighting both the potential benefits and the limitations of current research. As the field progresses, there is a clear call for more

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rigorous studies to elucidate the efficacy and mechanisms of omega-3 supplementation in anxiety disorders.

LITERATURE REVIEW

The article "Omega-3 fatty acids as treatments for mental illness: which disorder and which fatty acid?" by Ross, Seguin, and Sieswerda (M Ross et al., 2007) presents a critical examination of the role of omega-3 polyunsaturated fatty acids (PUFAs) in the treatment of anxiety disorders. The authors highlight that research in this area is still in its early stages, indicating a significant gap in the literature regarding the efficacy of omega-3 PUFAs specifically for anxiety symptoms.

The article notes that anxiety disorders encompass a range of conditions characterized by excessive fears and phobias, yet only two placebo-controlled trials have been conducted to date. The first trial, which involved a small cohort of 11 patients with obsessive-compulsive disorder (OCD), administered ethyl EPA at a dosage of 2 g/day. The results did not demonstrate a significant difference from the placebo, leading the authors to conclude that omega-3 fatty acids were not effective in this context. However, the authors critique the trial's limitations, particularly regarding its small sample size and the relatively brief duration of treatment, which may undermine the validity of the findings.

Conversely, the second trial referenced in the article yielded more promising results. Participants, consisting of 24 men undergoing treatment for substance use, were given a higher dose of 5 g DHA/day. This trial reported a significant improvement in tension and anxiety levels compared to the placebo group. However, the authors point out limitations in this study as well, including the lack of a clinically defined anxiety disorder among participants and reliance on self-rating scales, which may introduce bias.

The authors effectively argue that the current evidence is insufficient to draw definitive conclusions regarding the efficacy of omega-3 PUFAs in treating anxiety disorders. They advocate for further research involving larger sample sizes

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and more rigorously defined clinical populations to better assess the potential benefits of omega-3 supplementation in anxiety management. This call for additional studies underscores the necessity of exploring the therapeutic role of omega-3 fatty acids in a more systematic and comprehensive manner, particularly in well-defined anxiety disorder populations.

The article "Anxiolytic properties of compounds that counteract oxidative stress, neuroinflammation, and glutamatergic dysfunction: a review" by Patrícia Santos et al. (Santos et al., 2018) provides a comprehensive examination of the role of omega-3 polyunsaturated fatty acids (PUFAs) in modulating anxiety symptoms through their biochemical properties. The authors highlight the significance of omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), as critical components of neuronal cell membranes, influencing both structural and functional aspects of neuronal health.

A central theme of the article is the contrasting effects of omega-3 and omega-6 fatty acids on inflammation. The authors elucidate that omega-6 fatty acids are pro-inflammatory, while omega-3 fatty acids exert anti-inflammatory effects. This distinction is particularly relevant in the context of anxiety, as neuroinflammation has been implicated in the pathophysiology of anxiety disorders. By reducing neuroinflammation, omega-3 fatty acids may help alleviate anxiety symptoms, a proposition supported by various studies cited throughout the review.

Moreover, the article discusses the potential mechanisms through which omega-3 fatty acids may exert their anxiolytic effects. One significant mechanism proposed is the reduction of corticosteroid release from the adrenal gland, which is associated with decreased cortisol levels. Elevated cortisol has been linked to anxiety and mood disorders, suggesting that omega-3 supplementation could mitigate these effects and improve overall mood and anxiety levels.

However, the authors also point out a notable gap in the existing literature: most studies have primarily focused on anxiety symptoms across various conditions

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rather than specifically addressing anxiety disorders. This limitation suggests a need for more targeted research to better understand the efficacy of omega-3 fatty acids in clinical populations diagnosed with anxiety disorders.

The article "Diet, Inflammation, Gut Microbiome, and Mental Health" by Ashley R. Polokowski (R. Polokowski, 2019) provides a comprehensive examination of the relationship between omega-3 polyunsaturated fatty acids (PUFAs) and anxiety symptoms, exploring various physiological and clinical mechanisms. The systematic review presented in the article highlights several key insights into how omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), may influence anxiety through their effects on inflammation and gut microbiota.

Polokowski elucidates the role of omega-3 fatty acids in modulating inflammatory pathways, notably through the inhibition of cyclooxygenase-2 (COX-2) and the metabolism of arachidonic acid. This is significant as inflammation has been increasingly implicated in the pathophysiology of anxiety disorders. The article effectively discusses how the anti-inflammatory properties of omega-3s could contribute to a reduction in anxiety symptoms, thereby presenting a potential therapeutic avenue for individuals suffering from anxiety disorders.

Moreover, the review delves into the impact of omega-3 PUFAs on gut microbiota, which has garnered attention for its connection to mental health. Polokowski highlights evidence suggesting that omega-3 PUFAs can reverse the adverse effects of early-life stress on gut microbiota composition. This finding is particularly relevant, as it indicates that dietary interventions involving omega-3 fatty acids may not only alleviate anxiety symptoms directly but also promote a healthier gut microbiome, which in turn could further support mental well-being.

The article also references epidemiological studies, such as the Hordaland Health Study, which link cod liver oil consumption to reduced symptoms of depression. This association underscores the potential of omega-3 supplementation as a preventative or adjunctive treatment for anxiety and depression, although the

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article calls for further research to establish causality and the underlying mechanisms at play.

The article titled "Trim the fat: the role of omega-3 fatty acids in psychopharmacology" by Madeeha Nasir and Michael H. Bloch (Nasir & H. Bloch, 2019) provides a comprehensive examination of the relationship between omega-3 fatty acids and anxiety symptoms, particularly highlighting the biochemical differences in patients with social anxiety compared to healthy controls. The authors present compelling evidence that lower levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are found in the red blood cell (RBC) membranes of individuals suffering from social anxiety, suggesting a potential link between omega-3 fatty acid deficiency and anxiety disorders.

The article critically evaluates the existing literature on omega-3 supplementation and its effects on anxiety. Nasir and Bloch point out that many trials focusing on mood disorders have overlooked anxiety symptoms or excluded anxious patients altogether, despite the recognized comorbidity between anxiety and mood disorders. This gap in research is significant, as it limits the understanding of how omega-3 fatty acids may impact anxiety specifically, rather than mood disorders in isolation.

The authors reference randomized controlled trials (RCTs) that indicate omega-3 supplementation may lead to reductions in anxiety symptoms among various populations, including substance abusers and individuals undergoing acute stress, such as medical students preparing for exams. However, they also emphasize the need for caution in interpreting these findings, as the sole meta-analysis on the topic included non-placebo-controlled trials and did not adequately address publication bias. This raises questions about the robustness of the evidence supporting omega-3 supplementation as a treatment for anxiety.

Furthermore, the authors advocate for a more critical approach to the current literature, suggesting that the positive outcomes reported in some studies may not be as definitive as they appear. They call for more rigorous research designs that

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specifically investigate the effects of omega-3 fatty acids on anxiety symptoms, rather than relying on studies primarily focused on mood disorders.

The article titled "Polyunsaturated Fatty Acids: What is Their Role in Treatment of Psychiatric Disorders?" authored by Bozzatello, Rocca, Mantelli, and Bellino (Bozzatello et al., 2019) provides a comprehensive overview of the mechanisms through which omega-3 polyunsaturated fatty acids (PUFAs) may influence anxiety symptoms. The authors delve into the biochemical pathways involved, notably highlighting the roles of interleukin-6, brain-derived neurotrophic factor (BDNF), and cortisol modulation. These factors are critical in understanding how omega-3 fatty acids can exert their anxiolytic effects, particularly in individuals with various neuropsychiatric disorders or significant physical illnesses.

The review presents a meta-analysis indicating a modest anxiolytic effect of omega-3 fatty acids, which is particularly relevant given the growing interest in non-pharmacological treatments for anxiety. The authors underscore the importance of recognizing the relationship between omega-3 fatty acids and anxiety, especially in the context of post-traumatic stress disorder (PTSD). They note that PTSD is often accompanied by persistent oxidative stress and alterations in neural integrity, with specific reductions in omega-3 fatty acids, particularly docosahexaenoic acid (DHA), being observed in affected individuals.

A critical evaluation of the findings reveals that while the evidence suggests potential benefits of omega-3 fatty acids in alleviating anxiety symptoms, particularly in PTSD, the authors also acknowledge the limitations of current research. The scarcity of randomized controlled trials (RCTs) specifically examining the effects of DHA and eicosapentaenoic acid (EPA) in PTSD treatment is noteworthy. The article mentions that only three studies have been conducted, with mixed results regarding DHA's efficacy. For instance, one trial indicated that DHA supplementation did not outperform placebo in preventing PTSD symptoms, although subsequent analyses suggested a correlation between improved symptoms and increased blood levels of EPA.

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The article by Fatemi, Siassi, Qorbani, and Sotoudeh (Fatemi et al., 2020) explores the relationship between dietary fat quality and anxiety levels, particularly focusing on omega-3 polyunsaturated fatty acids (n-3 PUFAs). The authors present a compelling case that highlights the biochemical role of these fatty acids in maintaining membrane fluidity, which is crucial for proper synaptic transmission and the functioning of neurotransmitters such as serotonin and dopamine. This connection is particularly relevant given the established link between neurotransmitter dysregulation and anxiety disorders.

The authors note that a deficiency in n-3 PUFAs can lead to behaviors associated with depression and anxiety. Their findings align with a meta-analysis indicating that individuals with social anxiety disorders often exhibit lower blood levels of n-3 PUFAs, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), while presenting higher levels of n-6 PUFAs, such as arachidonic acid (ARA). This imbalance, characterized by a lower n-3:n-6 PUFAs ratio and a higher ratio of saturated fatty acids (SFAs) to monounsaturated fatty acids (MUFAs), is posited to adversely affect membrane fluidity and, consequently, brain function.

The article critically evaluates existing literature on the association between dietary fat quality and anxiety, acknowledging the limitations inherent in cross-sectional studies. While the authors report an inverse relationship between n-3 PUFA intake and anxiety symptoms, they also highlight the contradictory findings from prospective studies, such as one involving university graduates, which found no significant association. This inconsistency emphasizes the need for further research to clarify the role of dietary fats in anxiety disorders.

Moreover, the article discusses experimental studies that have yielded mixed results regarding the effects of n-3 PUFAs on anxiety. For instance, while some studies indicate that a daily consumption of 3 g of EPA and DHA can reduce anxiety symptoms in patients with obsessive-compulsive disorder, the overall evidence remains inconclusive. This variability suggests that individual differences,

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such as genetic predispositions or the presence of comorbid conditions, may influence the efficacy of n-3 PUFA supplementation in alleviating anxiety.

The article "Diet and Anxiety: A Scoping Review" by Aucoin et al. (Aucoin et al., 2021) provides a comprehensive exploration of the relationship between dietary fat intake, particularly omega-3 polyunsaturated fatty acids (PUFAs), and anxiety symptoms. The authors present a significant body of evidence suggesting that adequate or supplemental omega-3 fatty acids may exert anti-anxiety effects, highlighting the potential for dietary interventions in managing anxiety disorders.

One of the critical insights from the review is the role of inflammation in the pathogenesis of psychiatric disorders, including anxiety. The authors argue that omega-3 fatty acids contribute to reduced inflammation, which is a known factor in the development and exacerbation of anxiety symptoms. This connection is particularly pertinent given the increasing recognition of the gut-brain axis and the impact of diet on mental health. The review emphasizes that omega-3 fatty acids can influence not only inflammation but also oxidative stress, neurotransmission, and neuroplasticity—mechanisms that are crucial for understanding their therapeutic potential in anxiety management.

The article also contrasts the effects of different types of dietary fats on anxiety symptoms. It notes that diets high in total fat, cholesterol, or trans fats may have an anxiogenic effect, while omega-3-rich diets, derived from sources such as fish, seafood, flax seeds, chia, and hemp seeds, may provide protective benefits against anxiety. This distinction underscores the importance of dietary composition and quality when considering nutritional strategies for anxiety management.

Moreover, the authors reference a substantial number of animal studies that indicate a worsening of anxiety symptoms associated with high-fat diets, suggesting that not only the quantity but also the type of dietary fat consumed can significantly influence anxiety levels. Interestingly, the review mentions studies on ketogenic diets that propose potential therapeutic benefits, indicating a complex relationship between dietary fat types and mental health outcomes

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CONCLUSION

The literature review on omega-3 polyunsaturated fatty acids (PUFAs) and their association with anxiety symptoms reveals a multifaceted relationship that is still being explored. The early work by (M Ross et al., 2007) laid the groundwork, indicating that while there were initial findings suggesting potential benefits of omega-3 supplementation, the evidence was limited due to small sample sizes and short trial durations. This concern was echoed in subsequent reviews, such as that by (Santos et al., 2018), which highlighted the biochemical mechanisms through which omega-3s, particularly EPA and DHA, could influence anxiety, especially through their anti-inflammatory properties.

(R. Polokowski, 2019) expanded on these insights by systematically reviewing the physiological mechanisms linking omega-3s to anxiety, emphasizing their role in modulating inflammation and gut microbiota. This connection is significant as it suggests that omega-3 fatty acids may not only directly alleviate anxiety symptoms but also promote overall mental well-being through gut health. (Nasir & H. Bloch, 2019) further explored this relationship, presenting evidence of lower omega-3 levels in individuals with social anxiety, reinforcing the idea that deficiencies in these fatty acids could be linked to increased anxiety symptoms.

The review by (Bozzatello et al., 2019) provided a deeper understanding of the biochemical pathways involved in the anxiolytic effects of omega-3s, particularly focusing on interleukin-6, BDNF, and cortisol modulation. Their findings indicated a modest anxiolytic effect, particularly in neuropsychiatric disorders, while also acknowledging the need for more rigorous research specifically targeting anxiety disorders.

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benefits of omega-3-rich diets compared to other dietary fats, reinforcing the importance of nutritional strategies in addressing anxiety symptoms.

In conclusion, the collective body of literature indicates that omega-3 PUFAs may have a beneficial role in managing anxiety symptoms, primarily through their anti-inflammatory effects and influence on neurotransmitter function. However, the limitations of current research, including small sample sizes and methodological inconsistencies, highlight the necessity for more rigorous and targeted studies. Future research should focus on well-defined clinical populations to better understand the efficacy and mechanisms of omega-3 supplementation in anxiety disorders.

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