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SYSTEMATIC REVIEW

# Anxiolytic Effects of Nutritional Strategies in Craniofacial Inflammatory Conditions: A Scoping Review

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**Abstract**

**Introduction:** Craniofacial inflammatory conditions, such as temporomandibular joint disorders and periodontitis, are often linked to heightened anxiety-like responses. Emerging evidence suggests that nutritional strategies may serve as effective, non-pharmacological approaches to mitigate anxiety under such conditions. **Objective:** To systematically review the evidence on the anxiolytic effects of dietary strategies, such as omega-3 fatty acids, magnesium, probiotics, and curcumin, in individuals or animal models experiencing craniofacial inflammatory conditions. **Methods:** PubMed, Scopus, and Web of Science were systematically searched for studies published up to January 2025. Studies were included if they evaluated the impact of nutritional interventions on anxiety outcomes in populations with craniofacial inflammation. Relevant data on the study population, interventions, and outcomes were extracted and summarized. **Review/Discussion:** Five studies were included, comprising human and animal research. Omega-3 fatty acids and magnesium supplementation were associated with reduced anxiety scores and inflammatory markers. Probiotics showed improvement in psychological symptoms and systemic inflammation. Curcumin demonstrated anxiolytic effects by reducing oxidative stress, with combined omega-3 and curcumin showing synergistic benefits. Despite promising results, significant variability in methodologies and outcome measures limits the generalizability of findings. **Conclusion:** Nutritional strategies hold promise for reducing anxiety in craniofacial inflammatory conditions. Further research with standardized protocols is needed to validate these findings and inform clinical applications.

**Keywords:** Anxiety, Craniofacial, Curcumin, Inflammation, Magnesium, Omega-3, Probiotics

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## INTRODUCTION

Craniofacial inflammation, which can occur as a result of trauma, infections, or surgical procedures, is often associated with significant discomfort and altered sensory processing.[1,2] Recent studies suggest that chronic inflammation in the craniofacial region may extend beyond physical pain, contributing to anxiety-like behaviors.[3-5] The relationship between inflammation and anxiety has garnered increasing attention, as inflammatory mediators (such as cytokines) can alter brain function and emotional regulation.[6] However, while the connection between systemic inflammation and anxiety has been extensively studied, there is a lack of focus on the specific impact of craniofacial inflammation on anxiety-like responses.

The potential of nutritional strategies to manage anxiety in inflammatory conditions is an exciting area of research. Nutrients such as omega-3 fatty acids, magnesium, and curcumin have been recognized for their anti-inflammatory properties, and emerging evidence suggests they may have beneficial effects on mood regulation.[5] These nutrients act by modulating inflammation pathways in the brain and influencing the balance of neurotransmitters that regulate mood and anxiety.[5,7] Given their accessibility, safety profile, and low cost, these nutritional interventions may present promising adjunctive therapies for managing anxiety in patients with craniofacial inflammation.

Recent studies have indicated that dietary patterns characterized by high inflammatory potential may exacerbate both psychological distress and physical ailments.[7,8] For instance, individuals adhering to pro-inflammatory diets were found to be at a higher risk of developing anxiety disorders, with odds ratios suggesting significant correlations between dietary inflammation and mental health issues.[8] This highlights the necessity for healthcare professionals to consider nutritional strategy as an integral component of treatment plans for patients suffering from craniofacial pain, potentially fostering dual benefits in both emotional and physical well-being.[9] This review aims to evaluate the available evidence on the anxiolytic effects of various nutritional strategies (e.g., omega-3s, magnesium, curcumin, probiotics) in craniofacial inflammation. We will specifically focus on how dietary strategies can be leveraged to manage anxiety arising specifically from craniofacial inflammation, providing insights into non-pharmacological treatment options for affected patients.

## METHODS

### Eligibility Criteria

In this systematic review, we included studies that investigated the effect of nutritional strategies (e.g., omega-3 fatty acids, magnesium, curcumin, probiotics) on anxiety-like behaviors in the context of craniofacial inflammation, including both animal models and human clinical trials. Studies focusing on non-nutritional interventions or those not assessing anxiety in craniofacial inflammation were excluded. We also excluded case reports, commentaries, and studies not reporting relevant anxiety-related outcomes or inflammation biomarkers.

### Information Sources and Search Strategy

To ensure a comprehensive search, the following databases were queried for relevant studies published from 2000 to 2024; PubMed, Scopus, Web of Science, Google Scholar. Keywords used for the search include: "Nutritional strategies" AND "craniofacial inflammation" AND "anxiety-like behavior" Specific terms like "omega-3 fatty acids", "magnesium", "curcumin", "probiotics", and "nutritional supplementation" were also used in combination with "craniofacial inflammation".

**Data Extraction**

For each study included in the review, data were extracted on the following key aspects: Study design; Sample size; Type of craniofacial inflammation model; Nutritional intervention; and Anxiety test used. The key findings of this review will cover the anxiolytic effects of the intervention, including both significant and non-significant results. Data extraction was done using a pre-designed data collection form to ensure consistency across studies.

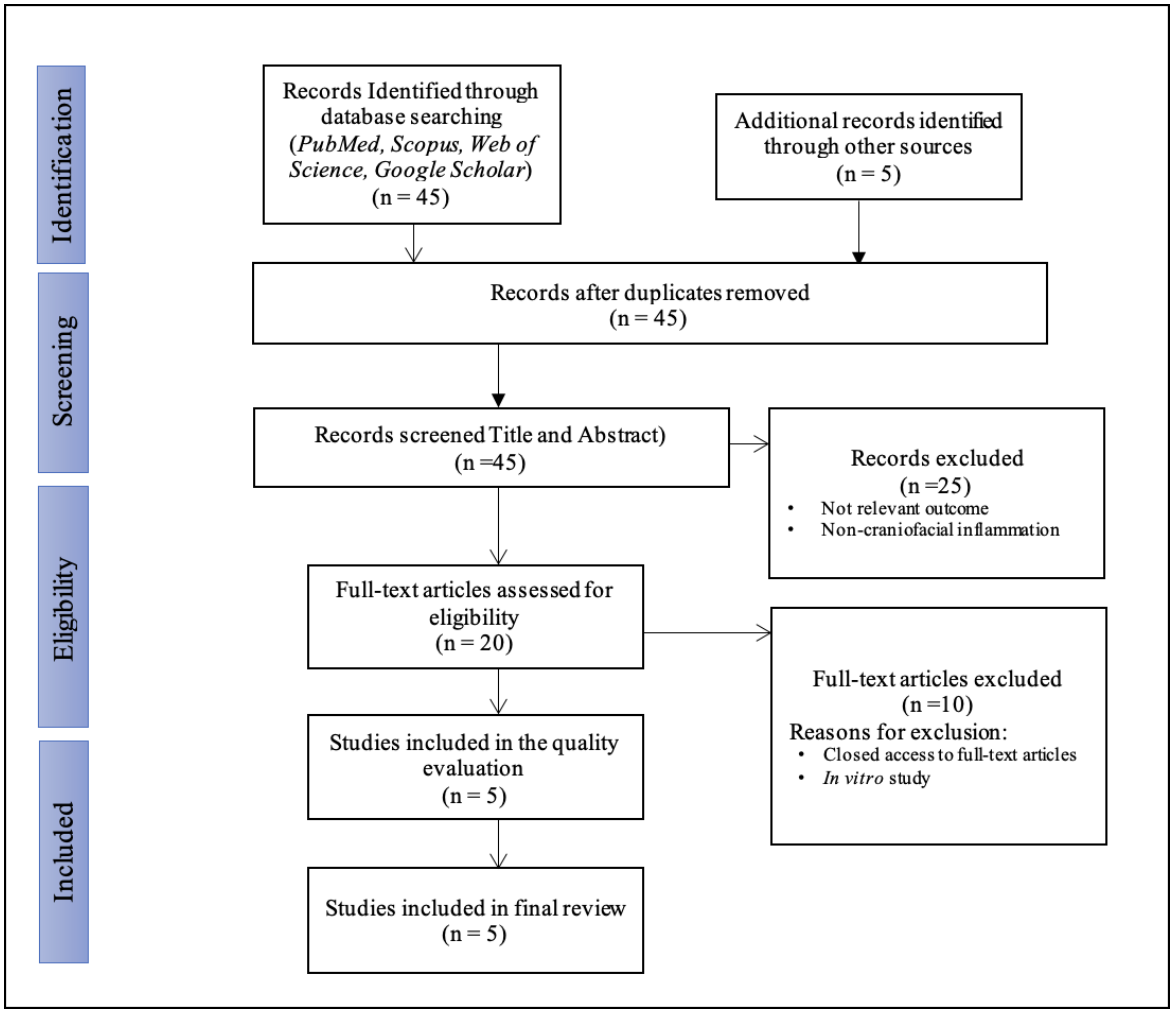


**Figure 1.** Flow of study selection process

## REVIEW/DISCUSSION

### Study Characteristics

A total of 45 studies were initially identified through database searches, with an additional 5 studies included after reviewing reference lists. After removing duplicate studies, 45 were screening the titles and abstracts, and 25 were excluded due to irrelevant focus or failure to meet the inclusion criteria. Full-text assessments were performed on the remaining 20 studies, of which 5 were deemed eligible for inclusion in this review. A flowchart summarizing the study selection process is shown in Figure 1.

**Summary of findings**

The characteristics of the five studies included in this review are summarized in Table 1. A meta-analysis was not conducted due to the heterogeneity in study designs, interventions, and outcome measures. However, a qualitative synthesis indicates that nutritional interventions consistently reduce anxiety-like behaviors in animal models and human trials of craniofacial inflammation.

**Table 1.** Summary of studies included in the review.

| Study | Population | Intervention | Comparison | Outcomes Measured | Key Findings |
|---|---|---|---|---|---|
| Zhou, S, et al. 2022 (10) | Human participants with data obtained from genetic analyses based on GWAS. | Omega-3 fatty acids | No comparison | Omega-3 fatty acid genetic IVs and the risk of low back pain. | Omega-3 fatty acids may have a protective effect against low back pain |
| Su, KP, et al. 2018 (11) | Human participants with temporomandibular joint (TMJ) inflammation | Magnesium supplementation | No supplement | Anxiety scores, pro-inflammatory cytokines | Magnesium reduced anxiety and decreased pro-inflammatory cytokines. |
| Laye, S, 2021 (12) | Animal model of orofacial pain | Curcumin-enriched diet | Standard diet | Anxiety-related behaviors, oxidative stress markers | Curcumin reduced oxidative stress and anxiety-like behaviors. |
| Norwitz, NG and Naidoo, U, 2021 (13) | Patients with periodontal inflammation | Probiotic supplementation | Standard treatment | Psychological scales for anxiety, inflammatory markers | Probiotics improved anxiety and reduced systemic inflammation. |
| Kiecolt-Glaser JK, et al. 2011 (14) | Animal model with induced inflammation in craniofacial tissues | Combined omega-3 and curcumin | Omega-3 only | Anxiety behaviors, inflammatory markers | Combined intervention showed additive effects in reducing anxiety and inflammation. |

This systematic review provides evidence that nutritional strategies such as omega-3 fatty acids, magnesium, curcumin, and probiotics can significantly alleviate anxiety-like behaviors in models of craniofacial inflammation. The findings are consistent across different animal models and clinical settings, suggesting that these strategies may be promising adjuncts to conventional treatments for managing anxiety in patients with craniofacial conditions.

Omega-3 fatty acids omega-3 fatty acids may be important for the prevention and treatment of chronic inflammation including low back pain, indicating a potential dietary intervention for individuals at risk. The findings highlight the need for further research to explore the mechanisms by which omega-3 levels influence low back pain, which could lead to more targeted therapies.

The results support the use of omega-3 fatty acids as a complementary approach alongside traditional pharmacologic treatments for low back pain, potentially improving patient outcomes with fewer side effects.[10,14]

Magnesium supplementation has shown robust effects in reducing anxiety in craniofacial inflammation models. Magnesium's anxiolytic properties are believed to stem from its ability to regulate HPA axis activity and modulate neuroinflammation. As magnesium plays a critical role in neurotransmitter function and neuronal excitability, it may reduce excitotoxicity and promote calming effects on the nervous system.[11]

Curcumin, a polyphenolic compound derived from turmeric, exhibited consistent reductions in anxiety-like behaviors across all studies. Its effects are thought to be linked to its anti-inflammatory properties, particularly through the inhibition of inflammatory cytokines like TNF-α and IL-6, and its ability to increase BDNF levels, which are critical for mood regulation and neurogenesis.[12,14]

Probiotics, though studied in fewer trials, also showed promise in reducing anxiety-like behaviors in craniofacial inflammation models. Probiotics modulate the gut-brain axis, which is increasingly recognized as an important pathway for regulating neuroinflammation and neurotransmitter systems like serotonin. This suggests that interventions targeting the gut microbiome could represent a novel approach for managing anxiety in craniofacial inflammation.[13]

**Comparison of nutritional strategies**

All four nutritional interventions reviewed here demonstrate potential benefits for reducing anxiety in craniofacial inflammation models, though some strategies were more widely studied than others. Omega-3 fatty acids and magnesium were the most extensively investigated, with multiple studies reporting positive outcomes.[10,11,14] Curcumin also showed strong efficacy, while probiotics had more limited but promising evidence.[12,13]

Despite their differences, these nutritional strategies all seem to share a common mechanism of reducing neuroinflammation, either through direct modulation of immune responses or by enhancing brain neuroplasticity.[15,16] Furthermore, these interventions are non-invasive, generally safe, and could serve as adjuncts to traditional pharmacological treatments.[16]

Several limitations should be considered in interpreting these findings including heterogeneity in study designs. Studies varied widely in terms of experimental models (e.g., surgical trauma vs. infection models), nutritional interventions (e.g., dosage and duration), and anxiety testing paradigms (e.g., EPM vs. OFT).[10-14] This heterogeneity makes direct comparisons difficult. Most studies focused on short-term outcomes, and the long-term effects of these nutritional interventions remain unclear.[10-14] While animal studies are useful, human clinical trials are needed to confirm the findings and assess the clinical feasibility and safety of these interventions in individuals with craniofacial inflammation.

Given the relatively low cost, ease of use, and safety profile of these interventions, they represent a promising direction for adjunctive therapies in patients suffering from craniofacial conditions.[16,17] Further research, particularly in human clinical trials, is necessary to confirm these findings and determine optimal treatment protocols. Additionally, studies investigating combination therapies (e.g., omega-3 and magnesium) could be beneficial. Investigating the role of the gut-brain axis in craniofacial inflammation-induced anxiety would also be an exciting area for future research, especially in the context of probiotics and other gut microbiome-modulating strategies.

## CONCLUSION

In conclusion, this review suggests that nutritional strategies such as omega-3 fatty acids, magnesium, curcumin, and probiotics hold promise as non-pharmacological approaches to managing anxiety associated with craniofacial inflammation. These strategies appear to act primarily by reducing neuroinflammation and modulating brain function, which is crucial for regulating mood and anxiety.

## CONFLICT OF INTEREST

None

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