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THE ROLE OF OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION IN MIGRAINE AND FIBROMYALGIA

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Annotation: Migraine and fibromyalgia are among the most common neurological disorders characterized by chronic pain syndromes in modern medicine. Recent scientific studies indicate that oxidative stress and mitochondrial dysfunction play a significant role in the pathogenesis of these conditions. This article analyzes the impact of oxidative stress in migraine and fibromyalgia, deficiencies in the antioxidant defense system, and the key mechanisms associated with mitochondrial dysfunction.

Keywords: Migraine, fibromyalgia, oxidative stress, mitochondrial dysfunction, antioxidant defense.

Introduction

Migraine and fibromyalgia are among the most prevalent neurological disorders characterized by chronic pain syndromes and complex pathophysiological mechanisms. These conditions are more commonly observed in women than in men. Both disorders frequently co-occur, leading to the exacerbation of symptoms and a significant reduction in quality of life [1,2]. Recent research has shown that oxidative stress and mitochondrial dysfunction play a central role in the chronic progression of these diseases [3,4]. This article explores the pathophysiological mechanisms and clinical significance of oxidative stress and mitochondrial dysfunction in migraine and fibromyalgia, as well as the therapeutic approaches relevant to clinical practice.

General Mechanism of Oxidative Stress

Oxidative stress is a condition in which the levels of reactive oxygen species (ROS) and reactive nitrogen species (RNS) exceed the neutralizing capacity of the body's antioxidant defense system. As a result, ROS can damage DNA, lipids, and proteins, and lead to the excessive production of inflammatory mediators [5].

Under normal physiological conditions, there is a dynamic balance between ROS (such as superoxide anion O_2^-, hydrogen peroxide H_2O_2, and hydroxyl radical OH^-) and antioxidants (such as superoxide dismutase [SOD], catalase [CAT], glutathione peroxidase [GPx], and glutathione [GSH]). However, factors such as stress, chronic inflammation, mitochondrial dysfunction, toxins, or genetic predisposition can lead to an excessive increase in ROS levels [11].

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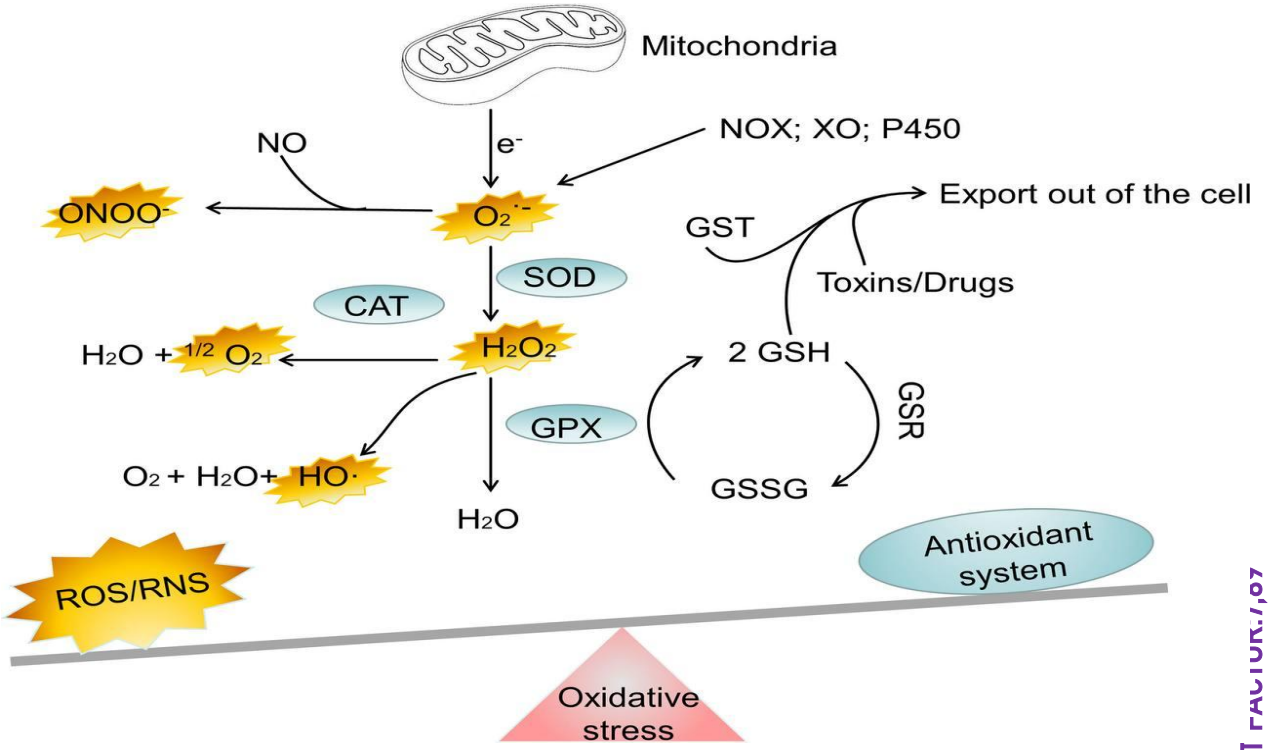

Figure 1. Mechanism of Free Radical Formation in Oxidative Stress

As a result of oxidative stress in the body, the following processes occur:

Lipid peroxidation – Damage to cell membranes, accompanied by an increase in malondialdehyde (MDA) levels.

Mitochondrial dysfunction – Disruption of energy production processes.

DNA damage – Activation of genes that promote inflammation.

Inflammation and apoptosis – Increased production of cytokines (such as IL-1 and TNF-α).

These processes enhance sensitivity within the nervous system, leading to central sensitization and the chronification of pain [6].

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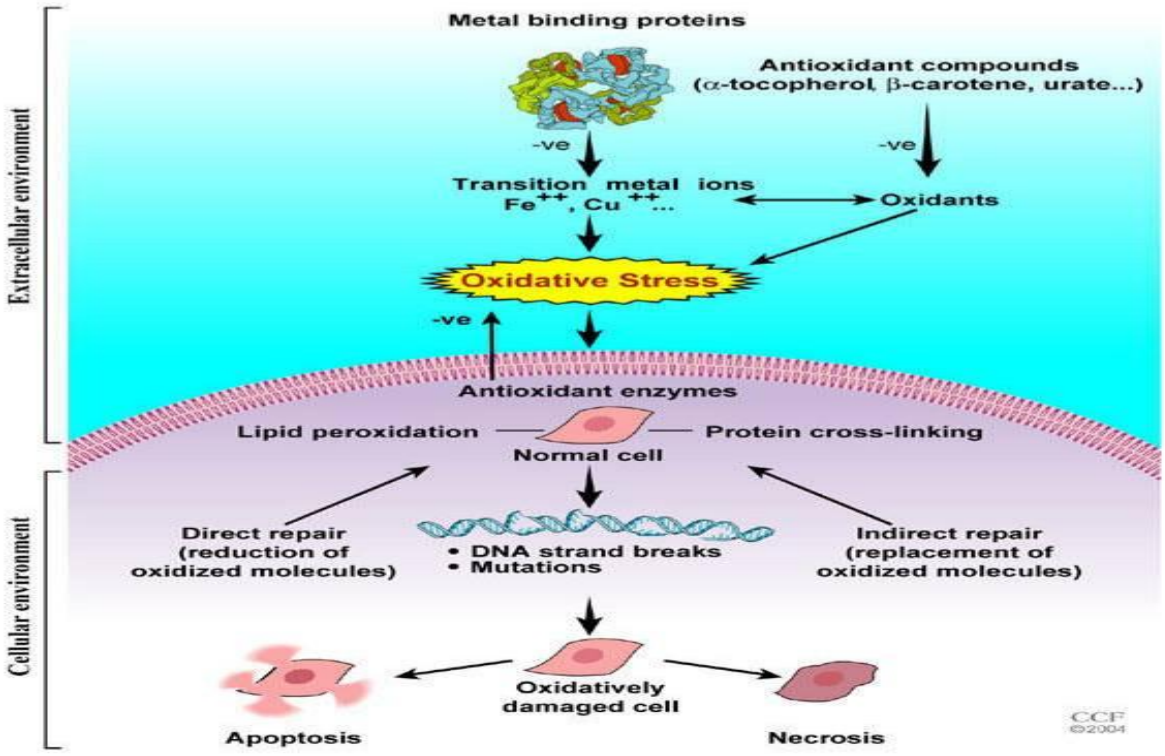

Figure 2. The Effect of Oxidative Stress on Cellular Processes

Oxidative Stress in the Context of Migraine

Oxidative stress and inflammation are among the key factors in the pathogenesis of migraine. During migraine attacks, neuropeptides released from the trigeminal nerve—especially calcitonin gene-related peptide (CGRP)—cause cerebral vasodilation and activate neurovascular inflammation. In patients with migraine, oxidative stress leads to the following changes:

- Elevated levels of MDA and 4-HNE (markers of lipid peroxidation)
- Decreased activity of antioxidant enzymes such as SOD, GSH, and CAT [9]
- Increased nitric oxide (NO) levels, contributing to cerebral vasodilation
- Reduced levels of Coenzyme Q10, resulting in impaired mitochondrial energy production

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In individuals with migraine, increased activity of inflammatory mediators such as CGRP, TNF-α, and IL-6 enhances ROS production, thereby intensifying the severity of migraine attacks [9,10].

A study conducted in 2024 reported a sustained elevation of oxidative stress biomarkers in patients with migraine [12].

Oxidative Stress and Mitochondrial Dysfunction in Fibromyalgia

In patients with both fibromyalgia and migraine, oxidative stress exacerbates clinical symptoms such as fatigue, sleep disturbances, and increased pain sensitivity [6]. In individuals with fibromyalgia, impaired mitochondrial function—specifically a reduction in ATP production—leads to increased ROS levels, thereby intensifying oxidative stress [7].

Recent studies have confirmed that patients with fibromyalgia exhibit mitochondrial dysfunction and reduced antioxidant levels. Coenzyme Q10 (CoQ10) supplementation has shown beneficial effects in alleviating symptoms [8]. Research conducted on fibromyalgia patients has demonstrated elevated levels of oxidative stress markers. For instance, a study by López and colleagues explored the relationship between oxidative stress and quality of life in fibromyalgia patients. They found that oxidative stress biomarkers were associated with cognitive dysfunction, insomnia, and fatigue [7].

Conclusion

In chronic neurological disorders such as migraine and fibromyalgia, oxidative stress and mitochondrial dysfunction are considered key pathogenic factors. The accumulation of reactive oxygen and nitrogen species, weakening of the antioxidant defense system, and disruption of cellular energy processes are directly associated with the worsening of clinical symptoms. According to the analysis of current scientific literature, elevated oxidative stress intensifies pain severity and contributes to psycho-emotional disturbances (particularly fatigue, cognitive decline, and sleep disorders), thus promoting the chronic course of the disease. Mitochondrial energy production deficits impair neuronal functional stability and facilitate the development of central sensitization.

Modern studies evaluating the clinical efficacy of antioxidant agents (such as coenzyme Q10, riboflavin, alpha-lipoic acid, and N-acetylcysteine) have demonstrated their positive role in symptom relief, restoration of cellular defense, and reduction of disease severity. Moreover, these compounds offer promising prospects for developing personalized treatment strategies for affected individuals.

Overall, in-depth investigation of the pathophysiological role of oxidative stress and mitochondrial dysfunction in migraine and fibromyalgia provides a strong scientific and practical foundation for the development of novel therapeutic approaches. In the future, patient profiling based on ROS/RNS biomarkers may usher in a new era in diagnosis and treatment.

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