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DISCOVERY SCIENTIFIC SOCIETY

The association between magnesium deficiency and the occurrence of anxiety disorders

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ABSTRACT

Magnesium (Mg) is a key mineral for mental health. Its deficiencies are common and may be linked to anxiety disorders. This paper reviews the evidence and mechanisms explaining this relationship. Neurobiologically, magnesium deficiency contributes to anxiety on several levels. It weakens the physiological blockade of NMDA receptors, which leads to neuronal hyperexcitability. It also disrupts the GABA system and causes hyperactivity of the HPA stress axis. Diagnosing the deficiency is complicated. Standard serum magnesium measurements are unreliable due to compensatory tissue release, but patients with anxiety often have lower ionized magnesium (iMg), correlating with symptom severity. Magnesium supplementation appears beneficial for anxiety, especially with well-absorbed organic forms.

Keywords: Magnesium, Anxiety, Magnesium Deficiency, Hypomagnesemia, Anxiety Disorders.

1. INTRODUCTION

Magnesium (Mg) is one of the key minerals necessary for the proper functioning of the human body. It takes part in hundreds of biochemical reactions that keep cells alive and active. The element is needed for energy production, protein synthesis, and the normal function of muscles and nerves. Because of these roles, magnesium is considered essential for maintaining both physical and mental balance. Magnesium helps regulate calcium movement across cell membranes and supports cell stability. In the nervous system, it takes part in maintaining normal communication between neurons and protects the brain from excessive stimulation (Boyle et al., 2017).

Magnesium has a calming effect on the nervous system. It blocks NMDA receptors, which prevents overexcitation of nerve cells, and helps maintain a balance between glutamate and GABA, the brain's main excitatory and inhibitory neurotransmitters. Emotional stability and the ability to withstand stress are both highly dependent on this balance. Magnesium also affects the stress response by influencing the hypothalamic–pituitary–adrenal axis and regulating the release of cortisol and ACTH (Boyle, 2017; Pickering et al., 2020).

A lack of magnesium is common in modern societies. Many people eat less magnesium than recommended, especially in Western countries. Studies show that

about two-thirds of adults in the United States and over 70% of middle-aged adults in France have an insufficient intake. Low magnesium levels are linked with a higher risk of hypertension, heart disease, and type 2 diabetes (Boyle et al., 2017).

Older adults are particularly at risk. Research from a hospital in Warsaw (2018–2020) found that 1 in 3 patients aged 65 or older had abnormal magnesium levels, and the risk increased with age (Malinowska et al., 2021). These results show that magnesium imbalance is common and clinically important in elderly people.

Even a mild deficiency can cause subtle symptoms such as irritability, anxiety, tiredness, and sleep problems. Because these signs are often vague, magnesium deficiency can remain undetected for a long time. Over time, low magnesium may gradually harm both physical and mental health. Anxiety disorders are among the most frequent mental health conditions worldwide, with complex causes involving both biological and environmental factors. Biologically, anxiety is associated with imbalances in neurotransmitters—particularly glutamate and GABA. Problems with the HPA axis, along with overactivity in brain regions controlling fear and emotion, are common as well.

Magnesium may influence these neurobiological systems in several ways. First, it calms the brain by blocking NMDA receptors and reducing glutamate activity. Second, it supports GABA signaling, which facilitates relaxation. Third, it may help regulate the stress response by reducing excessive cortisol release. Together, these actions suggest magnesium deficiency could increase sensitivity to stress and anxiety. This paper reviews current evidence on magnesium's neurobiological role and its link with anxiety disorders. Major themes include magnesium's biological importance, mechanisms of deficiency, clinical evidence, and diagnostic and therapeutic issues.

2. REVIEW METHODS

Search Strategy

This paper was prepared through a systematic literature review of major scientific databases, including PubMed. The process used combinations of keywords: magnesium, anxiety, magnesium deficiency, hypomagnesemia, and anxiety disorders. Publications from the last 13 years in English or Polish were included. The references of selected studies were also examined to identify additional relevant items.

Inclusion & Exclusion

The review included systematic reviews and meta-analyses that examined the relationship between chronic magnesium deficiency and anxiety disorders. It also covered experimental and interventional studies assessing the effects of magnesium supplementation on anxiety, as well as studies of cellular and neurobiological mechanisms (e.g., the HPA axis, NMDA receptors). Studies included adult populations, and key animal model research was used to explain pathophysiological mechanisms in detail. Case reports, editorial comments, and review articles without quantitative data were excluded from the analysis. Publications without full-text access and articles of low methodological quality (e.g., no control group, small sample sizes, which was a common limitation) were also excluded.

Study Selection & Data Extraction

The selection process was carried out by four independent authors, who evaluated titles and abstracts against pre-established criteria. In case of discrepancies, decisions were made by consensus. All data presented in this paper come from peer-reviewed scientific studies that met the above criteria. A preliminary database search identified [186] records. After removing duplicates and screening titles and abstracts, [84] articles remained for full-text review. Based on inclusion and exclusion criteria, [10] publications were selected for final synthesis. The selection process is depicted in the PRISMA diagram (Figure 1).

3. RESULTS & DISCUSSION

Neurobiological Pathomechanism

Magnesium (Mg) is vital for central nervous system (CNS) function, and its deficiency disrupts neurotransmitters, impairs stress response, and may enhance inflammation—mechanisms relevant to anxiety disorders.

The Role in Neurotransmitter Balance

Magnesium is essential for brain function, as it helps maintain the balance between excitatory and inhibitory systems. Anxiety is linked to excess excitatory signaling from glutamate (Boyle et al., 2017), and magnesium naturally inhibits this system (Botturi et al., 2020). It works by physically blocking the NMDA receptor. This receptor is the main channel through which glutamate acts (Boyle et al., 2017;

Pickering et al., 2020; Sartori et al., 2012). This block is essential. It prevents neurons from becoming over-excited or hyperexcitable (Boyle et al., 2017). With low magnesium, NMDA receptor blockade weakens, producing neuronal hyperexcitability and anxiety-like behaviors. This pathway mirrors the action of known NMDA antagonists. Simultaneously, magnesium supports the brain's main inhibitory (GABA) system (Boyle et al., 2017; Pickering et al., 2020). An imbalance between GABA and glutamate activity is a recognized biological marker for anxiety (Boyle et al., 2017). Tellingly, research by Sartori et al., (2012) showed that the anxiety they induced in mice (by using a low-Mg diet) could be reversed by diazepam, a drug that works by boosting GABA. This strongly suggests that magnesium and anxiolytic drugs are working on the same calming pathways.

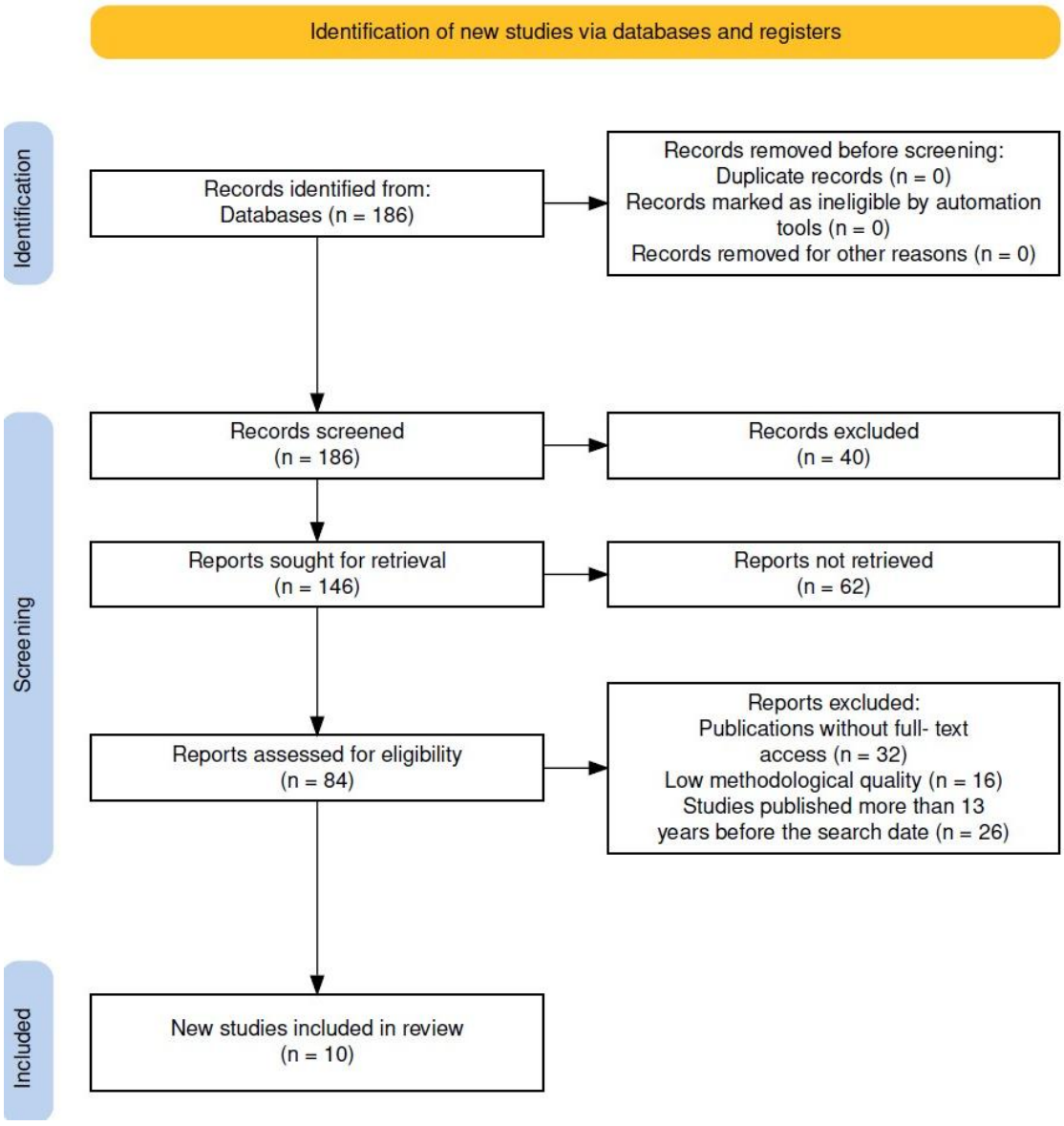

Figure 1: PRISMA flowchart

Influence on the Stress Axis (HPA)

A second major mechanism involves magnesium's control over the body's main stress system: the hypothalamic-pituitary-adrenal (HPA) axis (Boyle et al., 2017; Pickering et al., 2020). This system is our biological command center for stress, and its chronic dysregulation is a known driver of anxiety disorders (Botturi et al., 2020; Sartori et al., 2012). Magnesium deficiency throws this system out of balance. Key studies show that a lack of magnesium directly causes the HPA axis to become overactive. In low-magnesium models, researchers found higher levels of the CRH hormone in the brain. They also observed higher levels of ACTH in the blood. This indicates that the stress system remains continuously and excessively activated (Sartori et al., 2012). Magnesium's job is to act as an

inhibitory control on this axis (Pickering et al., 2020). Supplementation has been shown to suppress this overactivity, helping lower levels of stress hormones such as ACTH and cortisol (Boyle et al., 2017; Pickering et al., 2020). This ability to calm a hyperactive HPA axis is a primary reason for its anxiolytic effects (Boyle et al., 2017; Sartori et al., 2012).

Modulation of Monoamine Neurotransmitters (Serotonin and Dopamine)

Magnesium also appears to regulate the neurotransmitters serotonin and dopamine. Its benefits are partly explained by its interaction with the serotonergic system (Botturi et al., 2020). It works in two ways: it helps serotonin bind more effectively to its receptors, and it also acts as a cofactor for the enzyme that produces serotonin in the first place (Pickering et al., 2020).

Links to Oxidative Stress and Neuroinflammation

Finally, at the cellular level, a magnesium shortage is strongly linked to oxidative stress (OS) and inflammation (Pickering et al., 2020; Botturi et al., 2020; Zheltova et al., 2016). A systematic review by Zheltova et al., (2016) found that when magnesium is low, markers of cellular damage (lipids, proteins, and DNA) increase. This happens because low magnesium weakens the body's own antioxidant defenses.

Furthermore, the deficiency itself acts as a pro-inflammatory trigger. It causes immune cells (phagocytes) to activate and release various damaging free radicals. This process also causes mitochondrial dysfunction (Zheltova et al., 2016), leading to increased reactive oxygen species (ROS) and further nerve cell damage (Botturi et al., 2020; Zheltova et al., 2016).

Magnesium is essential for the proper functioning of the central nervous system, which is why its possible link to mental illnesses, including anxiety disorders, has become the subject of intense research (Kirkland et al., 2018; Botturi et al., 2020). In the context of anxiety, the mechanism of action of magnesium appears to be multifaceted. The key here is how magnesium works: it can uncompetitively block the NMDA (N-methyl-D-aspartate) receptor ion channel (Opanković et al., 2022). And since altered glutamate neurotransmission is often the source of anxiety disorders, it is precisely the inhibition of this pathway by magnesium that may explain its potential anxiolytic properties (Opanković et al., 2022; Kirkland et al., 2018). In addition, magnesium modulates the hypothalamic-pituitary-adrenal (HPA) axis, and its deficiency is associated with dysregulation of this axis, which is crucial in the pathogenesis of anxiety (Kirkland et al., 2018; Botturi et al., 2020).

Some systematic reviews have indicated no significant differences in serum magnesium levels in patients diagnosed with generalized anxiety disorder (GAD) or panic disorder compared to control groups (Botturi et al., 2020). However, it should be noted that most of these studies looked at total serum magnesium concentrations. It has been shown that altered glutamatergic neurotransmission often underlies anxiety disorders. Magnesium, which acts as a non-competitive antagonist of the NMDA (N-methyl-D-aspartate) receptor ion channel, may therefore be of key importance in this context (Opanković et al., 2022). It is precisely this ability to inhibit the aforementioned pathway that may be responsible for the potential anxiolytic properties of magnesium (Opanković et al., 2022; Kirkland et al., 2018). At the same time, however, the same group of anxiety patients showed significantly lower concentrations of ionized magnesium (iMg) compared to the control group (Opanković et al., 2022).

Furthermore, there is stronger evidence that magnesium levels are related to the severity of anxiety symptoms themselves. This was confirmed in a study by Opanković et al., (2022). The authors obtained statistically significant results showing a negative correlation between ionized magnesium concentration and anxiety scale scores (DAASA). It was therefore confirmed that lower levels of ionized magnesium were accompanied by greater severity of anxiety symptoms. This relationship is also supported by other reports indicating an inverse relationship between dietary magnesium intake and subjective assessment of anxiety levels (Kirkland et al., 2018) and a negative correlation between the severity of anxiety symptoms on the HAMA scale and magnesium concentration (Botturi et al., 2020).

The study by Opanković also showed a link between magnesium and oxidative stress. In people with anxiety disorders, the authors found a positive correlation between the concentration of ionized magnesium and the level of malondialdehyde, a common marker of oxidative stress. This finding led the authors to suggest that assessing ionized magnesium levels in conjunction with oxidative stress parameters (Mg-MDA) may serve as a biomarker in this patient group (Opanković et al., 2022).

Diagnostics and therapeutic potential of magnesium

Assessing the actual magnesium status in the human body remains a diagnostic challenge, mainly due to the limitations of the most commonly used methods (Fiorentini et al., 2021). Standard testing of serum magnesium concentration, although widely available, is considered an insufficiently reliable indicator of total body magnesium stores (Zhuang et al., 2025; Fiorentini et al., 2021).

The key problem lies in the distribution of this cation: more than 99% of magnesium in the body is located intracellularly, mainly in bones (50–65%) and muscles and soft tissues (34–39%). Magnesium homeostasis is strictly controlled. If its serum level drops, the body immediately compensates by releasing the element from bone reserves. This is because only a negligible amount of magnesium circulates in the serum itself – only about 0.3% of its total pool. Overall, the entire extracellular fraction, including plasma, accounts for less than 1–2% (Pickering et al., 2020). As a result, normal serum magnesium concentrations (usually in the range of 0.7–1.0 mmol/L) do not rule out the existence of a latent deficiency in tissues. In clinical practice, hypomagnesemia is usually defined as a serum concentration below 0.7–0.75 mmol/L, but it has been suggested that chronic latent magnesium deficiency, which has a potential impact on health, may already occur at values below 0.85 mmol/L (Pickering et al., 2020).

Due to the limitations of serum measurement, more comprehensive methods of assessment are being sought. The recently developed Magnesium Depletion Score (MDS) has been found to be a more valuable and reliable predictor (Zhuang et al., 2025). MDS is a clinical index calculated based on risk factors affecting magnesium homeostasis, including the use of diuretics, proton pump inhibitors (PPIs), reduced kidney function (eGFR), and high alcohol consumption. Other diagnostic methods, although less commonly used, include assessment of daily urinary magnesium excretion, analysis of concentrations in erythrocytes or platelets, as well as research methods such as phosphorus magnetic resonance spectroscopy (31P-MRS) to assess free Mg2+ in the brain and muscles, or fluorimetric chemosensors (Fiorentini et al., 2021).

Diagnostic difficulties are significant because magnesium deficiency is associated with numerous disorders, including neurological disorders such as depression and anxiety (Fiorentini et al., 2021; Pickering et al., 2020). Magnesium plays a key inhibitory role in the regulation and neurotransmission of the physiological response to stress. Magnesium supplementation helps alleviate common symptoms of mental stress, such as fatigue, irritability, and sleep problems. This has been confirmed in clinical trials. They showed that taking 300 mg of magnesium per day was associated with lower scores on the DASS (Depression Anxiety Stress Scale), and this effect was strongest in people experiencing high levels of stress. Other analyses have shown that a dose of 250 mg/day reduced serum cortisol levels in students, and 400 mg/day improved heart rate variability (HRV), which is an indicator of the parasympathetic response to stress (Pickering et al., 2020).

However, therapeutic efficacy depends on the preparation's bioavailability. Magnesium supplements include inorganic salts (e.g., oxide, sulfate) and organic salts (e.g., citrate, malate, taurate, pidolate) (Fiorentini et al., 2021). Soluble forms are generally better absorbed than less soluble forms. Although the data are inconclusive, it is suggested that organic salts have better bioavailability than inorganic compounds such as magnesium oxide. This is particularly important in the case of neurological disorders. Studies on animal models have shown that the organic form, magnesium acetyltaurate, effectively increased the concentration of this element in the brain (Fiorentini et al., 2021). A comprehensive summary of the key neurobiological mechanisms, diagnostic challenges, and therapeutic potential of magnesium in anxiety disorders is presented in Table 1.

Table 1: Summary of key neurobiological mechanisms, diagnostic implications, and therapeutic potential of magnesium in anxiety disorders

Area	Mechanism / Role of Magnesium	Outcome / Consequence of Deficiency	Detection / Intervention
Neurotransmitter Balance	Blocks the NMDA receptor, the main channel for excitatory glutamate signaling (Boyle et al., 2017; Sartori et al., 2012). Supports the GABA inhibitory system (Boyle et al., 2017).	Weakened NMDA blockade leads to neuronal hyperexcitability and anxiety-like behaviors (Boyle et al., 2017). GABA/glutamate imbalance is a marker of anxiety[1].	Anxiolytic drugs (e.g., diazepam) reversed anxiety induced by a low-Mg diet in mice, suggesting they act on shared pathways (Sartori et al., 2012).
HPA Axis Regulation	Acts as an inhibitory control on the hypothalamic-pituitary-adrenal (HPA) axis (Pickering et al., 2020).	Deficiency causes HPA axis hyperactivity, evidenced by elevated brain CRH and plasma	Supplementation suppresses this hyperactivity, lowering cortisol and ACTH levels (Boyle et al., 2017; Pickering et al., 2020).

		ACTH levels in animal models (Sartori et al., 2012).	
Monoamine Modulation	Acts as a cofactor for serotonin synthesis and enhances its receptor binding; regulates dopamine (Pickering et al., 2020; Botturi et al., 2020).	Disruptions in the serotonergic system may contribute to anxiety symptoms (Botturi et al., 2020).	-----
Oxidative Stress & Inflammation	Strengthens antioxidant defenses and prevents mitochondrial dysfunction (Zheltova et al., 2016).	Deficiency triggers oxidative stress (OS) and inflammation, activating phagocytes and increasing ROS (Zheltova et al., 2016).	A positive correlation was found between ionized magnesium (iMg) and malondialdehyde (MDA) (an OS marker) in anxiety patients (Opanković et al., 2022).
Diagnostics	Serum magnesium is unreliable as 99% of Mg is intracellular (bone/tissue) and levels are tightly homeostatically controlled (Pickering et al., 2020; Zhuang et al., 2025).	Patients with anxiety often show significantly lower ionized magnesium (iMg) despite normal total serum levels (Opanković et al., 2022).	iMg negatively correlates with anxiety severity (e.g., DAASA scale), making it a superior biomarker (Opanković et al., 2022). The Mg-MDA index is also suggested (Opanković et al., 2022).
Therapeutic Potential	Therapeutic efficacy depends on bioavailability (Fiorentini et al., 2021).	-------	Doses of 250–400 mg/day reduced cortisol or improved heart rate variability (HRV) (Pickering et al., 2020). Organic salts (e.g., acetyltaurate) show better bioavailability and brain tissue distribution than inorganic forms (Fiorentini et al., 2021).

4. CONCLUSION

Magnesium is crucial for mental health, and its deficiencies, common especially in the elderly, may be linked to anxiety disorders. Neurobiologically, magnesium deficiency contributes to anxiety by weakening the NMDA receptor blockade and disrupting the GABA system (leading to neuronal hyperexcitability), dysregulating and hyperactivating the HPA stress axis, and inducing oxidative stress. Diagnosing deficiency is complicated. Standard measurements of total serum magnesium are often unreliable because the body maintains its constant level at the expense of tissue reserves. However, newer research indicates that patients with anxiety disorders, even with normal total levels, may have significantly lower concentrations of the biologically active, ionized fraction (iMg). Organic formulations, by virtue of their more efficient absorption and tissue distribution, demonstrate a distinct clinical advantage over commonly used inorganic salts.

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Author's contribution

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Data and materials availability
All data associated with this study will be available based on reasonable request to the Corresponding Author.

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