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## **The Association between Hypothyroidism and Mental Health: A Literature Review**

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### **Abstract.**

**Introduction and purpose:** Hypothyroidism, characterized by reduced thyroid hormone production, is a common condition in patients. It can impact various bodily functions and beyond physical symptoms, significantly impacts mental health, contributing to conditions such as depression, anxiety, and cognitive impairment. This article explores the relationship between hypothyroidism and mental disorders, examining underlying mechanisms, clinical correlations, and management strategies to improve outcomes for affected individuals.

**State of knowledge:** It is well-established in scientific literature that hypothyroidism is strongly linked to mental health issues. Thyroid hormones play a key role in brain function, and their deficiency can disrupt mood regulation and cognitive process. Autoimmune thyroiditis, such as Hashimoto's disease, further links hypothyroidism to mood disorders due to chronic inflammation and autoimmunity. Treatment with levothyroxine often improves symptoms, highlighting the thyroid's critical role in mental health. However, the mechanisms remain under active investigation, with ongoing research into thyroid-brain interactions.

**Conclusion:** The correlation between hypothyroidism and mental disorders underscores the importance of recognizing thyroid dysfunction in psychiatric assessments. Early diagnosis and appropriate management of hypothyroidism can significantly improve mental health outcomes, emphasizing the critical interplay between endocrine and psychiatric health.

**Keywords:** hypothyroidism, mental health, depression, dementia, brain fog, Hashimoto disease

### **Introduction.**

Thyroid gland is an organ that produces hormones - thyroxine (T4) and triiodothyronine (T3). These hormones play a crucial role in growth, development and the regulation of metabolic functions [1]. Decreased production or inadequate action of thyroid hormones is named hypothyroidism. The diagnosis is based on blood levels of thyroid-stimulating hormone (TSH)

and free thyroxine (T4) [2]. There are different types of hypothyroidism: primary, secondary, tertiary, and peripheral. Primary hypothyroidism is caused by pathological processes within the thyroid gland, while secondary and tertiary hypothyroidism result from deficiencies in thyroid-stimulating hormone (TSH) or thyrotropin-releasing hormone (TRH) [3]. Subclinical hypothyroidism occurs when serum TSH level is elevated, but T4 and T3 levels remain normal [4].

The most common cause of hypothyroidism is Hashimoto disease (HD), also known as chronic autoimmune thyroiditis. It is characterized by the presence of serum antibodies against thyroid antigens, such as thyroperoxidase (anti-TPO) and thyroglobulin (anti-TG). Anti-TPO antibodies are the most reliable serological marker for diagnosing HD. Anti-TG antibodies are less sensitive and are detected in 60–80% of patients with HD [5]. Other causes of hypothyroidism include iodine deficiency, congenital abnormalities, medications (such as lithium, amiodarone, and tyrosine kinase inhibitors), radioiodine therapy, surgical thyroidectomy, and other rarer causes [1,6].

Hypothyroidism is a common condition worldwide, affecting between 0,3% and 3,7% of the population in the USA and between 0,2% and 5,3% in Europe [3]. It is more prevalent in females, individuals over the age of 65, and those with other autoimmune diseases, as well as in people with Down syndrome and Turner syndrome. Interestingly, the risk of hypothyroidism may be reduced by tobacco smoking and moderate alcohol intake [7].

Manifestations of hypothyroidism are nonspecific and can range from life-threatening to asymptomatic. In addition to the most common signs and symptoms, such as fatigue, cold intolerance, dry skin, constipation, vocal changes, and muscle aches, individuals with hypothyroidism often experience mood disturbances, anxiety, psychomotor retardation and other psychiatric symptoms [2]. Studies indicate that hypothyroidism may contribute to the development or exacerbation of mental disorders, highlighting the importance of assessing thyroid function in patients presenting with unexplained psychiatric symptoms.

### **Hypothyroidism and its impact to Central Nervous System (CNS):**

Thyroid hormones (THs), particularly T3, the active form, play a significant role in brain development and function. Their impact is crucial during fetal and postnatal development, and they continue to influence the brain throughout life.

THs regulate neuronal growth, differentiation, migration, myelination, and synaptogenesis. They act by the thyroid hormone nuclear receptors THRA and THRB, which are expressed on neural cells [8]. Additionally, the development and function of glial cells, such as astrocytes and oligodendrocytes, which are essential for maintaining neuronal homeostasis and supporting synaptic function, are dependent on THs [9]. Disturbances in thyroid hormone levels, whether hypothyroidism or hyperthyroidism, can lead to various neuropsychiatric manifestations [10].

Research shows that thyroid dysfunction affects neurotransmitter systems, including serotonin, dopamine, and norepinephrine, which are vital for mood regulation and cognitive processes [11]. Furthermore, hypothyroidism is associated with structural changes in the brain, such as a reduction in right hippocampal volume, a structure with a high density of thyroid hormone receptors. This reduction may contribute to impairments in learning and memory [12]. In patients with subclinical hypothyroidism, studies have shown decreased gray matter volumes in bilateral prefrontal cortices, cingulate gyrus, precuneus, left middle temporal gyrus, and insula. These changes suggest that individuals with subclinical hypothyroidism may have deficiencies in attentional control [13]. The condition may also affect cerebral perfusion, with some studies reporting diffuse global hypoperfusion [14], while others note deficits in posterior brain regions [15] or the parietal lobe [16].

### **Correlation between hypothyroidism and specific mental disorders:**

#### **DEPRESSION:**

Depression is a serious illness that affects approximately 4.4% of the global population, with a higher prevalence in females than males. It is a leading contributor to global disability and suicide rates [17]. Several factors increase the risk of developing depression, including genetics, psychosocial stressors, and the presence of other medical disorders [18]. A common link between hypothyroidism and depression is often observed, as both conditions share symptoms, such as depressed mood, apathy, emotional lability, decreased appetite, increased sleepiness, weight gain, fatigue, anergia, poor concentration, memory complaints, mental slowing, diminished libido, and suicidal ideation, which can complicate diagnosis [19]. Overt hypothyroidism is observed in 1–4% of individuals with affective disorders, while subclinical hypothyroidism is found in 4–40% of this group [20]. Studies estimate that up to 50% of patients with clinical hypothyroidism experience depressive symptoms [21], and over 40% suffer from clinically significant depression [22]. Autoimmune thyroiditis is also associated

with an increased risk of depression, potentially due to elevated antithyroid antibody levels, which are observed in up to 20% of patients with depression, compared to a 5–10% prevalence in the general population [10]. Researchers studying the relationship between depressive disorders and Hashimoto's disease found a strong association between elevated titers of anti-TPO antibodies and unipolar depression [23]. Additionally, hypothyroidism is a significant contributor to treatment-resistant depression, and levothyroxine therapy, when used adjunctively with antidepressants, can significantly improve mood disorders [24]. A study also indicates that a 3-months integrated yoga intervention can reduce depression and TSH levels in women with hypothyroidism [25].

#### BIPOLAR DISORDER:

Bipolar disorder is a mental health condition characterized by mood swings between emotional highs (mania or hypomania) and lows (depression). While mania is typically associated with hyperthyroidism, it has been rarely reported in cases of hypothyroidism. However, a few documented cases of mania in hypothyroid patients exist [26, 27]. Some studies suggest that bipolar disorder occurs at higher rates in patients with hypothyroidism, especially in those with a family history of mood disorders [28, 29]. The underlying mechanisms remain unclear, but may involve factors such as dysregulation of central nervous system catecholamine receptor sensitivity, thyroid inflammation, thyrotoxicosis, or circadian rhythm disturbances [27]. There is growing evidence linking anti-thyroid antibodies to bipolar disorder, with studies finding a higher prevalence of anti-TPO antibodies in patients with bipolar disorder compared to healthy controls [30]. Thyroid dysfunction is thought to contribute to mood instability and hypothyroidism is frequently observed in patients with rapid-cycling bipolar disorder [31]. Manic symptoms often resolve with thyroid hormone replacement therapy, although some cases require additional treatment with mood stabilizers or atypical neuroleptics [32].

#### ANXIETY DISORDERS:

Anxiety disorders are a group of mental health conditions characterized by excessive fear, worry, panic attacks, anticipatory anxiety, and avoidance behaviors. They often have a chronic course and interfere with daily life. Common types include generalized anxiety disorder (GAD), social anxiety disorder, panic disorder, and specific phobias [33]. Anxiety disorders affect approximately 3.4% of the population and are more common in women [17]. They are also prevalent among patients with thyroid dysfunction, occurring in about 30-40% of patients with

acute hypothyroidism. One study by Manish et al. suggested a prevalence as high as 63%. Patients with subclinical hypothyroidism may also experience anxiety, irritability, and difficulty concentrating [19]. Approximately 41.6% of individuals with autoimmune thyroiditis experience anxiety disorders. These patients are at a higher risk of developing both depression and anxiety disorders simultaneously. In patients with hypothyroidism, the initial symptoms of anxiety often include generalized agitation or intense restlessness [34]. Individuals with HD show significantly higher rates of lifetime generalized anxiety disorders and social phobia [35]. Other studies indicate that the most common anxiety disorder in HT is obsessive-compulsive disorder (OCD). Mood and anxiety disorders are prevalent in patients with HD, even in those who are euthyroid. It is believed that these disorders in HD patients are linked not only to abnormal thyroid hormone levels but also to the presence of thyroid autoimmunity. Therefore, all patients with HD should be evaluated for mood and anxiety disorders, regardless of their thyroid function test results [36].

#### COGNITIVE IMPAIRMENT AND DEMENTIA:

Hypothyroidism can lead to cognitive dysfunction, including impairments in working memory, slowed thinking, attention, verbal learning and processing speed [37-40]. These impairments are believed to result from the effects of low thyroid hormone levels on the hippocampus, a region critical for learning and memory [41]. Thyroid hormone imbalances are also associated with increased risk of dementia and Alzheimer's disease [42]. Prolonged hypothyroidism may worsen these effects, with each six-month period of elevated TSH levels increasing the risk of dementia by 12% [43]. While some studies suggest that thyroid hormone replacement therapy often alleviates cognitive symptoms [44-45], others indicate that it may not fully resolve issues related to psychological well-being or cognitive function, leaving some patients with persistent deficits despite normalized thyroid hormone levels [46-48]. Furthermore, psychiatric disturbances sometimes associated with hypothyroidism can complicate the assessment of cognitive performance [49].

#### BRAIN FOG:

Brain fog is a complex symptom associated with hypothyroidism and other conditions, including chemotherapy treatment, menopause, coeliac disease, chronic fatigue syndrome, lupus, post-COVID-19, and postural orthostatic tachycardia [50-56]. Symptoms typically include fatigue, depressed mood, memory problems, difficulty focusing, confusion, decision-

making challenges, and sleepiness. Many patients report experiencing these symptoms even before a formal hypothyroidism diagnosis. Brain fog significantly impacts quality of life and professional productivity. While rest and exercise are commonly reported as helpful remedies, standard treatments often fail to fully alleviate symptoms, leading patients to explore lifestyle adjustments and thyroid hormone modifications, often shared through online communities and forums [57].

#### MYXEDEMA PSYCHOSIS AND HASHIMOTO ENCEPHALOPATHY:

Myxedema psychosis (MP) and Hashimoto's encephalopathy (HE) are rare neuropsychiatric conditions associated with thyroid dysfunction, each with distinct underlying mechanisms. MP refers to psychotic symptoms in untreated hypothyroidism, characterised by delusions, primarily persecutory or paranoid and hallucinations, most often auditory [58]. Additional symptoms may include perception disorders, motor disturbances, formal thought disorders, and difficulties with concentration or attention [59]. Over half of the MP patients have no prior diagnosis of hypothyroidism, emphasizing the importance of considering thyroid dysfunction in cases of new-onset psychosis. Nearly all MP patients have normal CT/MRI and EEG results, while 75% test positive for thyroid peroxidase antibodies. This condition is effectively treated with oral thyroxine, often combined with short-term antipsychotics, leading to full recovery in most cases [58].

HE, on the other hand, should be considered as a differential diagnosis in hypothyroid patients presenting with psychosis. Unlike MP, where psychotic symptoms result from neurochemical changes due to thyroid hormone deficiency, HE stems from an autoimmune response independent of thyroid status [60]. Its autoimmune nature is supported by elevated thyroid antibody levels in the blood and cerebrospinal fluid and by a positive response to glucocorticosteroid therapy [61]. Symptoms of HE may include fluctuating consciousness, myoclonus, ataxia, tremors, seizures, and stroke-like episodes [62]. Cognitive impairments, memory issues, speech difficulties, sleep disturbances, and behavioral changes are also common [63, 64, 65]. Among neuropsychiatric symptoms, persecutory delusions and visual hallucinations are most frequently observed [66]. Clinical improvement is typically seen within 4-6 weeks of glucocorticosteroid therapy [67].



### **Diagnosis and assessment.**

Given the overlap of hypothyroidism and psychiatric symptoms, a thorough evaluation of thyroid function is essential for patients presenting with mental health disorders. Measuring serum levels of TSH, T4, and T3 is critical for diagnosing hypothyroidism and determining its severity. Elevated TSH level combined with low T4 typically indicate primary hypothyroidism. Testing for anti-thyroid peroxidase and anti-thyroglobulin antibodies can help identify autoimmune thyroiditis as the underlying cause [2]. Additionally, psychological assessment, including standardized tools like the Beck Depression Inventory and the Generalized Anxiety Disorder (GAD-7) scale, are valuable for quantifying the severity of depression and anxiety symptoms in hypothyroid patients [19].

### **Treatment and management strategies.**

Effective management of hypothyroidism is crucial for alleviating associated mental health symptoms. Levothyroxine (LT4) is the standard treatment, restoring hormone levels and often improving mood and cognitive function [68]. For patients who continue to experience mental health symptoms despite normalized thyroid hormone levels, additional treatments such as antidepressants or anxiolytics may be necessary. Selective serotonin reuptake inhibitors (SSRIs) are commonly prescribed for depression in hypothyroid patients [69]. Selenium supplementation may also support mood stability [70]. Additionally, regular exercise is essential for mental well-being and can enhance both thyroid function and psychiatric outcomes [71].

### **Conclusion:**

The correlation between hypothyroidism and mental disorders highlights the complex interplay between endocrine health and mental well-being. Thyroid hormone deficiency can significantly impact neurotransmitter balance, brain structure and brain diffusion, all of which contribute to psychiatric symptoms. Recognizing this correlation is critical for accurate diagnosis and treatment, as thyroid hormone replacement can substantially improve mental health outcomes for patients with hypothyroidism. Further research is necessary to better understand the mechanisms linking hypothyroidism and mental disorders, with the aim of optimizing treatment strategies and enhancing.

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