

From Glands to Nerves: Hypothyroidism's Underexplored Influence on Neurological Well Being-A Narrative Review

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Abstract

Review Article

Hypothyroidism is a clinical health condition in which the thyroid gland secretes insufficient levels of the thyroid hormones T3 and T4, resulting in high thyroid stimulating hormone (TSH) readings. The thyroid gland plays a key role in the development of the central nervous system. These hormones are essential for brain development and function. It has been found that thyroid disorders are among the most common diseases in worldwide. Thyroid disorders are one of the primary causes of cognitive decline, including Alzheimer's disease (AD). In this review, we had discussed about the various neurological complications that develops due to hypothyroidism.

Keywords: Increased TSH, cognitive impairment, canalicular neuropathies, neurodegenerative disorder, insomnia, myalgia.

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INTRODUCTION

The first endocrine gland that develops during fetal development is the thyroid gland [1]. Thyroid hormones (TH) are secreted by thyroid gland into the blood and help in several organ's biological functions [2]. This hormones, such as 3,5,3',5'-tetraiodo-L-thyronine (T4) and 3,5,3'-triiodo-L-thyronine (T3), are important for brain development in mammals, during embryonic and fetal stages, regulating processes of neuronal proliferation, migration and differentiation, neurite outgrowth, synaptic plasticity, dendritic branching, and myelination [3]. T4 and T3 crosses the blood brain barrier (BBB) of the choroid plexus through an MCT8 TH transporter or OATP1C1 TH transporter to enter into the brain [2]. The active form of T3 is an essential regulator of human metabolism, particularly for the central nervous system (CNS) [3]. It has been found that thyroid disorders are among the most common diseases in worldwide. The incidence rate of thyroid problems among adults is 0.2– 8%, this increases with age and is higher in women than in men [4]. TH and TSH values in the serum are used to categorize different types of thyroid dysfunction.

- Subclinical hypothyroidism exhibits normal T3 and T4 levels with increased TSH, while subclinical hyperthyroidism exhibits normal T3 and T4 levels with decreased TSH levels.
- Overt hypothyroidism exhibits decreased T3 and T4 levels and increased TSH, whereas overt hyperthyroidism exhibits increased T3 and T4 levels and decreased TSH [2].

Hypothyroidism is a clinical health conditions in which the thyroid gland secretes insufficient levels of the thyroid hormones T3 and T4, resulting in high thyroid stimulating hormone (TSH) readings. A significant effect of hypothyroidism is a slowing in cell metabolism. Lack of iodine (in water, plants, and foods) and Hashimoto's thyroiditis caused by autoimmune disease or thyrotoxicosis caused by Graves' disease are common causes of this disease condition [5]. Thyroid hormones (THs) have a variety of vital roles inside the central nervous system, from prenatal development to adulthood. Thyroid problems are one of the primary causes of cognitive decline, including Alzheimer's disease (AD). Recent studies have highlighted the possibility that AD and hypothyroidism/hyperthyroidism are related [6]. In this review we had discussed about the

various neurological complications that develops due to hypothyroidism.

COGNITIVE DISORDERS

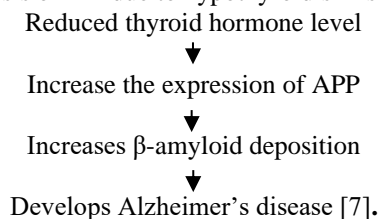
Low performance in one or more cognitive behaviors is known as cognitive impairment; if it develops, in its more advanced state, it can be referred to as dementia, which includes severe or more severe types of cognitive impairment/decline. Nearly 50 million people worldwide have dementia, and 10 million new cases are reported each year. Adults with abnormal thyroid function have long been known to experience psychological and cognitive problems. The first reports of the connection between mental illnesses and thyrotoxic diseases present back to the late nineteenth century [4]. Neurodegenerative conditions like dementia are closely associated with TH dysfunction in the CNS. The development of neurological disorders including Alzheimer's disease and depression is closely related to subclinical and overt hypothyroidism, both of which cause mood dysregulation, anxiety, attention, psychomotor function, and cognitive impairment. Hippocampal atrophy was present in hypothyroid patients, which causes

- Memory loss
- Reduced cerebral blood flow
- Decline in memory [2].

The metabolism of carbohydrates is controlled by THs, and hypothyroidism has been linked to:

- Decreased glucose availability and altered glucose absorption.
- Slow down gluconeogenesis
- Lowering the production of insulin.

In fact thyroid malfunction has been observed in up to 11% of diabetic patients. Being that the brain's primary energy source is glucose hence cognitive function also depends on it, an energy imbalance may have a significant impact on the brain's vital functions. The bilateral amygdala, hippocampus, perigenual anterior cingulate cortex (ACC), left sub-genual ACC, and right posterior cingulate cortex have all revealed decreased activity in PET studies of hypothyroidism patients. These areas are essential for attention and memory [5]. Hypothyroidism interferes with the maintenance of the normal energy-consuming processes required for vital brain functions including neurotransmission and memory [6]. A link between subclinical hypothyroidism (SCH) and cognitive performance was found in 14 out of 23 studies. The pathogenesis of AD due to hypothyroidism is as follow



CARPELTUNNEL SYNDROME

One of the most prevalent compressive, canalicular neuropathies of the upper extremities and a frequent source of hand pain and reduced function is carpal tunnel syndrome (CTS). The median nerve of the wrist is either compressed or injured in carpal tunnel syndrome. Typical symptoms of CTS include pain, tingling, numbness, and swelling over the hand's median nerve distribution area [8]. The transverse carpal ligament and carpal bones form the small space known as the carpal tunnel. The median nerve travels through this area to supply the first four fingers and palm of the hands with motor and sensory function. According to Werner *et al.*, those with a BMI > 29 are 2.5 times more likely to develop CTS than those who are underweight [9]. Long-term postures with excessive dynamic stretching or extensions, repetitive usage of the flexor muscles, and vibration exposure are the main environmental factors [10]. One of the disorders that has been linked to an increased prevalence and incidence of CTS is hypothyroidism [11]. In a study by Karne *et al.*, found that of 36 adult patients with primary hypothyroidism, 16.7% of individuals had CTS [10]. A major risk factor for CTS in people with hypothyroidism is

- An increased BMI.
- Buildup of mucinous substance or mucopolysaccharides on the median nerve in hypothyroidism may be the cause of CTS.

It may also be brought on by swelling of the synovial membrane around the tendons in the carpal tunnel in cases with uncontrolled hypothyroidism [9]. The correlation between hypothyroidism and CTS was weaker than the correlation between hypothyroidism and surgery for CTS. Concurrent hypothyroidism can interfere with the effectiveness of conservative CTS treatment and need surgery [11].

PARKINSON DISEASE

Early-stage loss of dopaminergic neurons in the substantia nigra pars compacta characterizes Parkinson's disease (PD), the second most prevalent neurodegenerative illness after Alzheimer's disease. Numerous studies have been conducted since the 1970s to determine whether hypothyroidism affects a person's vulnerability to Parkinson's disease. Although some studies have indicated a higher chance of developing PD in hypothyroid patients, no causal link between these two conditions has been established. Iodine deficiency and pituitary dysfunction brought on by hypothalamic dysfunction are thought to be two possible correlated factors that affect the likelihood of developing PD. In addition to longitudinal investigations, certain cross-sectional studies have also found low thyroid hormone levels to be related to the severity of motor symptoms. Patients with Parkinson's disease have also shown abnormal thyroid test results, which were identified as subclinical hypothyroidism. Furthermore, patients with drug-resistant PD may need to be evaluated for

hypothyroidism if they have clinical indications of hypothyroidism and vice versa [12].

Psychiatric Disorder: Depression and Bipolar

Neuropsychiatric symptoms are sometimes associated with hypothyroidism. Cognitive and emotional problems are common but modest in subclinical hypothyroidism. Although the stated prevalence of clinical hypothyroidism is modest, the severity of the emotional and cognitive symptoms might be high. Neuropsychiatric illnesses can resemble endocrine conditions like hypothyroidism. Through interactions with the serotonin and norepinephrine systems, thyroid hormone regulates mood. Depression and hypothyroidism both lower serotonin (5-HT) activity. Lower serotonergic endocrine responses and the presence of depression are predicted by higher TSH levels. The chance of getting depression may increase as a result of this drop in 5-HT. The first test for detecting thyroid dysfunction is serum TSH, which is followed by free T4 estimations. When it comes to the diagnosis of thyroid diseases, serum TSH is more sensitive and specific than free T4. Patients with psychiatric diseases may have aberrant thyroid status results from laboratory tests ¹³.

Sleep Disorder & RLS

Iodine-containing substances called iodothyronines, which make up thyroid hormones (active T3 and T4 precursors), are crucial for growth, normal cell development, and production of heat and metabolism [14]. The general quality of sleep may be impacted by hypothyroidism, which is characterised by decreased thyroid hormone production. According to Song *et al.*'s research, individuals with subclinical hypothyroidism or low thyroid hormone levels typically have

- Longer sleep latency
- Shorter sleep duration and
- Decreased satisfaction with their sleep quality.

The symptoms of thyroid hormone deficiency may lead to sleeplessness, which may be one reason why hypothyroidism and insomnia frequently co-occur. For instance, an underactive thyroid is linked to symptoms including muscular and joint pain, a cold intolerance, and heightened anxiety, all of which can make it difficult to fall asleep. The increased risk of restless legs syndrome (RLS) associated with inadequate thyroid function is a well-known example of thyroid dysfunction causing sleep problems. When they rest, people with RLS experience an uncomfortable or unpleasant sensation in their legs or bodies. Therefore, RLS symptoms, which typically appear while a person is attempting to sleep, might cause insomnia and sleep problems [15].

Effect on Auditory Function

Congenital hypothyroidism (CH) is an endocrine disorder that is frequently observed in neonates and is associated with a lack of or decrease in thyroid hormones (THs) [16]. CH is a prevalent

endocrine illness that affects neonates, occurring in between 1:2,000 and 1:4,000 live births globally. About 2:1 of people who are affected are women [17]. Newborn screening (NS) can identify it as a public health problem [16]. It is unknown how common hearing impairment is among CH patients; however, up to 20% of them are affected. According to recommended practices, blood obtained on filter paper should be used for neonatal screening before the seventh day of life in order to measure thyroid-stimulating hormone (TSH). When there is elevated serum TSH (>10 mU/L), or low thyroxine or T4 levels, the diagnosis is considered to be made [17]. CH is typically categorised as permanent or temporary, with primary, secondary, and tertiary aetiologies. Because of the hormone shortage persists, the irreversible condition necessitates lifetime care. However, temporary CH recovers usual TH production over the first several years or months of life. Lack of an early diagnosis and appropriate care can lead to irreversible mental impairment and alterations in neurological and motor development [16].

MYOPATHY

Fibromyalgia is thought to affect 2%–3% of people worldwide. Fatigue, widespread muscle pain, paresthesia, cognitive impairment, and non-restorative sleep are only a few of the somatic symptoms of fibromyalgia [18]. A skeletal muscle condition called hypothyroid myopathy (HM) is brought on by hypothyroidism. The symptoms of myopathy, which include myasthenia, muscle spasm after exercise, myalgia, and muscle stiffness, appear between 30% - 80% of hypothyroidism patients. Although the symptoms of hypothyroid myopathy are often modest, they can become more severe in cases of severe hypothyroidism that go untreated. Due to glucosaminoglycan deposition in type II fast muscle fibres and type I slow muscle fibres, impaired contractility of the actin-myosin unit, decreased myosin ATPase activity, and slower ATP turnover, hypothyroid myopathy damages skeletal muscle [19].

CONCLUSION

This review concludes that hypothyroidism causes various neurological dysfunctions. Hence early diagnosis, following proper treatment regimen and regular follow up helps to reduce such complication in patients suffering from hypothyroidism.

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