İCMAL MƏQALƏ **AÇIQ GİRİŞ (OPEN ACCESS)**

THE EFFECT OF THYROID HORMONE IMBALANCE ON THE NERVOUS SYSTEM.

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Abstract

This review presents current data on the effect of thyroid hormone imbalance on the nervous system and discusses the role of neuron-specific enolase as a marker of neuronal damage. Thyroid disorders are widespread and often accompanied by damage to the central and peripheral nervous systems, manifesting as cognitive impairment, mood changes, and acute neurological conditions. Thyroxine and triiodothyronine play a key role in the development and functioning of the nervous system, affecting neurogenesis, synaptogenesis, myelination, neuronal metabolism, and cognitive function at all stages of life. Hormone imbalances lead to decreased attention, impaired memory, slowed psychomotor reactions, and emotional instability. Autoimmune processes, including Hashimoto's thyroiditis and Graves' disease, can further affect the nervous system through autoantibodies and systemic immune dysregulation. Neuron-specific enolase is considered a potential biomarker of early neuronal damage, reflecting the impact of hormonal imbalance on nervous tissue. The limited nature of existing data highlights the need for further research to understand the pathogenetic mechanisms, improve early diagnosis and prognosis, and develop individualised therapeutic approaches for patients with neurological complications of thyroid disease.

Keywords: thyroid gland, hypothyroidism, hyperthyroidism, cognitive impairment, autoimmune mechanisms, neuronal damage, neuron-specific enolase.

Introduction

Thyroid disorders are widespread and often accompanied by damage to the central and peripheral nervous systems [1, 2, 3]. Clinical manifestations range from subclinical cognitive impairment and mood changes to acute neurological conditions — from thyrotoxic periodic paralysis, manifested by episodes of muscle weakness, to myxedema coma [4, 5]. Understanding the mechanisms by which thyroid hormone imbalance affects nerve tissue is important for both diagnosis and the identification of sensitive biomarkers of neuron damage. This review presents current data on the effects of triiodothyronine (T3) and thyroxine (T4) imbalance on the nervous system and reviews information on neuron-specific enolase (NSE) as a marker of neuronal damage in thyroid diseases.

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The effect of thyroid hormones on the activity of the nervous system.

It is well known that thyroxine and triiodothyronine play a key role in the development and functioning of the nervous system throughout a person's life [6]. In the embryonic and early postnatal periods, thyroid hormones are necessary for neurogenesis, neuron migration, synaptogenesis, and myelination. Hormone deficiency leads to irreversible cognitive impairment [7]. In adults, T3 and T4 support neuron metabolism, modulate the expression of genes responsible for synaptic plasticity, and affect mood and cognitive function [8, 9, 10]. These hormones enter cells through special transporters and are then activated or inactivated by the enzymes D2 and D3 deiodinases. They then bind to nuclear receptors, which leads to the regulation of gene transcription, affecting their function. Disruptions in these mechanisms, which occur in clinical and subclinical hypo- or hyperthyroidism, can lead to difficulties with concentration, impaired ability to retain and process information (working memory), slowed psychomotor reactions, and increased emotional instability [11, 12].

Hypothyroidism and the nervous system.

Clinical hypothyroidism is one of the most significant endocrine causes of cognitive impairment. Thyroid hormone deficiency slows down neurometabolic processes, reduces neurotransmitter levels, and impairs synaptic plasticity. Adult patients often suffer from slowed psychomotor activity, memory impairment, decreased attention, and mood swings. It should be noted that congenital hypothyroidism remains the most common preventable cause of mental retardation, with a prevalence of 1:2000–1:4000 newborns [13]. Low levels of thyroid hormones, especially in the first months of life, slow down the myelination of nerve fibres. This also reduces the accumulation of lipids and glycoproteins in nerve tissue, leading to morphofunctional disorders of the membranes of neurons in the brain's conduction pathways [14]. Since the clinical manifestations and course of hypothyroidism vary significantly among individuals of different ages, unfortunately, at one year of age, when early diagnosis is extremely important, the clinical picture typical of this condition is observed in only 10–15% of cases [15]. Timely diagnosis and replacement therapy can prevent serious cognitive impairment, although in some cases minor language or learning difficulties may persist [16]. It should also be noted that in elderly patients, hypothyroidism can manifest with symptoms similar to dementia, sometimes leading to misdiagnosis; replacement therapy often improves cognitive function, but complete recovery is not always achieved [17].

Hyperthyroidism and the nervous system.

Hyperthyroidism, on the contrary, is associated with hyperactivation of the central nervous system. Patients often complain of restlessness, irritability, sleep disturbances, poor concentration, and fatigue [18]. Studies have shown that patients with newly diagnosed hyperthyroidism perform worse on tests of attention, memory, and executive function than patients with normal thyroid function [19]. In older people, hyperthyroidism can also mimic dementia, accompanied by confusion and cognitive decline, but restoration of normal thyroid function often leads to improvement [20]. There are opinions that cognitive and behavioural changes in hyperthyroidism may be partly associated with adrenergic hyperactivity,

which is confirmed by the beneficial effect of beta-blockers on attention and concentration [21]. In addition, autoimmune hyperthyroidism (Graves' disease) may be accompanied by neurological autoimmune disorders, such as myasthenia gravis, exacerbating the clinical picture [22].

Autoimmune mechanisms and cross-associations.

The effect of thyroid dysfunction on the nervous system is not limited to hormonal disorders alone. Autoimmune diseases, primarily Hashimoto's thyroiditis and Graves' disease, which are the most common forms of thyroid pathology, can play a significant role. Neuropsychiatric manifestations in these conditions are due to complex and multifactorial pathogenetic mechanisms [23]. Autoantibodies to thyroid antigens can indirectly affect the function of neurons and glial cells [24], and in some cases can penetrate the disrupted blood-brain barrier, contributing to inflammation [25]. In this context, according to several authors, neuron-specific enolase (NSE) may be elevated in autoimmune thyroid diseases. Given that NSE is a cytosolic enzyme of neurons and neuroendocrine cells, an increase in its serum concentration is considered to reflect neuroendocrine activation and possible subclinical neuronal damage in the context of immune-mediated inflammatory processes associated with thyroid dysfunction. Such alterations may indicate the involvement of the nervous system in the pathogenesis of autoimmune thyroid pathology [26]. There is also a well-established link between Graves' disease and myasthenia gravis, which occurs more frequently than would be expected by chance [27]. Hashimoto's thyroiditis is associated with an increased risk of developing multiple sclerosis and autoimmune encephalopathies [28]. Systemic dysregulation of the immune system, including cytokine imbalance and oxidative stress, further contributes to the development of neuropsychiatric manifestations. This can occur even when thyroid hormone levels remain close to normal [29].

Neuron-specific enolase as a marker of neuronal damage.

NSE is an isoform of a glycolytic enzyme that is predominantly expressed in neurons and neuroendocrine cells. Normally localized within cells, NSE is released into the bloodstream after neuronal damage, making it a widely used biomarker of neuronal damage. Elevated NSE levels are observed in traumatic brain injury, stroke, and hypoxic-ischaemic encephalopathy, where they correlate with severity and prognosis. They are also elevated in neurodegenerative diseases, including Alzheimer's disease and amyotrophic lateral sclerosis [30]. According to recent studies, elevated levels of neuron-specific enolase are also associated with the development of diabetic neuropathy, reflecting damage to neuronal tissue [31]. In clinical studies of patients with primary hypothyroidism, serum neuron-specific enolase (NSE) has been evaluated as a marker of nervous system involvement. In a cohort of individuals with primary hypothyroidism, serum NSE levels were assessed alongside neurological status and electrophysiological evaluations, revealing that NSE activity varied with clinical factors such as symptom severity, disease duration, and presence of neurological signs, and that changes in NSE correlated with treatment dynamics. These findings support the view that elevated serum NSE in hypothyroidism may reflect underlying neurophysiological alterations associated with the endocrine disorder [32]. In addition to these clinical observations, several other neurobiochemical markers are widely used

to assess nervous system involvement, including S100B and glial fibrillary acidic protein (GFAP). While NSE primarily reflects neuronal metabolic activity and neuronal injury, S100B and GFAP are predominantly associated with astroglial activation and structural glial damage. S100B is considered a marker of blood–brain barrier disruption and astrocytic stress, whereas GFAP represents cytoskeletal alterations within astrocytes. In contrast, NSE may be more sensitive to subtle metabolic disturbances affecting neuronal integrity, such as those observed in endocrine disorders, including thyroid hormone imbalance. Therefore, comparative evaluation of these biomarkers may improve the interpretation of neurobiological changes in hypo- and hyperthyroid states [33]. In this context, thyroid hormone imbalance may have a similar effect on NSE levels, potentially reflecting neuronal damage in thyroid pathology. However, the available data in this area remain limited, highlighting the need for further research. Given the insufficient sensitivity of existing diagnostic methods for the early detection of neurological disorders in thyroid diseases, NSE can be considered a promising biomarker of early neuronal damage in this group of patients.

Conclusion

Thyroid hormone imbalance has a significant impact on the nervous system, manifesting itself in a wide range of cognitive and neurological disorders. Despite the well-documented role of T3 and T4 in brain development and function, quantitative indicators of neuronal damage in thyroid dysfunction remain limited. Further research will provide a deeper understanding of the mechanisms of neurological complications arising from thyroid disease and enable the development of more accurate diagnostic and therapeutic approaches tailored to the individual needs of patients.

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QALXANABƏNZƏR VƏZİNİN HORMONLARININ DISBALANSININ SINIR SISTEMINƏ TƏSIRI

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Xülasə

Bu icmal qalxanabənzər vəzi hormonlarının disbalansının sinir sisteminə təsirinə həsr olunmuşdur və neyronların zədələnməsinin göstəricisi kimi neyron-spesifik enolazanın rolu nəzərdən keçirilir. Qalxanabənzər vəzinin xəstəlikləri geniş yayılmışdır və tez-tez mərkəzi və periferik sinir sisteminin pozulmaları ilə müşayiət olunur. Bu dəyişikliklər koqnitiv funksiyaların zəifləməsi, əhval dəyişiklikləri və müxtəlif nevroloji əlamətlərlə özünü göstərə bilər. Tiroksin və triiyodtironin sinir sisteminin normal inkişafı və fəaliyyəti üçün vacibdir. Bu hormonlar neyrogenez, mielinizasiya, neyronların maddələr mübadiləsi və yaddaş da daxil olmaqla koqnitiv funksiyalara təsir göstərir. Hormon balansının pozulması diqqətin azalmasına, yaddaşın zəifləməsinə, psixomotor reaksiyaların ləngiməsinə və

emosional qeyri-sabitliyə səbəb ola bilər. Haşimoto tireoiditi və Qreyvs xəstəliyi kimi autoimmun xəstəliklər immun mexanizmlər vasitəsilə sinir sisteminə əlavə təsir göstərə bilər. Neyron-spesifik enolaza sinir toxumasının zədələnməsini əks etdirən həssas biomarker hesab olunur. Mövcud məlumatların məhdudluğu bu sahədə əlavə tədqiqatların aparılmasının, erkən diaqnostikanın yaxşılaşdırılmasının və qalxanabənzər vəzi xəstəlikləri olan pasiyentlər üçün daha effektiv müalicə yanaşmalarının işlənib hazırlanmasının vacibliyini göstərir.

ВЛИЯНИЕ ДИСБАЛАНСА ГОРМОНОВ ЩИТОВИДНОЙ ЖЕЛЕЗЫ НА НЕРВНУЮ СИСТЕМУ.

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Резюме

В данном обзоре представлены современные данные о влиянии дисбаланса гормонов щитовидной железы на нервную систему и обсуждается роль нейронспецифической энолазы как маркера повреждения нейронов. Заболевания щитовидной железы широко распространены и часто сопровождаются повреждением центральной и периферической нервной системы, что проявляется в виде когнитивных нарушений, изменений настроения и острых неврологических состояний. Тироксин и трийодтиронин играют ключевую роль в развитии и функционировании нервной системы, влияя на нейрогенез, миелинизацию, метаболизм нейронов и когнитивные функции на всех этапах жизни. Гормональный дисбаланс приводит к снижению внимания, ухудшению памяти, замедлению психомоторных реакций и эмоциональной нестабильности. Аутоиммунные процессы, включая тиреоидит Хашимото и болезнь Грейвса, могут дополнительно влиять на нервную систему через аутоантитела и системную иммунную дисрегуляцию. Нейронспецифическая энолаза считается потенциальным биомаркером раннего повреждения нейронов, отражающим влияние гормонального дисбаланса на нервную ткань. Ограниченность существующих данных подчеркивает необходимость дальнейших исследований для понимания патогенетических механизмов, улучшения ранней диагностики и прогнозирования, а также разработки персонализированных терапевтических подходов для пациентов с неврологическими осложнениями заболеваний щитовидной железы.