THE ASSOCIATION BETWEEN HYPOTHYROIDISM, MENTAL DISORDERS AND PHYSICAL ACTIVITY: A COMPREHENSIVE REVIEW

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Abstract
Hypothyroidism refers to the common pathological condition of thyroid hormone deficiency. Multiple studies have concluded that undiagnosed and undertreated patients with hypothyroidism are at increased risk of developing mental disorders. Moreover, there are proven cases of symptom remission with or without antidepressants after a euthyroid state was established. Studies suggest that exercise can have positive effects on thyroid function as well as improving mental state. However, patients with untreated hypothyroidism often experience decreased exercise tolerance, weakness, fatigue, and feelings of low energy, which often prevent them from engaging in physical activities. This review strengthens the link between hypothyroidism, mental health issues and struggles that come with thyroid hormone deficiency and physical activity. It also demonstrates how treating the underlying hypothyroidism, as well as promoting regular physical activity, can be significant ways to improve health outcomes in these patients.

Methods
A systematic literature search was conducted using PubMed and Google Scholar data bases, focusing on studies published in English and Polish that examined the relationship between untreated hypothyroidism, mental health disorders, and engaging in regular physical activities. Keywords included "untreated hypothyroidism," "mental illness," "depression," "anxiety," "exercise tolerance," and "quality of sleep".

Aim of the study:
The aim of our work is to review and summarize the most interesting conclusions from the research on the impact of hypothyroidism on developing mental disorders as well as outcomes on physical activity performance.

Key words
Hypothyroidism, depression, anxiety, physical activity, quality of sleep, mental disorders
Introduction

The thyroid gland maintains an optimal level of metabolism in various tissues for their proper functioning. The main hormones secreted by the thyroid are thyroxine (T4) and triiodothyronine (T3). Hypothyroidism refers to the common pathological condition of thyroid hormone deficiency, which among adults often manifests in a reduced basal metabolic rate, cold intolerance, weight gain, constipation, dry skin, slow speech, slower cognitive processes, impaired memory, and severe mental disorders, but clinical presentation can differ with age and sex, among other factors. Untreated patients may also report experiencing reduced exercise tolerance, low mood, and decreased energy levels.

Importance of diagnosing hypothyroid among patients with mental diseases

Common symptoms of psychological dysfunction encountered in hypothyroidism include forgetfulness, mental slowness, lethargy and emotional lability. [1] Hypothyroidism even when occult or subclinical can cause changes in energy, mood, anxiety level or cognition. Antidepressants and mood stabilizers appear not to be as effective in patients with abnormal thyroid function. [2] Levothyroxine therapy is known to improve the symptoms of depression rapidly when compared to antidepressants alone. [3] Both increase and decrease in thyroid function can cause mood abnormalities. [4] Recognizing and correcting hypothyroidism by adequate treatment, including subclinical presentations, can alleviate symptoms similar to those of affective disorders. [2]

Most common mental diseases among patients with hypothyroidism

Depression

Many studies support the association between hypothyroidism and depression. A vast body of research demonstrated that somatostatin and serotonin influence the hypothalamus-pituitary-thyroid axis. There is also a possible association between autumine mechanisms involving the thyroid gland and depressive disorders, but the available evidence is so far not clear. However, studies demonstrate that antithyroid antibodies are elevated among many people with depression. [3] Hypothyroid patients usually tend to experience concentration difficulties, lassitude, low libido, and pessimism or sadness that can be linked with major depressive episodes. [2] Thyroid hormones not only participate in the pathophysiology of depression, but also influence the development of psychotic symptoms. [5] Studies show that subclinical hypothyroidism is also highly correlated with major depressive disorder. [6] The treatment protocol usually entails the treatment of hypothyroidism appropriately with thyroid
replacement therapy and antidepressants. Levothyroxine functions to improve the action of antidepressants, potentiating their effects in treating and improving the symptoms of depression. [3] In addition it is important to remember that the endocrine system presents different features throughout a lifetime and age may significantly influence in thyroid function’s role in depression with psychotic symptoms. [5]

Bipolar affective disorder
One of the most common mental illness associated with hypothyroidism is depression. However, an increasing number of scientific articles are highlighting the important role of thyroid hormone deficiency among patients who suffer from bipolar affective disorder. Mood disorders are intimately associated with suboptimal thyroid function. [7] Studies from 2014 done by Dr. Bindu Menon from the Department of Psychiatry in India showed a significant correlation between a family history of mood disorder in the first degree relatives and patients with hypothyroidism. [8] Moreover, studies done in 2016 also suggested a possible correlation in thyroid antibodies among possible endophenotypes for bipolar disorder. [9] A recent large sample sized cross-sectional study in China shown a correlation between decreased serum FT4 level a high prevalence of psychotic depression among depression adolescents and recommended that adolescents with depressive disorders regularly screen their serum FT4 levels for better clinical outcomes. [5]

Poor sleep quality
Studies show poor sleep can trigger mania, psychosis or paranoia, as well as make existing symptoms worse. Hypothyroidism may affect overall sleep quality. Although no direct biochemical connection has been established between hypothyroidism and insomnia, some studies have shown a relationship between untreated subclinical hypothyroidism and poor sleep quality. [10]

Anxiety
Although anxiety is usually associated with hyperthyroidism, studies show that occasionally this type of disorder may also be observed among patients with T3 and T4 deficiency. The symptoms include panic disorder, agoraphobia, social phobia, performance anxiety, post-traumatic stress disorder and generalized anxiety disorder. [2]

**The beneficial role of physical activity in mental health**
Numerous epidemiological studies have demonstrated the beneficial role of physical activity in healthy living and preventing many disorders. Adequate exercise is proven to lower physical conditions such as cardiometabolic illness, breast and colon cancer, osteoporosis, obesity. Regular activity is associated not only with lower risk of developing mental health
problems but is also a promising way to manage them. Exercise has been evaluated as an adjunct intervention for mood disorders including major depressive disorder and bipolar disorder. [11], [12] Neuroplasticity is increasingly characterized as a central mechanistic component of mental health improvements and is highly influenced by physical activity. [11] Neuroplasticity is the brain's ability to reorganize itself by forming new neural connections throughout life. It is an ongoing process that allows the neurons in the brain to compensate for injury and disease and to adjust their activities in response to new situations or changes in the environment. Neuroplasticity also plays a crucial role in learning and memory. Increased neuroplastic capacity is one hypothesized mechanism underlying the mental health benefits of several widely used somatic psychiatric treatment modalities. Exercise is one of the few behavioral processes that appears to increase neuroplasticity. [11]

**Regular physical activity in hypothyroidism**

Decreased exercise tolerance is a common symptom among people with hypothyroidism, as well as weakness, fatigue, and feelings of low energy. Therefore, for untreated patients, exercising regularly can be more challenging and less appealing compared to the rest of the population. Recent studies showed a strong association between the amount of daily physical activity of American adults and changes in thyroid function, including thyroid hormone levels and thyroid diseases. [13] People with hypothyroidism engage in sports less frequently, which may be due to the influence of hypothyroidism on the lungs, heart and muscles, which can cause impaired exercise tolerance. [14] Hypothyroidism results in increased vascular resistance, decreased cardiac output, decreased left ventricular function, and changes in several other markers of cardiovascular contractility. [15] However, due to a lack of physical activity, there is a higher risk for patients with hypothyroidism of developing mental disorders, to which they are already more susceptible compared to the general population. Studies from 2021 has uncovered several novel factors that are associated with exercise intolerance in patients with hypothyroidism. Main reported long-term physical activity limitations among partcipants were muscle pain, fatigue after exercise and arthralgia. Two-thirds of the respondents indicated that their current condition of hypothyroidism limited their physical activity performance. [16] Surprisingly, other studies, also done in 2021, showed that more patients engaged in sports activities compared to the general population. However, two-thirds of the patients indicated that the current condition of hypothyroidism was limiting their physical activity performance. [17]

**Discussion**

Research shows a strong association between the occurrence of mental illnesses and undiagnosed hypothyroidism. Clinical symptoms of hypothyroidism can also be notoriously variable. The degree of impairment may depend on the patient’s normal functional level. [2]. In addition, symptoms often overlap, which can cause problems with diagnosing patients as
well as removing the source of the underlying issue. On the other hand, there is a risk that individuals suffering from psychiatric disorders may overly attribute low mood to diagnosed hypothyroidism and not seek help for their mental health.

Conclusion
There is a proven association between developing mental disorders and patients with hypothyroidism. There are also described cases demonstrating a significant remission in symptoms among patients after their euthyroid state was established. Healthcare providers should consider routine screening for thyroid dysfunction in patients presenting with psychiatric symptoms. In addition, one proven beneficial way to improve mental state is regular exercise, but as mentioned earlier, due to reduced exercise tolerance and lack of quality sleep, it can be more challenging and not as appealing for people with untreated hypothyroidism. Further research is needed to establish proper therapeutic guidelines and strengthen the link between hypothyroidism, mental disorders, and challenges in engaging in regular physical activities.

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