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Neuropsychological Changes in Patients with Congenital Hypothyroidism Treated with Levothyroxine: Associated Factors and Thyroid Hormone Resistance

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Introduction

Congenital hypothyroidism is a condition characterized by an insufficient production of thyroid hormones from birth, which can significantly affect growth, metabolism, and neurodevelopment. Early diagnosis and treatment with levothyroxine, a synthetic thyroid hormone, have dramatically improved outcomes for individuals with CH, particularly in preventing severe intellectual disability. However, despite adequate treatment, some patients exhibit persistent neuropsychological alterations, suggesting that factors beyond simple hormone replacement therapy may contribute to these deficits. Understanding the mechanisms behind these neuropsychological changes and the potential role of thyroid hormone hyposensitivity is essential for optimizing management and improving patient outcomes [1].

Thyroid hormones are critical for brain development, especially during the fetal and early postnatal periods. They influence processes such as neurogenesis, synaptogenesis, myelination, and neuronal migration. Any disruption in thyroid hormone availability during critical developmental windows can lead to long-lasting effects on cognitive, emotional, and behavioral functions. Although levothyroxine therapy aims to normalize thyroid hormone levels, there is evidence that some patients with CH continue to experience difficulties in areas such as attention, memory, executive function, and emotional regulation. These neuropsychological alterations suggest that the replacement therapy may not fully replicate the natural hormonal dynamics required for optimal neurodevelopment or that other underlying factors may be at play [2]

One possible explanation for these persistent neuropsychological deficits is the phenomenon of thyroid hormone hyposensitivity, wherein tissues, including the brain, exhibit reduced responsiveness to circulating thyroid hormones. Thyroid hormone action is mediated by thyroid hormone receptors and regulated by intracellular deiodinases, transporters, and cofactors that control hormone availability and receptor sensitivity. Any disruption in these pathways can impair the ability of target tissues to respond to thyroid hormones, even when serum levels are normalized by levothyroxine therapy. In CH patients, genetic variations or epigenetic modifications affecting these regulatory mechanisms could contribute to thyroid hormone hyposensitivity and associated neuropsychological changes.

Description

Several factors have been linked to the neuropsychological outcomes of CH patients treated with levothyroxine. The timing of diagnosis and initiation of treatment plays a critical role. Early initiation of therapy, ideally within the first two weeks of life, is crucial for minimizing neurodevelopmental impairments. Delayed treatment increases the risk of neuropsychological deficits, as critical periods for brain development may be missed. Even with early treatment, the adequacy of levothyroxine dosing is important. Both under-treatment and over-treatment can have adverse effects. Suboptimal dosing may fail to fully correct hypothyroidism, while excessive dosing can lead to hyperthyroidism-like symptoms, which are also detrimental to brain function. The quality of hormone regulation during treatment is another critical factor. Maintaining stable thyroid hormone levels within the target range is essential for normal neurodevelopment. Fluctuations in hormone levels, as evidenced by variability in TSH or free T4 measurements, have been associated with worse neuropsychological outcomes. Such fluctuations may reflect challenges in achieving precise dosing or individual variability in hormone metabolism and sensitivity [3].

In addition to treatment-related factors, intrinsic characteristics of CH itself may influence neuropsychological outcomes. The severity of the thyroid hormone deficiency at diagnosis, as indicated by extremely high TSH levels or undetectable thyroid hormones, is associated with greater risks of cognitive and behavioral impairments. This may be due to the longer duration of uncorrected hypothyroidism during critical developmental periods. Furthermore, certain etiologies of CH, such as thyroid agenesis or ectopia, are associated with a higher risk of neuropsychological deficits compared to cases caused by transient or mild dysfunction. Genetic factors may also contribute to neuropsychological outcomes in CH patients. Variants in genes involved in thyroid hormone transport, metabolism, and signaling, such as SLC16A2, DIO2, or THRB, could affect brain sensitivity to thyroid hormones. These genetic factors might partially explain the variability in outcomes among patients receiving similar treatment regimens. Research into these genetic mechanisms is ongoing, but their role highlights the complexity of thyroid hormone action and its impact on neurodevelopment [4].

The role of thyroid hormone resistance, a condition in which tissues exhibit reduced responsiveness to normal or elevated levels of thyroid hormones, is particularly intriguing in the context of CH. Resistance to thyroid hormone can be caused by mutations in the THR genes, particularly THRB. While RTH is rare, subclinical forms of thyroid hormone hyposensitivity may be more common and could contribute to neuropsychological alterations in CH patients. For example, impaired function of THRs in the brain could limit the effects of levothyroxine on neurodevelopment, even when serum hormone levels are normalized. Similarly, abnormalities in thyroid hormone transport across the blood-brain barrier, mediated by proteins such as MCT8, could reduce hormone availability in the central nervous system. Environmental and psychosocial factors also play a role in shaping neuropsychological outcomes in CH patients. Access to healthcare, adherence to treatment, and family support are critical for ensuring effective management of the condition. Additionally, the presence of comorbid conditions, such as attention-deficit/hyperactivity disorder or learning disabilities may complicate the neuropsychological profile of CH patients. These factors underscore the importance of a multidisciplinary approach to care, involving endocrinologists, neurologists, psychologists, and educators.

Addressing neuropsychological alterations in CH patients requires a

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comprehensive understanding of the underlying mechanisms and contributing factors. Routine neuropsychological assessments should be incorporated into the long-term follow-up of CH patients to identify and address deficits early. Interventions such as cognitive-behavioral therapy, educational support, and pharmacological treatments for comorbid conditions may help improve quality of life and functional outcomes. Additionally, optimizing levothyroxine therapy, including more precise dosing strategies and the use of combination therapies, could enhance treatment effectiveness. Future research should focus on elucidating the molecular and genetic mechanisms underlying thyroid hormone hyposensitivity in CH patients. Advances in genomics and transcriptomics could identify biomarkers of thyroid hormone resistance and guide personalized treatment approaches. Furthermore, studies investigating the role of novel therapeutic agents, such as selective thyroid hormone receptor agonists, could offer new strategies for addressing tissue-specific hyposensitivity [5].

Conclusion

While levothyroxine therapy has significantly improved the prognosis for patients with congenital hypothyroidism, neuropsychological alterations remain a concern for some individuals. These deficits may be linked to thyroid hormone hyposensitivity, variability in treatment effectiveness, and intrinsic factors related to the severity and etiology of CH. By addressing these challenges through personalized treatment, multidisciplinary care, and ongoing research, it is possible to further improve outcomes and ensure that individuals with CH reach their full cognitive and developmental potential.

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Conflict of Interest

None.

References

1. Razón-Hernández Karla Cristina, Norma Osnaya-Brizuela and Armando Valenzuela-Peraza, et al. "Neuropsychological Alterations in Patients with Congenital Hypothyroidism Treated with Levothyroxine: Linked Factors and Thyroid Hormone Hyposensitivity." *J Clin Med* 11 (2022): 3427.
2. Pardo Campos María L, Mariel Fernanda Musso, Ana Keselman and Laura Gruñeiro, et al. "Cognitive profiles of patients with early detected and treated congenital hypothyroidism." (2017).
3. Sawicka-Gutaj Nadia, Natalia Zawalna, Paweł Gut and Marek Ruchała. "Relationship between thyroid hormones and central nervous system metabolism in physiological and pathological conditions." *Pharmacol Rep* 74 (2022): 847-858.
4. Stagi Stefano, Giovanna Municchi, Marta Ferrari and Malgorzata Gabriela Wasniewska. "An overview on different l-thyroxine (l-t4) formulations and factors potentially influencing the treatment of congenital hypothyroidism during the first 3 years of life." *Front Endocrinol* 13 (2022): 859487.
5. Salerno Mariacarolina, Roberto Militerni, Carmela Bravaccio and Maria Micillo, et al. "Effect of different starting doses of levothyroxine on growth and intellectual outcome at four years of age in congenital hypothyroidism." *Thyroid* 12 (2002): 45-52.

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