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Original Article

Dependence of Cognitive and Mental Development in Children with Autism Spectrum Disorder on Thyroid Dysfunction and Cortisol Imbalance

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Abstract

Causal relationships and statistically proven correlations have been established between hypothyroidism and / or cortisol imbalance and negative behaviors and violations of mental and cognitive development in children with autism spectrum disorder. Also, correcting hormonal disorders led to a decrease in negative behaviors and noticeable improvements in mental states and cognitive functions. Successful therapeutic strategies are proposed for all types of hormonal disorders considered.

Clinicians should pay attention to subclinical forms of hormonal disorders in children with ASD. Parents and correctional professionals working with these children should consider that negative behaviors and developmental delays may be associated with a disruption in the hormonal levels of a child.

Keywords: Anxiety; ASD; Autism; Cognitive impairment; Cortisol imbalance; HPA; Hypothyroidism; Obsessive-compulsive disorder; thyroid gland

Purpose of the Study

- Identify and systematize pathological changes in the hypothalamic-pituitary-adrenal (HPA) axis
- Establish causal relationships between these changes and mental disorders and cognitive development in children with Autism Spectrum Disorder (ASD)

Research objectives

- Study the relationship between impaired cognitive development, interpersonal interactions, and communication in children with ASD with the development of hypothyroidism and / or cortisol imbalance
- Describe any pathological changes in the HPA axis in children with ASD
- Suggest therapeutic strategies for stabilizing cortisol levels and restoring / supporting thyroid function

Research materials

Research on the impact of HPA imbalance on behavior, mental health, and cognitive functions in children was conducted at the Center for Integrative Medicine, Miraculum (Tbilisi, Georgia; www.facebook.com/autism.ge), during a period of 16 months as part of a general study of the relationship between negative behavior in children with ASD and various pathological conditions. During this period, 86 patients with ASD, ages 3 to 16 years, were involved. Diagnoses: childhood autism (F.84) and atypical autism (F.84.1).

For this article, the considered sample was limited to patients with confirmed HPA imbalance. This was 37% of the entire sample or 32 children. In this group, hypothyroidism was diagnosed in 8 patients. Cortisol imbalance was found in 17, including 9 with low and 8 with high cortisol levels. In 7 children, hypothyroidism was combined with a cortisol imbalance.

Research methods

- Study of the history of the disease in a child's life
- Assessment of physical development
- Examination by the following specialists: neurologist, endocrinologist, clinical psychologist, pediatrician
- Laboratory diagnostics: measurement of levels of TSH, T3,T4, cortisol (daily level of saliva, ELICA method, morning / night) (Mrcheveli Laboratory; Tbilisi, Georgia)
- Assessment of a child's basic skills at his / her developmental level. Sparrow et al.'s (1985) Vineland Adaptive Behavior Scales: Classroom Edition was used as the assessment instrument

Conclusion

- A stable relationship (including a statistically high degree of positive or negative correlation) was established between
  - Thyroid dysfunction and impaired cognitive development in children with ASD
  - Cortisol imbalance and disorders in mental health, communication, and socialization

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- The correction of hormonal disturbances (with the correction of disturbances in other major bodily systems) leads to a decrease or elimination of negative behavior and an improvement in mental state and cognitive development.
- In view of the above; clinical practitioners, pediatricians, parents, and correctional specialists working with ASD children should pay attention to possible hormonal imbalances as a cause of negative behavior and delayed mental and cognitive development.

Introduction

Unlike other basic systems in a child's body (gastrointestinal tract, immune system, nervous system, genetic diseases, gene polymorphisms), HPA disorders in children with ASD have been the subject of independent research relatively rarely [1]. It is worth noting that only a few works have been carried out in recent years in the following areas:

- Dysfunction of the thyroid gland and delayed development of a child [2-4]
- Thyroid function in mothers of children with ASD, with women diagnosed with hypothyroidism giving birth to children who quite often, at the age of 14 months, showed signs of autism with impaired intelligence and delayed cognitive development [5,6]
- Imbalance in the level of steroid hormones, especially cortisol, in children with ASD compared with neurotypical children [7]
- Imbalance in the levels of testosterone and oxytocin in children with ASD compared to neurotypical children [8]
- Comparative studies of cortisol, melatonin, and oxytocin levels in neurotypical children and in children with ASD, confirming the frequent imbalance in the levels of these hormones in children with ASD [9].

The lack of medical science's attention to the problems of the HPA axis in children with ASD leads to neglecting its disruptions in clinical practice. For example, over the past decade, many studies and publications have appeared, and hundreds of conferences held, where the existence of a close relationship between the intestinal microbiocenosis and a child's brain has been proven. Because of this; clinicians, psychologists, and parents in recent years began giving priority to diagnosing and correcting pathological changes in the gastrointestinal tract of children with ASD. This approach is gradually becoming an irreversible trend.

However, the situation with ASD children is completely different in the field of endocrinology. There are very few evidence-based publications, and clinicians rarely examine hormonal levels in autistic children. Moreover, they do not associate, and do not try to associate, changes in hormonal levels with the cognitive development and mental state of children with ASD.

This article, describing research that occurred, is intended to contribute to a change in this situation. Its task is to show clinical practitioners, pediatricians, parents, and correctional specialists working with ASD children that, in some cases, negative behaviors and mental and cognitive developmental delays can be associated with hormonal imbalances. In these cases, the correction of hormonal disorders (with the correction of disorders in other basic bodily systems) leads to a decrease or elimination of negative behaviors and an improvement in mental states and cognitive development. If, after successful correction of the gut microbiome, a child does not improve his or her behavioral and cognitive abilities, psychotropic drugs should not be resorted to immediately. It is necessary to first check whether the HPA axis is working correctly and, if necessary, make subsequent corrections.

Behavior Assessment Methodology

This research studied the effects of decreased thyroid function with high or low levels of cortisol on the cognitive status of children and their level of socialization, communication, motor skills, and household skills.

The Vineland Adaptive Behavior Scale (VABS) was used to assess the behavior and condition of children in the study. This scoring test was chosen because the patient sample was predominantly composed of children with severe autism who are not able to respond to detailed testing and evaluation. The results of the Vineland Scale, based on conversations conducted with people from a child's immediate environment and parents, give the most reliable information when a child is non-verbal. The immediate environment included teachers, educators (tutors), and relatives living with a child. A child, if unable to provide the required information, did not participate in the diagnostic study.

This study is based on a scoring system for data interpretation. For each available skill, the child was awarded 1 point; in the absence of a skill, 0 points. For the purposes of this study, the Classroom Edition of the VABS was divided into 3 independent blocks (Figure 1).

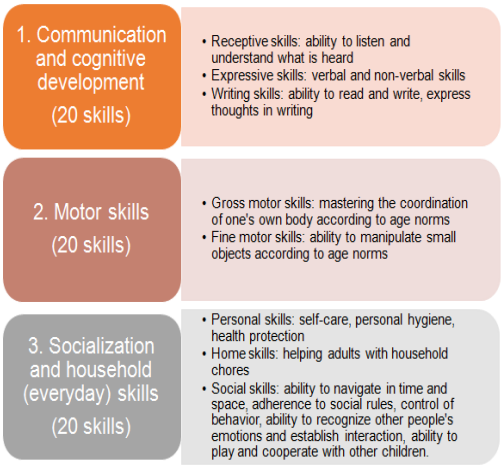


Figure 1: Contents of VABS's three blocks.

Research Results

We established the following causal relationships between thyroid dysfunction and cortisol imbalance and mental, behavioral, and cognitive impairments in children with ASD (Figure 2).

Hypothyroidism in the absence of a cortisol imbalance led to impairments, primarily in the area of cognitive development and the acquisition of motor skills. This is confirmed by the statistical processing of research data (Graph 1). A negative correlation means

that, with an increase in the TSH level; i.e., with a high level of thyroid hormone deficiency in children; communication, socialization, and cognitive functions deteriorate, and fine and gross motor skills are impaired. It should be noted that hypothyroidism most strongly affects fine and gross motor skills, probably due to a general decrease in tone and metabolism with hypothyroidism (Figure 3).

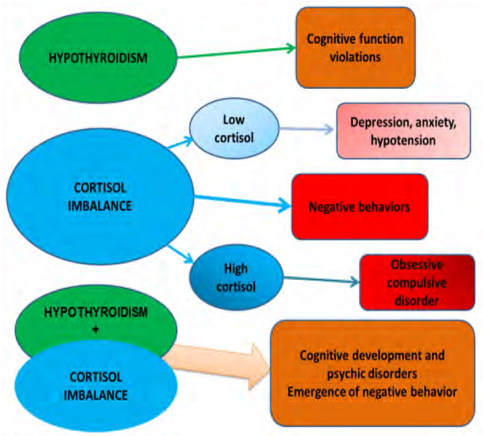
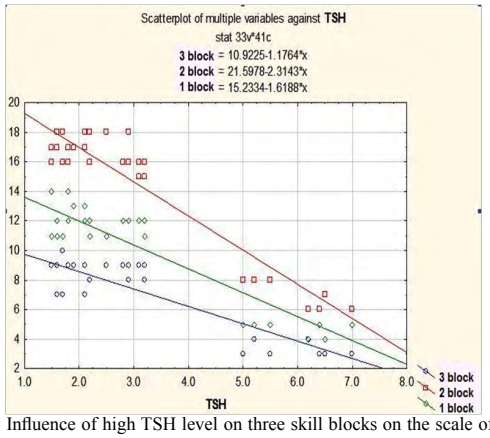


Figure 2: External symptoms of hormonal disorders in children with ASD (based on the results of a study by the Miraculum Center).



Graph 1: Influence of high TSH level on three skill blocks on the scale of adaptive behavior.

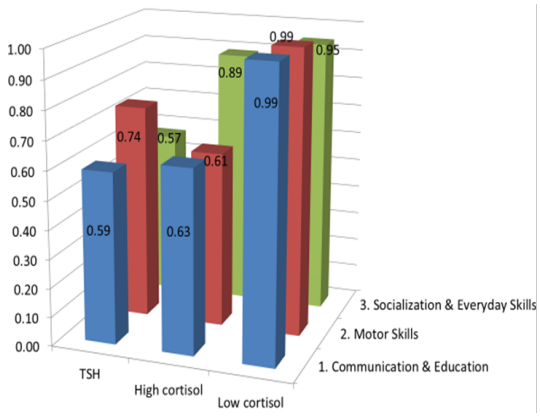
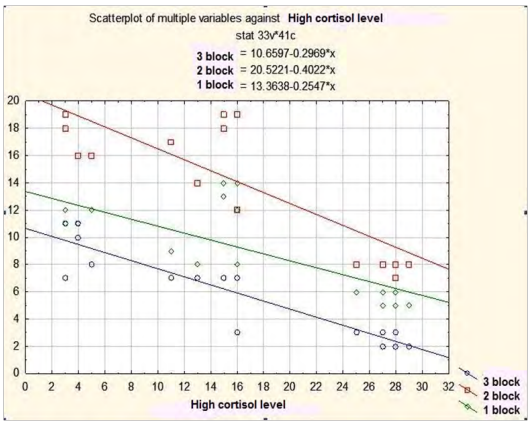


Figure 3: Statistical correlations between TSH, high / low cortisol, and (1) communication & education skills, (2) motor skills, (3) socialization and everyday skills.

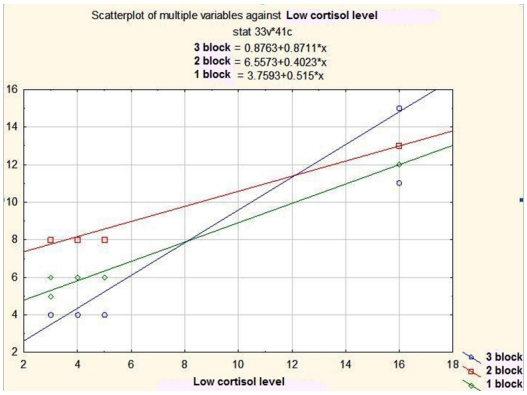
High levels of cortisol led to high anxiety; an increase in repetitive, persistent, and obsessive thoughts (obsessions); and repetition of stereotypic actions and movements. With this group of disorders,it can be stated that high cortisol can bring children in this group to borderline Obsessive-Compulsive Disorder (OCD).

Statistical processing of the data (Graph 2) showed that the high level of cortisol affects the level of socialization and communication (Figure 3). This is most likely due to the high level of anxiety and emotional lability recorded at high levels of cortisol [10].



Graph 2: Influence of high cortisol level on three skill blocks on the scale of adaptive behavior.

Low cortisol levels also led to manifestations of negative behavior and, at the same time, contributed to the development of depression, high anxiety, and hypotension (arterial hypotension). With a low level of cortisol in children, significant impairments were recorded in the cognitive sphere, communication, socialization, and everyday skills (Graph 3). This is due to the significant physiological changes that occur in all systems when there is a low level of cortisol (hypotension, depression, or a high level of anxiety) [10]. Statistical processing of data resulting from a low level of cortisol showed the highest correlations for all three blocks (Figure 3).



Graph 3: Influence of low cortisol level on three skill blocks on the scale of adaptive behavior.

The combination of hypothyroidism and an imbalance of cortisol led to the most severe and systemic disorders in both behavior and cognitive development. Statistical processing in this case could not be

done due to the many multidirectional indicators. However, clinical observations were sufficient for this conclusion.

Statistical Processing of Data

The method of nonparametric processing, namely Spearman's rank correlation coefficient, was used for statistical data processing. To assess the strength of correlations between the variables, we used the Chaddock scale, which interpreted the value of the coefficient. During the study, the following direct correlations were identified and statistically evaluated:

- Negative correlations between the level of TSH (deficiency of thyroid hormones) and the skill level in block 1 (communication and cognitive development), block 2 (motor skills), and block 3 (social and everyday skills);
- Positive correlations between low cortisol levels and skill levels in blocks 1, 2, 3;
- Negative correlations between high cortisol levels and skill levels in blocks 1, 2, 3.

Spearman correlation coefficient between TSH and:

- Block1 – 0.5923 (strong negative dependence),
- Block 2 – 0.7419 (very strong negative dependence),
- Block3 – 0.5725 (strong negative dependence).

Spearman correlation coefficient between high cortisol and:

- Block1 – 0.6340 (strong negative dependence),
- Block2 – 0.6069 (strong negative dependence),
- Block3 – 0.8875 (very strong negative).

Spearman correlation coefficient between low cortisol and:

- Block 1 – 0.9941 (very strong positive dependence),
- Block 2 – 0.9879 (very strong positive dependence),
- Block 3 – 0.9468 (very strong positive dependence).

Therapeutic Strategies Used in the Study

Hypothyroidism

This group of children underwent L-thyroxine hormone replacement therapy with the addition of co-factors selenium, chromium, and iodine. It is emphasized that the stabilization of thyroid hormone levels began with the stabilization of the gastrointestinal tract [10-12]. The latter is a necessary condition for the successful correction of hormonal disorders.

In diagnosing patients, the low level of iron in the blood was noted. In 7 out of 8 patients; the total level of iron and ferritin was significantly lower than normal. Low iron levels were treated with Ferropol. Correction took from 1 to 1.5 months under laboratory control. It should be noted that correcting iron levels began with stabilization of the gastrointestinal tract.

After the iron level was stabilized, the TSH level also decreased, which means that thyroid functioning improved. Accordingly, the dose of L-thyroxine could be reduced. It is important that the relationship between low iron levels in the body and decreased thyroid function be considered when correcting thyroid functioning.

All 8 children with hypothyroidism had latent (subclinical) hypothyroidism. Against the background of high TSH levels (5 and above), T4 remained relatively normal. It is crucial for clinicians to consider this when diagnosing and treating this cohort of patients. Even with latent hypothyroidism, it must be emphasized that impairments associated primarily with cognitive development and motor skills in children with autism begin to be noted.

Hormone replacement therapy was conducted for several months with constant monitoring of hormonal blood levels. After about two months, parents and professionals began to see a noticeable improvement in children's cognitive development: an accelerated pace in learning new skills and a generalization of skills, an increase in activities and a wider range of interests, the development of more expressive speech and understanding of verbal speech.

A high cortisol level was correlated with obesity, low concentration, and increased anxiety. High cortisol levels were corrected using:

- Paleo nutrition protocol -- aimed at stabilizing the hypothalamic-pituitary axis, among other things
- Pro / pre / symbiotics -- based on the results of microbiome research
- Dietary supplements -- particularly magnesium sulfate, melatonin (as a cortisol antagonist), Omega-3, B vitamins, and CoQ10
- Anxious-depressive emotional background – if recorded in a child, St. John's wort tea used as an antidepressant
- Treatment was continued for at least 3 months. In all cases, parents noted positive dynamics after about 1.5 months from the start of treatment, including weight loss, increased concentration, and decreased anxiety.

A low cortisol level correlated with severe muscular dystonia, sarcopenia, outbursts of aggression, and sleep disturbances. Low cortisol levels were much more difficult to correct. The correction was carried out continuously for at least 3 months and included:

- Anti-inflammatory nutritional protocol
- B vitamins, in particular B5, and liposomal vitamin C
- Adaptogens; including licorice, St. John's wort, and Eleutherococcus senticosus (Siberian ginseng)

Approximately 3-4 months after the start of treatment, parents noted improvements in behavior: a decrease in repetitive behavior and obsessions and an improvement in mental status. However, in terms of muscular dystonia and sarcopenia, there were no changes or improvements were insignificant.

Hypothyroidism Combined with a Cortisol Imbalance

These were the most difficult patients in terms of physical condition and dynamics of changes, with all groups of impairments observed, including cognitive development, mental status, communication, socialization, and motor skills. With this cohort, treatment also focused on stabilizing the balance of the gastrointestinal tract, correcting cortisol levels, hormone replacement therapy, and diet therapy. The treatment was carried out over several months. It should also be noted that, during treatment, the emotional background and mental status was first stabilized. Then, after about 2 months, a gradual improvement in cognitive and motor functions began.

Because of the results of this study, it is strongly recommended that children with ASD be checked for hormonal disruptions. Additionally,

since indicators are often at the norm border, this possibility should be left open, even when they do not cause alarm in an endocrinologist.

Unfortunately, many clinicians do not pay attention to subclinical forms of hypothyroidism or to borderline indicators of cortisol imbalances. However, an exception must be made for children with ASD. For many of them, at the border of the norm, there may be indicators not for just one but for several main, bodily systems. Separately, a borderline state may not be dangerous, but, when several systems interact, the sluggish process of pathological changes in a child's body can lead to catastrophic consequences. The sooner they are attended to, the more effective the correction of existing or emerging violations will be.

It is difficult to overestimate the role that the hormonal system plays, at the same time, in starting this pathological process. Anything associated with hormonal disruption often causes irreparable harm, not only to the brain but to the entire body. The hormonal system, as a system that maintains homeostasis, balances the stable functioning of a child's entire body.

Naturally, one cannot be limited only to stating the dependence of the mental and cognitive development of children on hypothyroidism, cortisol imbalance, and other hormonal disruptions. New systemic studies are needed to further research and study the pathophysiological mechanisms of triggering developmental disorders due to hormonal disturbances. In the future, this will make it possible to create and increase the effectiveness of both targeted pharmacological therapy and timely diagnosis of disorders to avoid damage and / or delay in the development of the cerebral cortex.

Conclusion

The hormonal disorders considered had the following consequences in children's development:

- Hypothyroidism in the absence of a cortisol imbalance resulted in delayed cognitive development and motor skills.
- A cortisol imbalance did not significantly slow cognitive development but did cause negative behavior with impaired communication and socialization.
- High cortisol levels led to high anxiety; an increase in repetitive, persistent, and obsessive thoughts (obsessions); repetition of stereotypic actions; low concentration;and impaired interpersonal interaction and communication.
- Low cortisol levels led to negative behavior but also contributed to the development of depression, high anxiety, and arterial hypotension [1].
- A combination of hypothyroidism and a cortisol imbalance led to the most severe and systemic impairments, both in behavior and in cognitive development.

Correction of thyroid dysfunction and / or cortisol imbalance led to improved behavior and increased mental and cognitive development in a child. Normalization of intestinal microbiocenosis was a necessary condition for successful correction of hormonal disorders. It must be noted that correction of the gastrointestinal tract was unstable and fraught with the possibility of relapses without subsequent correction of the hormonal background. This also applies to other basic systems in a child's body when violations occur.

When diagnosing hormonal problems in children with ASD, subclinical forms of hypothyroidism and cortisol imbalance cannot be ignored. Also, attention must be given to a possibly low iron level in the blood.

Psychologists, psychiatrists, and other professionals who work with children identified as having ASD and other associated diagnoses should bear in mind that negative behaviors and other developmental disorders that are the basis for the diagnosis of autism may have medical origins, including hormonal ones. It is not recommended that psychotropic drugs be administered for negative behaviors in children before checking their hormonal state.

Patient Consent Statement

All guardians of patients signed an agreement to participate in this study.

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