The possible relationship between thyroid dysfunctions, weight gain, and attention deficit/hyperactivity disorder (ADHD) among children and adolescents: A consultation-liaison psychiatry sample with pediatric endocrinology

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Date submitted: Aug 01, 2018
Date accepted: Aug 10, 2018
Online publication date: December 15, 2018

ABSTRACT
Aims: Attention Deficit/Hyperactivity Disorder (ADHD) is a common neuropsychiatric disorders in the pediatric population. Genetic, biological and psychosocial factors are involved in the occurrence of ADHD but the exact etiology is still unknown. Thyroid functions are critical to neurocognitive development in childhood. The aim of this study was to investigate the relationship between ADHD, thyroid functions and weight gain in children.

Methods: Children aged 7 to 15 years having a diagnosis of ADHD who were consulted to the pediatric endocrinology unit for weight gain were recruited. Anthropometric measurements, blood levels of thyroid stimulating hormone (TSH), free (F) T3, FT4, Anti (thyroglobuline) TG and Anti (thyroid peroxidase) TPO were obtained and a thyroid sonography was performed for each patient.

Results: Among the participants (n=11), 4 (36.4%) were obese and 4 (36.4%) had subclinical hypothyroidism. Two patients (18.2%) were both obese and had subclinical hypothyroidism. Patients with ADHD and subclinical hypothyroidism had higher mean TSH level than patients those with ADHD and obese ones, but had lower FT4 levels. Thyroid volume of a 13-year-old girl who had subclinical hypothyroidism was>+2SD.

Conclusions: Although there is not enough evidence that hypothyroidism is an important problem in ADHD, we found a higher ratio of subclinical hypothyroidism and obesity in this sample. This is an important result and should be carried out in consultation-liaison patients.

Introduction
Attention deficit-hyperactivity disorder (ADHD) is one of the most common neuropsychiatric disorders in the pediatric population that has a negative effect on cognitive functions. The three core symptoms of ADHD are attention deficit, hyperactivity, and impulsivity (1). The disorder has an estimated prevalence of 5-10 % among children and adolescents boys are affected 2-10 times more than the girls (2). ADHD persists into adulthood for approximately two-thirds of the patients and understanding this fact has heightened the interest of professionals on the common etiological factors of both ADHD and other medical problems (3).

Some known genetic, biological, environmental and psychosocial factors have a role in the development of ADHD (4) but still, the certain etiology of the disorder is unknown. Among biological-endocrinological variables, thyroid functions play a vital role on neurocognitive development in childhood (5) and thyroid dysfunction both hyperthyroidism and hypothyroidism are common in ADHD children (6). Recent studies suggest that the other common endocrine problem in ADHD children is overweight and obesity (7). Although the relationship between hypothyroidism-obesity is known, this relationship has not been previously investigated in children with ADHD.

The aim of this study was to investigate whether there is a relationship between subclinical thyroid dysfunction and ADHD among children and adolescents who were consulted to pediatric endocrinology for regional fat gain, overweight or obesity.

The sample consists of 11 ADHD children and adolescents who were between 7-15 ages and consulted to pediatric endocrinology department for regional fat gain, overweight or obesity problem. ADHD was diagnosed by a child and adolescent psychiatrist by clinical interviews using ‘The Schedule for Affective Disorders and Schizophrenia for School-Aged Children Present and Lifetime Version (K-SADS-PL)’. K-SADS-PL is a semi-structured psychiatric interview developed by Kaufman and colleagues to investigate psychiatric diagnosis of children and adolescents between ages 6-17 (8). Its validity and reliability study was conducted for Turkish children by Gokler et al.(9). All of the cases were also evaluated with the detailed physical
examination, pubertal staging (according to Tanner stage system) and anthropometric measures (chronological age, height, weight, standing height, which was expressed as SD score and body mass index (BMI: weight(kg)/height (meters)).

Obesity was defined as a BMI greater than the 95th percentile for age and sex. BMI reference curves for Turkish children were used for evaluation.

The thyroid gland was assessed by palpation and graded according to the goitre classification system proposed by WHO. Serum free T3, free T4, TSH, antithyroglobulin (anti-TG), antithyroid peroxidase antibody (anti-TPO) levels of all the children were measured using the venous blood sample. Serum free T3, T4 levels were measured by competitive immunnoassay method using immunodiagnostic products while anti-TG and anti-TPO were measured using immunometric assay method. Thyrotropin releasing hormone (TRH) test was also performed for all of the children with ADHD. TSH response to TRH was considered to be normal between levels 5-25 mIU/L and the values above 25 mIU/L were accepted as exaggerated and those below 5 mIU/L were accepted as suppressed. Thyroid sonography was performed by high-resolution ultrasound, using 7.5 mHz probes and thyroid volumes were calculated by the Neu reference criteria (11). Accordingly, cases with thyroid volumes above the 97th percentile were accepted as goitre. The protocol was approved by the local research ethics committee of Ufuk University and all subjects gave informed consent. All data were evaluated by SPSS-16.0 version. All statistics are reported two-tailed; standard deviations are reported throughout.

**Results**

Among the sample nine patients (81.8%) were male and two (18.1%) were female. Mean age was 11.7±0.67 years old and mean BMI was 19.10±1.33. Four patients (36.4%) were obese and four patients had subclinical hypothyroidism. Two patients (18.2%) were both obese and also had subclinical hypothyroidism. Patients with both ADHD and subclinical hypothyroidism had higher TSH level than patients with ADHD and obese, but had lower FT4 levels (Table 1). Thyroid volume of the 13-year-old girl who had subclinical hypothyroidism was > +2SD. The parenchyma of her thyroid gland has found in heterogeneous configuration. Among the cases, there was no anti-TG or anti-TPO positivity.

**Table 1. Antropometric Measures and Thyroid Hormone Levels of the Group**

<table>
<thead>
<tr>
<th>Parameter (kg)</th>
<th>ADHD (n=11)</th>
<th>ADHD+SH (n=4)</th>
<th>ADHD+O (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>43.6±5.3</td>
<td>43.7±7.7</td>
<td>50±8.0</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>151.2±6.3</td>
<td>147.7±9.2</td>
<td>146.2±8.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>19.1±1.3</td>
<td>20.7±2.3</td>
<td>23.4±1.4</td>
</tr>
<tr>
<td>TSH (IU/L)</td>
<td>3.6±0.4</td>
<td>5.2±0.5</td>
<td>3.4±0.8</td>
</tr>
<tr>
<td>FT4 (ng/dl)</td>
<td>1.2±0.1</td>
<td>1.0±0.1</td>
<td>1.3±0.1</td>
</tr>
<tr>
<td>FT3 (µg/dl)</td>
<td>0.4±0.1</td>
<td>0.4±0.1</td>
<td>0.4±0.0</td>
</tr>
</tbody>
</table>

Kg: kilogram; cm: centimeter; m²: square meters; IU/L: International Units Per Litre; ng/dl: nanogram/deciliter; µg/dl: microgram/deciliter

**Discussion**

To our knowledge, this is one of the few studies investigating the relationship between ADHD and thyroid functions and/or subclinical hypothyroidism among children who consulted to pediatric endocrinology clinics for regional fat gain, overweight or obesity. Thyroid dysfunction and obesity had high ratios in our sample. A prospective study which screened thyroid abnormalities in 277 children with ADHD at the University of Chicago found that the prevalence of thyroid abnormalities is high (5.4%) in children with ADHD than in the normal population (<1%) (10). Thyroid hormones are known to be very important for the development of the central nervous system, especially for the developing brain of the pediatric age population. Problems arise from thyroid gland and the thyroid hormones have the capacity to form neuropsychiatric syndromes and symptoms including attention deficit hyperactivity disorder, autism, and associated neurodevelopmental and behavioral problems (11). Haddow et al. found that fetus who had thyroid gland disturbance had lower IQ levels than the controls (12). The results of their study demonstrated that synthetic chemicals even in very low concentrations can interfere with the thyroid system, and affect intellectual and behavioral development of embryo and lead to a serial of neurological problems including ADHD. Attention deficit-hyperactivity disorder has been related to many factors such as allergens, toxicity of heavy metals, low protein diets with a high carbohydrate content, unbalanced minerals, amino acid deficits, thyroid disorders, and vitamin B complex disorders (13). In a Spanish study thyroid hormones (free T4 and T3) and TSH concentrations were measured in preschoolers and their relation with ADHD symptoms had been investigated. Children with TSH concentrations in the upper quartile of the normal range had been found at higher risk for ADHD (14). Another study from the USA found that higher concentrations of normal FT4 levels were associated with mood lability, preoccupations, and lower ratings of attention problems (15).

On the other hand, epidemiologic studies suggest that obesity in children may be associated with a reduced level of physical activity so the expectation was the low prevalence of obesity/overweight in children with ADHD but the result is different. Studies demonstrated that ADHD is not a preventive factor for obesity (7, 16). Also Curtin et al. reported that the prevalence of overweight was %29 and the prevalence of obesity as %17.3 in ADHD children ages between 3-18 years. Especially the prevalence of obesity was 42.9% in children between 2-5 ages (16). Our results are in accordance with these studies and the general population.

The high ratios of thyroid dysfunction and obesity in the current study may be an important finding to highlight the importance of consultation-liaison studies between child psychiatry and endocrinology departments and detailed endocrinological examination in children with ADHD.

The major limitation of the study is the small sample size. The results of the investigation may be conceived as preliminary findings of the relationship between subclinical thyroid dysfunction, weight gain and ADHD. So that this relation should be studied in the larger number of ADHD populations.

**Acknowledgments**

This study was designed by ATE and AG. Data was collected and analyzed by ATE, AG and HG. Manuscript was written by AG, ATE and HG. There was no financial assistance with the project.

**Conflict of Interest**

The authors declared they do not have anything to disclose.
regarding conflict of interest with respect to this manuscript.

References