ORIGINAL ARTICLE

Assessment of serum levels resistin in girls with anorexia nervosa.

Part II. Relationships between serum levels of resistin and thyroid, adrenal and gonadal hormones

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Abstract

OBJECTIVES: Thyroid, adrenal glands and gonadal hormones play a role in maintaining metabolic homeostasis of the body via the receptors located in the adipose tissue. The correlations between serum resistin (RES) and function of other hormonal axes in patients with AN have not been established, yet. Therefore, the aim of this study is: 1) assessment of concentrations of thyroid hormones (FT4, TSH), adrenal hormones (ACTH, cortisol), sex hormones (LH, FSH, estradiol, testosterone); 2) establishing their relationship with BMI and 3) analysis of correlations between examined hormones and RES serum concentrations in adolescent female patients with AN.

DESIGN AND SETTING: Serum RES (ELISA) and fT4, TSH, ACTH, LH, FSH, estradiol and testosterone (ECLIA) concentrations have been assayed in 195 adolescent girls: 87 with restrictive AN, 17 with not otherwise specified eating disorders (NOS), 30 with simple obesity (OB) and 61 healthy (H) subjects.

RESULTS: Mean serum FT4, LH and estradiol concentrations were significantly lower (p=0.015; p<0.0001; p<0.0001, respectively) in AN than in OB group, and cortisol increased (p<0.001) compared to OB and H subjects. In all examined subjects BMI correlated positively (p<0.0001) with LH (r=0.61) and estradiol (r=0.30), and negatively with cortisol (r=–0.35; p=0.008). Also the significant positive relationship between serum RES and FT4 (r=0.34), LH (r=0.57) as well as estradiol (r=0.28) was observed, whereas serum cortisol correlated negatively with RES (r=–0.40).

CONCLUSION: Changes in resistin serum concentrations in eating disorders may be involved in the altered regulation of hypothalamic-pituitary-adrenal, thyroid and gonadal axes.

INTRODUCTION

Anorexia nervosa (AN) in young women is an example of chronic body fat deficit. This disease may serve as a biological model of chronic loss of body fat and body energy imbalances.

The adipose tissue is the source and reservoir of adipocytokines, showing endocrine and auto-/paracrine effects, including resistin (RES), as well as the site where steroid hormones and thyroid hormones are metabolised. The adipose tissue contains receptors of the adrenergic system as well as receptors for thyroid hormones, glucocorticoids, androgens, oestrogens, cytokines, lipoproteins, growth factors (Kershaw & Flier 2004). This clear association of the adipose tissue with hormones and cytokines suggests the possibility of mutual relations and cooperation in the mechanisms of energy, metabolic and immune homeostasis of the body.

Little is known about the relationship between the RES and the hormones of the thyroid, adrenal glands and gonads, which, the same as insulin, catecholamines, and growth hormone play a role in maintaining energy and metabolic homeostasis of the body *via* the receptors located in the adipose tissue. Until now, the relationship between RES and insulin aroused the greatest interest of researchers (Anderlová *et al.* 2006; Koerner *et al.* 2005; Li *et al.* 2006; Steppan *et al.* 2001). However, there are still unresolved questions about the correlations between serum RES and function of other hormonal axes in patients with eating disorders, including AN. Therefore, the objectives of this study are: 1) assessment of concentrations of thyroid hormones (FT4, TSH), adrenal hormones (ACTH, cortisol), sex hormones (LH, FSH, estradiol, testosterone); 2) establishing their relationship with BMI and 3) analysis of correlations between examined hormones and resistin serum concentrations in adolescent female patients with AN.

MATERIAL AND METHODS

The study was performed 195 girls aged 11 to 19 years included into four groups: the group of anorectic girls (AN), as well as the following control groups: NOS (not otherwise specified eating disorders), OB (simple obesity) and H (healthy) (Table 1).

BMI (Body Mass Index: BMI = (weight [kg]/height [m]^2) and BMI-SDS (body mass index standard deviation score) using the following formula: BMI-SDS = (current patient's BMI [kg/m^2] – BMI at 50th percentile [kg/m^2])/ (½ × BMI at 50th percentile [kg/m^2] – BMI at 3rd percentile [kg/m^2]) were calculated in all study subjects. The assessment was performed using sex- and age-specific BMI percentile charts, currently valid for the Polish population (Palczewska & Niedźwiecka 2001).

The AN group consisted of 87 girls (mean age: 15.2 ± 0.3 years) with the restrictive subtype of AN and the NOS group included 17 girls (mean age: 16.4 ± 0.9 years), who failed to meet all the criteria for AN. The diagnosis of AN was established based on the DSM-IV diagnostic criteria (American Psychiatric Association DSM IV 1994).Mean weight in patients with AN was 38.46 ± 1.2 kg, mean BMI: 14.67 ± 0.33 kg/m^2, mean BMI-SDS: –2.65 ± 0.2 (Table 1). Mean weight in the NOS group was 47.5 ± 2.9 kg, mean BMI: 17.86 ± 1.04 kg/m^2, mean BMI-SDS: –1.4 ± 0.68. The OB group consisted of 30 girls with simple obesity (mean age: 14.6 ± 0.8 years; BMI > 97th centile; BMI-SDS > 2 SD). No binge eating disorder was observed in any patient. Mean weight was 85.87 ± 7.58 kg, mean BMI: 31.86 ± 2.19 kg/m^2, mean BMI-SDS: 6.91 ± 1.23. Sixty one female volunteers were included in the H group (mean age: 15.4 ± 0.8 years). None of the healthy subjects used any weight loss diets or other slimming methods within the last three months before the study. Mean weight in the H group was 52.26 ± 3.66 kg, mean BMI: 19.75 ± 1.12 kg/m^2, mean BMI-SDS: –0.18 ± 0.54 (Table 1).

Tab. 1. Characteristics of examined groups of girls.

	AN (n = 87)	**NOS** (n = 17)	**OB** (n = 30)	**H** (n = 61)
		mean ± 1.96 SE (range)		
Age [years]	15.18±0.32 (11.3–18.5)	16.35±0.85* (11.9–18.9)	14.62±0.84* (11–18.3)	15.36±0.8 (11.7–17.9)
Body weight [kg]	38.46±1.2 (26.7–51.6)	47.5±2.9** (39.2–60.7)	85.87±7.58*** (57.7–134.0)	52.26±3.66*** (31.5–71.7)
Height [cm]	162.0±1.49 (143.5–175.0)	163.40±4.50 (146.5–178.0)	163.57±3.51 (145.0–186.5)	162.60±3.49 (138.0–183.0)
BMI [kg/m^2]	14.67±0.33 (10.85–17.85)	17.86±1.04** (14.34–21.85)	31.86±2.19*** (25.5–52.0)	19.75±1.12*** (15.29–23.93)
BMI-SDS	–2.65±0.2 (–5.21–1.08)	–1.42±0.68* (–3.23–1.41)	6.91±1.23*** (3.23–17.83)	–0.18±0.54*** (–2.11–1.89)

H – healthy group; AN – anorexia nervosa group; NOS – not otherwise specified eating disorders group; OB – simple obesity group; SE – standard error; BMI-SDS – body mass index standard deviation score
$^{*}p<0.05$ - NOS vs OB; $^{**}p<0.05$ - NOS vs AN; $^{***}p<0.00001$ - OB and H vs AN

In all study subjects the development of secondary sexual characteristics according to the Tanner scale (Tanner 1962) was consistent with the chronological age. In all patients with AN primary (14 girls) or secondary (73 girls) amenorrhea was observed. One girl in the NOS group was premenarcheal, and 13 others had secondary amenorrhea. All other study subjects had regular menstruations.

The study was approved by the Bioethics Committee of the Medical University of Silesia in Katowice (Register No. KNW-6501-62/08). Informed consent for participation in the study was obtained from all study subjects and their parents or legal guardians.

Serum RES levels were determined in all study subjects by the ELISA method (enzyme-linked immunosorbent assay) using commercial assay kits of Bio-Vendor LLC (USA). The lowest RES concentration determined was 0.1 ng/ml, intra-assay error was 3.4%, and inter-assay was 6.8%. Additionally, serum fT4, TSH, ACTH, LH, FSH, estradiol and testosterone concentrations were determined by the ECLIA (Roche, Switzerland).

The results were analyzed using a licensed version of Statistica v. 3.0 software. In statistical analysis, the distribution of results was tested for consistency with normal distribution using the Shapiro-Wilk test. Significance of differences in mean values was assessed using the analysis of variance (ANOVA) and the homogeneity of variance was evaluated using the Levene's test. As the Shapiro-Wilk test demonstrated that study variable distributions are significantly different from normal distribution, and the Levene's test indicated lack of homogeneity of variance, the non-parametric Kruskal-Wallis test and the median test were used in the final assessment. To verify differences between mean values, the HSD (Honestly Significant Difference) Tukey's multiple comparison test was used for different sample sizes. Correlations were tested using the Spearman test.

RESULTS

Mean body weight and BMI in the AN group were statistically significantly lower compared to the NOS group ($p<0.05$) as well as the OB and H groups ($p<0.00001$). BMI-SDS in the AN group was significantly lower compared to BMI-SDS in the OB and H groups ($p<0.00001$). BMI-SDS of the NOS patients was significantly lower ($p<0.05$) compared to the OB group (Table 1).

Mean TSH concentrations remained within the normal range and were similar between the study groups (AN, NOS, OB, H). Mean FT4 concentrations in the AN group (1.16 ± 0.24 ng/dl) although within the normal limits, but were statistically significantly lower ($p=0.015$) as compared to OB group (1.33 ± 0.27 ng/dl).

In AN patients, mean cortisol concentrations (23.9 ± 11.9 μg/dl) were significantly higher ($p<0.001$) than the mean values obtained in the OB and H groups (14.0 ± 4.9 μg/dl and 13.3 ± 4.8 μg/dl, respectively). Mean serum ACTH levels were normal in all study groups and there were no significant differences between these values in each group.

Mean LH values were below normal and also the lowest in the AN group (0.90 ± 1.3 IU/ml), and the highest in the OB group (7.34 ± 4.5 IU/ml). In the NOS group, mean LH concentrations were 2.7 ± 4.8 IU/ml and among the healthy subjects, 4.8 ± 2.5 IU/ml. The differences between the different LH concentrations obtained in the AN, OB and H groups were statistically significant ($p<0.0001$). There were no statistically significant differences between mean FSH values between the study groups, and these values were within the normal range. Mean serum estradiol concentrations were reduced below normal in the AN group (31.2 ± 18.9 pg/ml) and did not significantly differ from mean values obtained in the NOS group (55.9 ± 60.3 pg/ml), but were significantly lower ($p<0.01$) than these obtained in the OB and H groups (72.7 ± 57.7 pg/ml and 71.1 ± 72.2 pg/ml, respectively). Mean testosterone concentrations were within the normal limits and did not differ significantly between the groups (Table 2).

In the AN group, no correlation was found between concentrations of the examined thyroid, adrenal and gonadal hormones and BMI. However, BMI values in all subjects analyzed together were statistically significantly positively correlated with serum LH (r=0.61; $p<0.0001$) (Figure 1) and estradiol concentrations (r=0.30; $p<0.0001$) (Figure 2), as well as negatively correlated with serum cortisol levels (r=−0.35; $p=0.008$) (Figure 3).

There was no correlation between RES and thyroid, adrenal and gonadal hormones concentrations in the AN group. However, the analysis of these relationships in all subjects combined revealed the significant positive correlations between serum FT4 (r=0.34; $p<0.0001$), LH (r=0.57; $p<0.0001$) and estradiol (r=0.28; $p<0.0002$) concentrations and RES levels. Moreover, the significant negative correlation between cortisol and RES blood levels (r=−0.4; $p<0.0001$) has been stated (Table 3).

DISCUSSION

AN is a good model for the analysis of the relationship between the degree of adipose tissue hormonal disorders and physical, mental and behavioural symptoms of malnutrition. These patients commonly have somatic, metabolic and mental complications resulting from cachexia (Levine 2002; Nogal *et al.* 2008; Palla & Litt 1988; Ziora *et al.* 2006; Żechowski & Jakubczyk 2000). The underlying causes include changes in the secretion of various hormones and neurotransmitters (serotonin, NPY, NA, dopamine, enterohormones), which are responsible for food intake and involved in the pro-

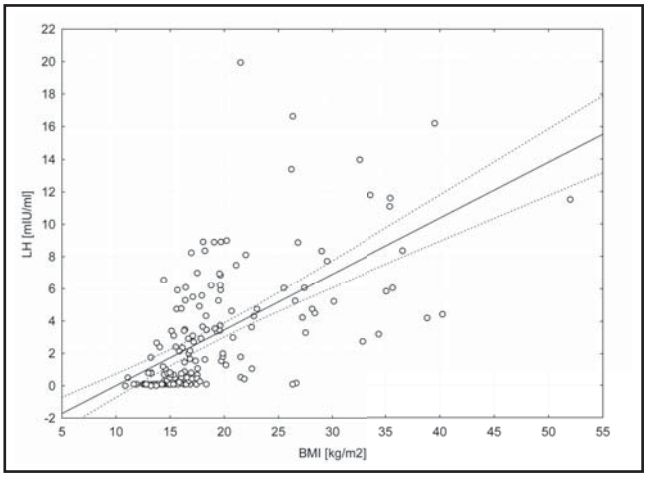

Figure 1. Correlation between BMI (kg/m^2) and serum LH concentration (mIU/ml) in all examined subjects (r=0.61; p<0.0001).

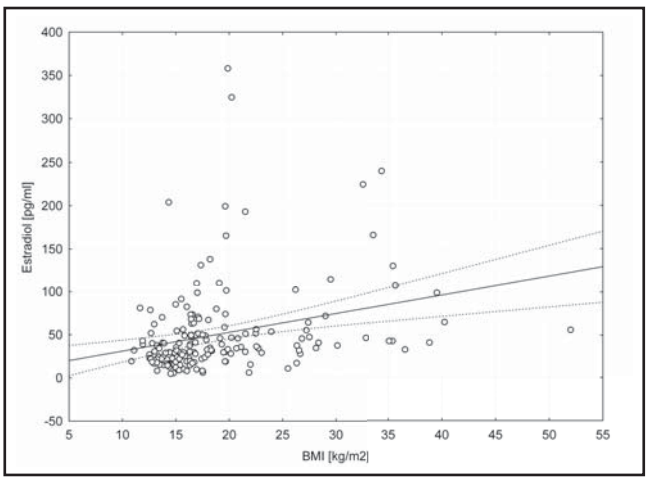

Figure 2. Correlation between BMI (kg/m^2) and serum estradiol concentration (pg/ml) in all examined subjects (r=0.30; p<0.0001).

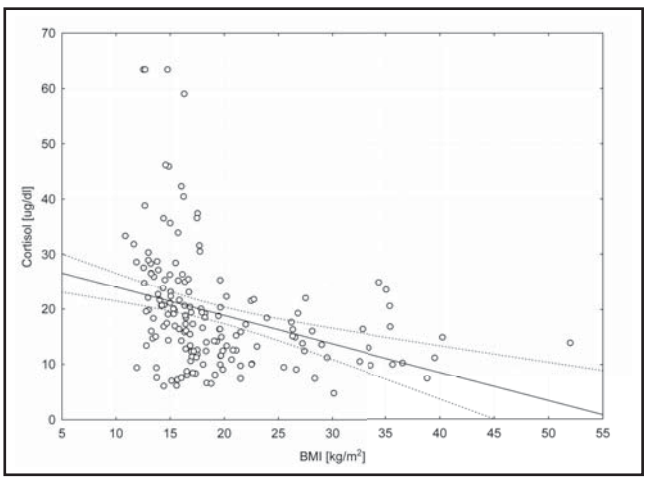

Figure 3. Correlation between BMI (kg/m^2) and serum cortisol concentration (µg/dl) in all examined subjects (r=–0.35; p=0.008).

cesses of thermoregulation and energy expending. The resulting from malnutrition endocrine disturbances in the hypothalamus-GH-IGF-I, hypothalamic-pituitary-thyroid, -adrenal, -gonads axes may affect the functions of many organs (Levine 2002; Nogal *et al.* 2008; Palla & Litt 1988). Adipose tissue hormones such as leptin, adiponectin, and probably also resistin play a role in the processes of body adaptation to chronic malnutrition,

In our subjects with AN LH and estradiol levels were significantly below normal that is consistent with our previous results obtained in a group of 89 girls with AN (Ziora *et al.* 2006).

All our anorectic subjects were in the acute phase of the disease. They had primary or secondary amenorrhoea, and decreased levels of sex hormones (estradiol, LH) in the blood indicating hypogonadotrophic hypogonadism. This hormonal disorder is typical for AN and its consequences, such as amenorrhoea, or inhibited sexual development, are considered diagnostic criteria for AN (American Psychiatric Association (DSM IV), 1994; Ziora *et al.* 2006).

Hypothalamic hypogonadotrophic hypogonadism, seen in patients with anorexia nervosa, is an example of the body's adaptation to chronic malnutrition (Støving *et al.* 2001). In the conditions associated with chronic loss of adipose tissue, adaptive mechanisms regulating appetite, thermogenesis and voluntary energy expenditure are activated. In the case of long-term negative energy balance, the reproductive functions are inhibited, among other disorders. The activation of regulatory mechanisms, leading to suppression of the hypothalamic-pituitary-gonadal axis, resulting in a secondary inhibition of hormonal and reproductive functions of the gonads, is an important aspect of the body's adaptation to a state of malnutrition (Støving *et al.* 2001).

In all subjects analyzed together, we demonstrated significant positive correlations between serum LH and estradiol concentrations and BMI. Furthermore, LH and estradiol concentrations were strongly positively correlated with serum resistin levels. There was no such relationship in the AN group, which can be explained by too low dispersion of body weight and BMI values within a single group. No correlation was also shown between serum FSH either testosterone and RES concentrations in any individual group or in all subjects analyzed together.

The literature data on the relationship between resistin levels and sex hormones concentrations in the blood are scarce.

According to some authors (Körner *et al.* 2005), men have higher concentrations of RES in the blood than women. The others (Lee *et al.* 2003), report RES concentrations about 20% higher in women than in men. In children, RES concentrations correlate positively with the phase of sexual development (Gerber *et al.* 2005). Animal experiments have demonstrated that testosterone and reduced oestrogen concentrations

Tab. 2. Mean resistin, thyroid, adrenal and gonadal hormones serum concentrations in examined groups of girls.

Hormone [unit]	**AN** (n= 87)	**NOS** (n= 17)	**OB** (n= 30)	**H** (n= 61)
	mean±1.96 SE (range)			
Resistin [ng/ml]	2.81±0.59*** (1.35–3.97)	3.12±0.86 (1.54–4.23)	4.78±0.45*** (3.97–5.78)	4.11±0.36*** (3.37–5.02)
FT4 [ng/dl]	1.16±0.24* (0.50–1.85)	1.15±0.23 (0.887–1.66)	1.33±0.27* (0.89–2.04)	1.31±0.15 (1.04–1.7)
TSH [μIU/ml]	2.39±1.0 (0.34–5.05)	1.99±0.86 (0.705–4.09)	2.27±1.09 (0.41–4.29)	2.05±0.87 (0.767–4.2)
Cortisol [μg/dl]	23.91±11.92** (6.14–63.44)	21.90±10.93 (7.49–42.33)	14.02±4.93** (4.82–24.85)	13.31±4.78** (6.22–25.32)
ACTH [pg/ml]	22.18±20.47 (0.64–124.5)	28.47±17.57 (8.41–63.21)	27.88±15.67 (11.37–63.00)	30.82±14.51 (10.5–61.42)
LH [IU/ml]	0.90±1.29*** (0.001–6.55)	2.75±4.83 (0.1–19.94)	7.34±4.59*** (0.1–16.63)	4.79±2.48*** (0.504–9.00)
FSH [IU/ml]	3.80±3.48 (0.09–15.07)	5.90±3.67 (0.18–12.15)	4.49±1.95 (0.62–8.19)	5.02±1.88 (0.94–10.9)
Estradiol [pg/ml]	31.19±18.87** (5.00–91.40)	55.92±60.29 (6.21–204.00)	72.71±57.73** (11.00–239.70)	71.11±72.19** (15.61–358.1)
Testosterone [ng/dl]	30.05±26.26 (1.04–161.50)	53.0±43.84 (12.15–166.50)	38.16±24.44 (4.01–105.30)	32.10±16.26 (11.23–75.34)

H – healthy group; AN – anorexia nervosa group; NOS – not otherwise specified eating disorders group; OB – simple obesity group; SE – standard error; *p<0.05 AN vs OB; **p<0.001 AN vs OB and H; ***p<0.0001 AN vs OB and H

directly increase RES expression in the adipose tissue (Ling *et al.* 2001).

Nogueiras *et al.* (Nogueiras *et al.* 2003) showed *in vivo* in rats that RES mRNA expression in the adipose tissue was higher in male than female rats. Orchidectomy resulted in a decrease in RES expression, whereas ovariectomy did not cause any change in the expression.

Kapoor *et al.* (2007) reported no changes in blood resistin levels after a 3-month treatment with testosterone in men with hypogonadism and type 2 diabetes.

Chen *et al.* (Chen *et al.* 2007) studied the effect of estrogens (estradiol, estriol and estrone) as well as selective oestrogen receptor modulators, including genistein and diethylstilbestrol, on resistin gene expression in cultures of 3T3-L1 adipocytes in vitro. In this study, estrogens activated the expression of the RES gene in the adipocytes, leading to increased synthesis of this protein. Other authors (Hong *et al.* 2007) found no correlation between estradiol and estrone concentrations in the blood and resistin levels.

Our patients with AN had low serum levels of estradiol, similar to the values observed in postmenopausal women. We found no correlation between serum estradiol and resistin in the AN group, similarly as Hong *et al.* (2007), in post-menopausal women. Kulik-Rechberger *et al.* (Kulik-Rechberger & Rechberger 2003) also showed no correlation between the concentrations of estradiol, LH and FSH and RES levels in the blood of healthy girls aged 9 to 14 years. Other authors have reported that mean RES concentrations in pre-menopausal women was approximately twice higher than RES concentration in peri- and post-menopausal women and it did not depend on the levels of estradiol, testosterone, FSH and SHBG (Sowers *et al.* 2008).

Tab. 3. Correlations between resistin and thyroid, adrenal and gonadal serum concentrations in anorexia nervosa (AN) group and in all examined subjects analyzed together.

Hormone	**Resistin** [ng/ml]	
	AN (n=87)	**All subjects** (n=195)
TSH [μIU/ml]	r=-0.02; p=0.86	r=-0.12; p=0.11
FT4 [ng/dl]	r=0.0009; p=0.89	r=0.34; p<0.0001*
Cortisol [μg/dl]	r=0.13; p=0.25	r=-0.40; p<0.0001*
ACTH [pg/ml]	r=-0.009; p=0.94	r=-0.18; p=0.03*
LH [IU/ml]	r=-0.0009; p=0.99	r=0.57; p<0.0001*
FSH [IU/ml]	r=-0.07; p=0.53	r=0.17; p=0.06
Estradiol [pg/ml]	r=-0.22; p=0.55	r=0.28; p=0.0002*
Testosterone [ng/dl]	r=-0.06; p=0.62	r=0.11; p=0.17

In patients with AN, we found a significantly higher mean serum cortisol concentration compared to obese and normal girls. We also observed a negative correlation between BMI and serum cortisol in the group of all patients combined. Additionally, serum cortisol levels correlated negatively with RES concentrations in all

patients. Plasma ACTH concentrations were similar in all examined groups.

It has been demonstrated that the conditions involving low or high body weight are associated with hypothalamic-pituitary-adrenal axis (HPA) disorders. Patients with AN present abnormalities suggesting impaired HPA function (Misra *et al.* 2006). It has been suggested that they arise from the central activation of HPA in a situation of chronic stress, which is supported by high levels of CRH in the cerebrospinal fluid of patients with AN (Douyon & Schteingart 2002; Støving *et al.* 2001). The CRH stimulation test shows a decrease in their ACTH response. It is believed that the discrepancy between the increased secretion of hypothalamic CRH and normal levels of ACTH result from the dysfunction in negative feedback regulation only at the level of the pituitary, but not the hypothalamus (Douyon & Schteingart 2002).

Many patients with AN have hypercortisolemia with increased mean concentration of cortisol in the blood in 24-hour assays, as well as increased urinary secretion of free cortisol; however, serum ACTH levels are usually normal (Bannai *et al.* 1988; Misra *et al.* 2006). It is believed that hypercortisolism is caused by the increased production and secretion of cortisol in the adrenal glands and decrease in its clearance (Boyar *et al.* 1977). The coexistence of hypercortisolism with normal ACTH levels may result from an increase in adrenal cortical sensitivity to ACTH. In fact, excessive cortisol response to ACTH stimulation has been reported in patients with AN. Contrary to other syndromes associated with hypercortisolaemia (Cushing's disease or syndrome), serum cortisol concentrations in AN and free urine cortisol are only slightly elevated compared to normal and the circadian rhythm of secretion is preserved in AN (Boyar *et al.* 1977; Douyon & Schteingart 2002; Støving *et al.* 2001).

Hormones of the adipose tissue may certainly have an impact on the function of the adrenal cortex, but the mechanisms of this action are not known, yet. On the other hand, the production and secretion of adipocytokines, including leptin, adiponectin, resistin, is also the subject to regulation by other hormones such as glucocorticoids (Fonseca-Alaniz *et al.* 2007).

In all our subjects, blood TSH levels were within normal limits. The mean concentration of FT4 in the blood of patients with AN was significantly lower than in the obese subjects.

Quantitative disorders of the adipose tissue in the states of low or high body weight may be accompanied by secondary dysfunction of the thyroid, which is an expression of adaptation of the body to starvation or overfeeding. Malnutrition seen in chronic wasting diseases such as AN leads to disturbances in the functioning of the hypothalamic-pituitary-thyroid axis. A well-known example is euthyroid sick syndrome with low serum T3, increased rT3, and normal or low TSH (Douyon & Schteingart 2002). This syndrome is due to triggering adaptive mechanisms in chronically malnourished patients, leading to reduced basal metabolic rate.

Studies concerning the assessment of thyroid hormone concentrations in the blood of patients with AN have been conducted, and their results are generally consistent (Bannai *et al.* 1988; Nedvídková *et al.* 2000; Ziora *et al.* 2006). The most common abnormality is a decrease in blood concentrations of T4, FT4, T3 and FT3 below the normal levels, and increase in rT3 levels, but usually with normal TSH concentrations (Bannai *et al.* 1988; Natori *et al.* 1994; Nedvídková *et al.* 2000; Reinehr *et al.* 2008). Our current and previous (Ziora *et al.* 2006) observations, concerning serum FT4 and TSH concentrations of patients with AN in the acute phase of illness, are also similar. Normalization of body weight in patients with AN is usually accompanied by restoration of thyroid hormone concentrations (Palla *et al.* 1988).

To the best of our knowledge, there is no literature data on the relationship between the concentrations of thyroid hormones and resistin levels in the blood of patients with AN.

Our study found no relationship between serum TSH, FT4 and RES concentrations in patients with AN. However, there was a positive correlation between serum FT4 levels and resistin levels in all subjects taken together.

The observations in people with thyroid dysfunction reflect the role of thyroid hormones in maintaining the energy homeostasis of the body (Iglesias & Díez 2007). Thyrotoxicosis leads to weight loss and reduced body fat and muscle tissues (Dimitriadis & Raptis 2001; Iglesias & Díez 2007; Weetman 2000). Hypothyreosis is also associated with changes in body weight and composition. Patients with hypothyroidism show a slow weight gain caused by fluid retention in the hydrophilic glycoprotein deposits in the tissues with concomitant reduced oxygen consumption, reduced basal metabolic rate and lower heat production (Pucci *et al.* 2000).

Studies concerning the relationship between the serum RES concentrations and the thyroid hormones were carried out experimentally in animal models and in humans with thyroid dysfunction. It has been shown that in rats the concentration of RES in the blood is regulated by thyroid hormones (Nogueiras *et al.* 2003; Weinstein *et al.* 1990). The high expression of RES mRNA in the adipose tissue of rats with hypothyreosis and low expression in rats with hyperthyreosis (Syed *et al.* 1999) has been shown.

RES concentrations in the blood of patients with hyperthyroidism were lower compared to those in healthy patients (Iglesias *et al.* 2003), but this has not been confirmed in other studies (Krassas *et al.* 2005; Yaturu *et al.* 2004). Yaturu *et al.* (2004) reported a positive correlation between serum RES concentrations and FT3 and FT4 levels, and a negative correlation with TSH. Other authors (Krassas *et al.* 2005), similarly to

Iglesias *et al.* (2003), showed a reduction of elevated blood levels of RES in patients with hyperthyroidism after achieving the euthyroid state. However, they found no correlation between RES concentrations in the blood and body weight, BMI or body fat either in hyperthyroidism or in euthyroid state (Krassas *et al.* 2005). According to some authors (Iglesias *et al.* 2007), this cannot entitle to conclude that resistin plays a role in maintaining energy balance in patients with hyperthyroidism.

The results of studies on blood concentrations of RES in patients with hypothyreosis are also divergent (Iglesias *et al.* 2007; Pontikides & Krassas 2007). Some authors have demonstrated reduced (Iglesias *et al.* 2003; Owecki *et al.* 2008), others increased (Botella-Carretero *et al.* 2006) or unchanged (Krassas *et al.* 2006) RES concentrations in the blood of patients with hypothyroidism. Owecki *et al.* (2008) found no correlation between RES concentrations in the blood and concentrations of thyroid hormones (FT3, FT4 and TSH) in women with hypothyroidism after thyroidectomy and radioiodine treatment of thyroid cancer. Krassas *et al.* (2006) saw no differences in RES concentrations in the blood of patients with hypothyroidism in Hashimoto's disease compared with those in euthyreosis. However, Iglesias *et al.* (Iglesias *et al.* 2003) reported lower resistin concentrations in the blood of patients with hypothyreosis, concluding that thyroid dysfunction may affect blood RES levels.

We conclude that changes in resistin serum concentrations in eating disorders may be involved in the altered regulation of hypothalamic-pituitary-adrenal, thyroid and gonadal axes.

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