Increased circulating levels of betatrophin in patients with Hashimoto thyroiditis.

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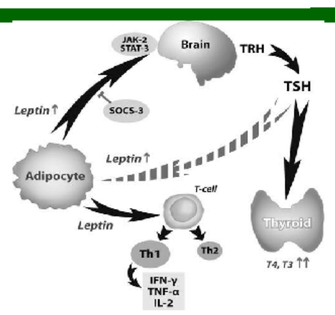

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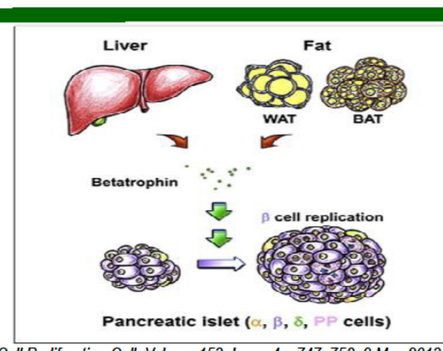


Peng Yi et al. Betatrophin: A Hormone that Controls Pancreatic β Cell Proliferation Cell. Volume 153, Issue 4, p747–758, 9 May 2013

INTRODUCTION

Hashimoto thyroiditis (HT) - is one of the most common autoimmune thyroid disorders and the most common cause of hypothyroidism, but the relation between HT and body mass is still unclear.

Leptin is a pleiotropic adipokine, produced mainly by white adipose tissue. Increased leptin plasma level is observed in obesity and is critical for regulating food intake and energy expenditure, crucial for a number of physiological processes, such as inflammation, angiogenesis, hematopoiesis. Leptin influences immune reactivity and autoimmunity

Betatrophin, also known as TD26/RIFL/lipasin/ANGPTL8/C19orf80, is a novel protein predominantly expressed in human liver and adipose tissue.

Betatrophin concentration is increased in patients with diabetes and obesity and is associated with insulin secretion. It also positively correlates with insulin resistance and BMI in non-diabetic subjects. Stimulators of betatrophin, such as thyroid hormones are usually relevant to thermogenesis.

In the present study we aimed to find out the relation between HT, obesity and betatrophin concentration.

MATERIAL AND METHODS

The study comprised 175 subjects, including 133 patients with diagnosed HT (mean age 44.6 15.3 years, F/M 90.6%/9.4%) and 42 healthy individuals (mean age 40.8 15.6 years, F/M 89.3%/10.7%), who had never been treated for any autoimmune diseases.

Serum TSH and betatrophin concentration were measured using an enzyme-linked immunoassay (DiaSource, Louvain-la-Neuve, Belgium). Anti-peroxidase antibodies (TPOAb), leptin and TNFα levels were also determined by immunoassays (Euroimmun, Lubeck, Germany and R&D Systems, Minneapolis, USA, respectively).

All patients were checked with body analyzer INBODY 220 (Direct Segmental Multi-frequency Bioelectrical Impedance Analysis Method; *Biospace, Korea*), which allows measurements of body mass, total body water (TBW), fat and free fat mass, skeletal muscle mass (SMM), BMI, the percent of body fat (PBF) and basic metabolic rate (BMR).

Reliability of an estimated BMR was confirmed by calorimetric method performed in 5 patients with HT. Differences between these results were smaller than 5%.

Concentrations of betatrophin and leptin were measured in group of patients with HT and controls in which differences of body composition measurements were not statistically significant.

STATISTICA 12.0 for Windows (StatSoft.Inc, USA) and IBM SPSS Statistics 21.0 (Predictive Solutions, USA) Software were used for the statistical analysis.
Before analysis data were tested for normality of distribution using Kołomogorow-Smirnow (Lillefors adjustment) and Shapiro-Wilk tests. Differences between the groups were compared by U Mann-Whitney test and relationships between variables were tested using Spearman's rank correlation test. P value lower than 0.05 was considered statistically significant.

RESULTS

Increased body mass was observed in 72% of the HT patients, including overweight in 38% and obesity in 35% of them.
In the control group overweight or obesity was observed in 38% of the subjects studied.

Body composition analysis in patients with HT compared with the control group.

	HT (N=133)	Control group (N=42)	p
Body mass (kg)	**74.1 (63.5-91.60)**	**65.0 (60.0-74.1)**	0,008
BMI (kg/m^2)	**27.2 (23.9-32.1)**	**22.12 (20.7-27,1)**	0,02
TBW	33.0 (31.0-36.9)	34.4 (30.5-41.1	ns
Fat mass (kg)	34.4 (30.5-41.1	**26.8 (20.6-37.1)**	0,02
PBF((%)	**38.0 (31.8-41.5)**	**26.8 (20.6-37.1)**	0,005
BMR	1383(1278-1581)	1342(1282-1455)	ns

Body composition analysis in patients with HT compared with the control group matched for body mass.

	HT (N=53)	Control group (N=28)	p
Body mass (kg)	**74,1(45,00-82,0)**	**70,00(51,5-109,0)**	ns
BMI (kg/m^2)	**26,46(18,5-37,4)**	**25,95(18,7-39,3)**	ns
TBW	**34,1(21,6-63,8)**	**33,5(27,9-51,8)**	ns
Fat mass (kg)	**25,8(8,3-49,0)**	**26,35(6,9-446)**	ns
PBF (%)	**29,4(22,6-32,2)**	**27,8(20,6-33,8)**	ns
BMR	**1372(1011-2261)**	**1354(1188-1893)**	ns

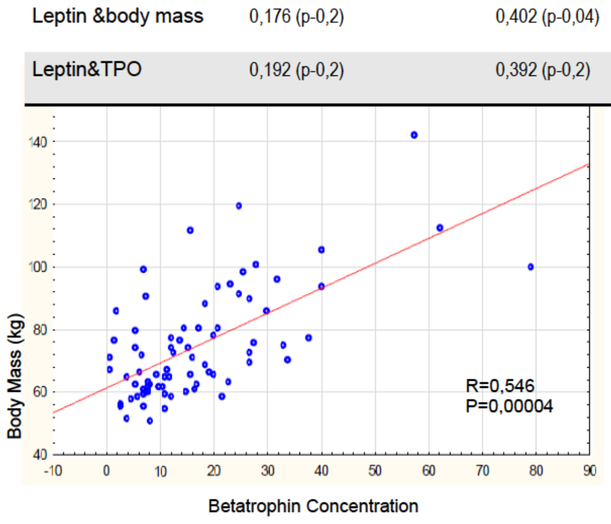
Biochemical characteristics of patients with HT compared with the control group mached for body mass.

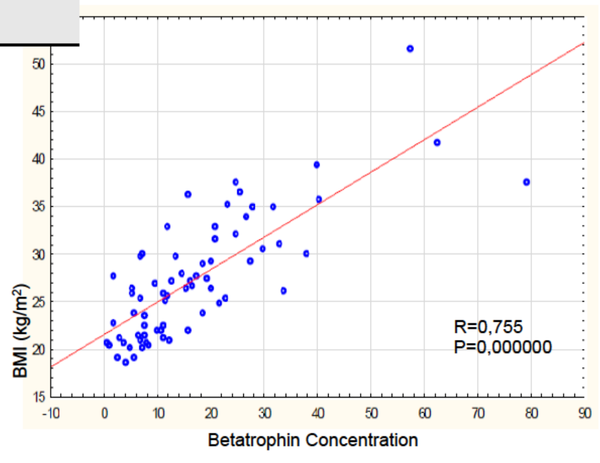
	HT (N=53)	Control group (N=28)	p
TSH [IU/ml]	**1,55 (0,016-9,32)**	**1,67 (0,4-2,5)**	**ns**
TPOAb[IU/ml]	**171,04 (4,2-715)**	**6,36 (4,46-556,2)**	**0,000**
Leptin [ng/ml]	**1,64 (0,38-7,7)**	**1,67 (0,4-2,5)**	**ns**
Betatrophin [ng/ml]	**17,34 (0.7-78.98)**	**9,75 (0.61-40.14)**	**0,008**
TNFa [pg/ml]	**6,14 (0.21-14.42)**	**5,27 (2.96-14.52)**	**0,012**

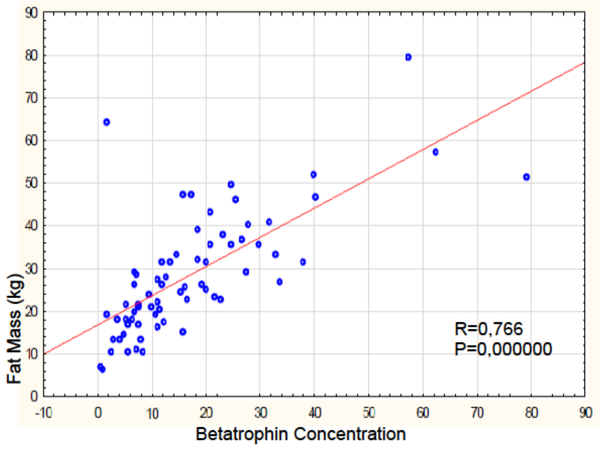
Data are shown as medians (interquartile range),

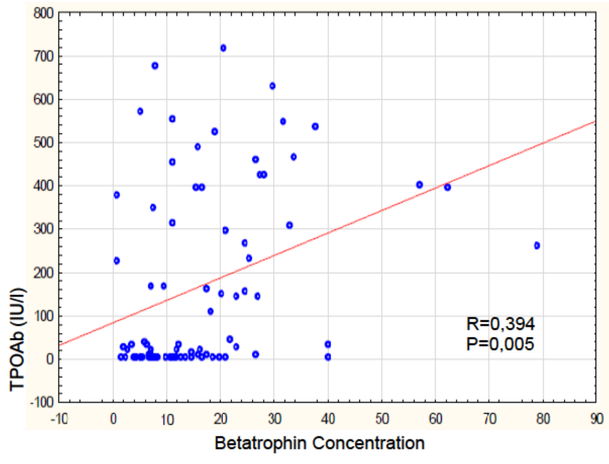
Spearman's correlation coefficient s of leptin concentrations and other variables studied in patients with Hashimoto thyroiditis.

	HT [R(p)]	Control group
Leptin &age	0,322 (p-0,02)	0,27 (p-0,02)
Leptin &body mass	0,176 (p-0,2)	0,402 (p-0,04)
Leptin&TPO	0,192 (p-0,2)	0,392 (p-0,2)









CONCLUSIONS:

Among the patients with HT, even in euthyreosis, the problem of overweight and obesity is significantly more common than in the healthy individuals.

Patients with HT, have significantly higher betatrophin concentrations than healthy individuals, even in euthyreosis with normal body mass.

Our results suggest that betatropthin could cause the increase in fat mass, especially in patients with autoimmunity of thyroid gland.

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