Role of thyroid hormones on serum leptin levels

G Sesmilo, R Casamitjana 1, I Halperin, R Gomis and E Vilardell
Endocrinology and Diabetes Unit, and 1Hormonal Unit, Hospital Clínic, Barcelona, Spain
(Correspondence should be addressed to R Gomis, Endocrinology Unit, Villarroel 170, 08036 Barcelona, Spain)

Abstract
Leptin is an adipose tissue hormone whose plasma levels reflect energy stores. Although pathological thyroid function is related to changes in energy expenditure and body composition, its possible influence on leptin levels remains to be determined. The objective of the study was to provide new data on the relationship between plasma leptin levels and thyroid function.

Sixteen patients with primary autoimmune hypothyroidism, and seventeen patients with primary autoimmune hyperthyroidism were prospectively studied from the time of clinical diagnosis and then every 6–8 weeks until thyroid function was completely restored (plasma tri-iodothyronine, free thyroxine and TSH within normal ranges). Fasting immunoreactive plasma leptin levels and body composition (bioelectrical impedance) were assessed at every visit.

Plasma leptin levels were correlated with percentage body fat, as previously described, both at the time of diagnosis (r = 0.60, P < 0.001) and after normalisation of thyroid function (r = 0.63, P < 0.001). There was no correlation between serum leptin and thyroid hormone levels at any time during the study. Plasma leptin levels as well as percentage body fat (BF) did not change significantly from the beginning until the end of the study, either in the hypothyroid (leptin: 14.54 ± 2.61 vs 16.92 ± 2.61 ng/ml, BF: 25.25 ± 2.47 vs 25.90 ± 3.22%) or in the hyperthyroid (leptin: 10.69 ± 1.81 vs 12.36 ± 2.19 ng/ml, BF: 22.01 ± 2.31 vs 25.39 ± 1.13%) group of patients.

In conclusion, these results suggest that thyroid function per se is not a major determinant of plasma leptin levels.

European Journal of Endocrinology 139 428–430

Introduction
Leptin, the ob gene product, is an adipose tissue hormone which has been closely linked to the amount of body fat stores (1). Furthermore, it has been found to increase energy expenditure in rodents (2). Although its plasma levels have some relationship with other hormones such as glucocorticoids and insulin (3, 4), its precise role in the endocrine system remains to be determined. Abnormal thyroid function is associated with changes in body weight and energy expenditure, but it remains to be established whether thyroid hormones independently affect plasma leptin levels in humans. Several studies with diverse methodologies have addressed the field of leptin and thyroid function in humans (5–9). Only one of them found decreased leptin levels in the hypothyroid state (5). On the other hand, thyroid hormones exert a negative influence on serum leptin levels in rats (10).

To provide new data on the possible relationship between thyroid hormones and leptin, we have prospectively followed a group of hypothyroid and hyperthyroid patients from the time of clinical diagnosis and then every 6–8 weeks until thyroid function was restored. We have determined serum leptin concentrations and parameters of body composition at every visit. Our results suggest that thyroid hormones are unlikely to play an important role in the regulation of plasma leptin levels.

Subjects and methods
Thirty-three patients with primary autoimmune disease were studied. Subject characteristics are shown in Table 1. There were 16 hypothyroid patients (12 women and 4 men) with a mean age of 49.13 ± 3.25 years, a mean body mass index (BMI) of 28.40 ± 1.08 kg/m², reduced serum thyroid hormone levels (tri-iodothyronine (T₃): 0.65 ± 0.06 ng/ml, normal range: 0.80–1.60 ng/ml; free thyroxine (FT₄): 0.56 ± 0.06 ng/dl, normal range: 0.80–2 ng/dl), and elevated thyrotrophin (TSH) (63.34 ± 17.9 mU/l, normal range: 0.40–4 mU/l). The hyperthyroid group consisted of 17 patients (13 women, 4 men) with a mean age of 45.41 ± 4.47 years, BMI: 21.81 ± 0.86 kg/m², elevated serum thyroid hormone levels (T₃: 3.58 ± 0.57 ng/ml, FT₄: 4.48 ± 0.43 ng/dl), and reduced serum TSH (<0.03 mU/l). Both groups were
studied at the time of clinical diagnosis and then every 6–8 weeks until thyroid function (T3, FT4, and TSH) was within the normal range. Hypothyroid patients were treated with L-T4 (100–150 μg/dl), and hyperthyroid patients with methimazole (MTZ; 10–15 mg/dl) to achieve normal thyroid function. The mean time for restoring thyroid function was 3.6 ± 0.5 months for hypothyroid and 2.8 ± 0.3 months for hyperthyroid patients. The dietary habits of all subjects were monitored during the follow-up to confirm that they were not on a calorie-restricted diet that could influence plasma leptin levels. Informed consent was obtained from all patients and the study was approved by the hospital’s ethical committee.

At every visit, blood samples were extracted in the morning after an overnight fast, weight and height were measured and body composition was assessed by bioelectrical impedance. All serum specimens were frozen at −20°C until assayed.

Serum T3, FT4 and TSH were measured by enzyme immunoassay (Technicon Immuno 1, Bayer, Tarrytown, NY, USA), Leptin was determined by RIA (Linco Research, St Charles, MO, USA).

Statistical analyses were carried out with SPSS for Windows using simple correlation, the t-test for paired data and multiple regression analysis. Data are presented as means ± S.E.M.

**Table 1 Subject characteristics at the beginning and at the end of the study. Data are means ± S.E.M.**

<table>
<thead>
<tr>
<th></th>
<th>Hypothyroid</th>
<th>Hyperthyroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3 (ng/ml)</td>
<td>0.65 ± 0.06</td>
<td>3.58 ± 0.57</td>
</tr>
<tr>
<td>FT4 (ng/dl)</td>
<td>0.56 ± 0.06</td>
<td>4.48 ± 0.43</td>
</tr>
<tr>
<td>TSH (mU/ml)</td>
<td>63.34 ± 17.9</td>
<td>2.18 ± 0.46*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.40 ± 1.08</td>
<td>27.65 ± 1.04*</td>
</tr>
<tr>
<td>BF (%)</td>
<td>25.25 ± 2.47</td>
<td>25.90 ± 3.22</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>14.54 ± 2.61</td>
<td>16.92 ± 2.66</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>12 F/4 M</th>
<th>13 F/4 M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.13 ± 3.25</td>
<td>46.41 ± 4.47</td>
</tr>
</tbody>
</table>

* P < 0.05 comparing baseline with euthyroid state for each group.

Although there was a small change in BMI (a decrease in hypothyroid and an increase in hyperthyroid patients) after normalisation of thyroid function, parameters of body composition such as percentage body fat (BF), fat mass, free fat mass and body water did not change significantly between the beginning and the end of the study. Furthermore, plasma leptin levels did not change during this period, either in the hypothyroid (leptin: 14.54 ± 2.61 vs 16.92 ± 2.66 ng/ml) or in the hyperthyroid (leptin: 10.69 ± 1.81 vs 12.36 ± 2.19 ng/ml) group of patients (Fig. 1).

**Discussion**

Although much has been learnt regarding the leptin hormone, its physiology and the precise role it plays in the endocrine system remain to be defined. One of the difficulties inherent to these studies lies in the fact that leptin physiology seems to be rather different in humans and rodents. Not only is the circadian rhythm of its plasma levels different but also its regulation and the relationship with other hormones have been shown to

![Figure 1](https://example.com/leptin_concentrations.png)

**Figure 1** Plasma leptin concentrations in hypothyroid (Hypo) and hyperthyroid (Hyper) groups at the beginning of the study, and at the end of the study (after T4 or MTZ treatment) when euthyroid. Horizontal bars represent means.
differ (11, 12). Nevertheless, it is known that glucocorticoids stimulate the synthesis of leptin both in humans and rodents (3, 13). Insulin also has an effect on leptin in both species, but while it has an acute effect in rodents (9), in humans this acute effect does not exist, although some groups have shown a chronic effect in prolonged clamp studies (14).

Recently, some studies in rats have demonstrated a negative influence of thyroid hormones on leptin levels, independently of the changes in body weight due to the thyroidal effect (10). In sharp contrast, our study reveals that in humans there is not a major independent effect of abnormal thyroid state on serum leptin. When leptin levels in the same group of patients were compared at the time of diagnosis of the thyroid illness and when thyroid function was restored, no difference in plasma levels was seen. Of note the percentage body fat in these patients did not undergo major changes. This is relevant as body fat was the only parameter independently related to plasma leptin in a stepwise regression analysis. These results agree with other clinical studies in humans: one of them showed no effect of a short term T₃-induced hyperthyroidism (6); others did not find differences when comparing leptin levels amongst euthyroid, hyperthyroid and hypothyroid individuals (7, 9). Only one group found lower leptin levels in the hypothyroid state (5). Our prospective analysis is not consistent with a major effect of thyroid hormones on leptin levels, as leptin levels did not change in the same group of individuals when thyroid function was restored. This suggests that plasma leptin concentrations in humans do not reflect the changes in energy expenditure due to the thyroidal effect.

In summary, while inhibition of serum leptin by thyroid hormones has been demonstrated in rodents treated with both T₃ and T₄ (10), in humans with either hypo- or hyperthyroidism, plasma leptin concentrations do not change with the restoration of thyroid function. We conclude that although thyroid hormones have effects on energy expenditure and body weight, they do not have an independent effect on circulating serum leptin levels.

Acknowledgements
We thank Dr J Ferrer for advice.

References
7 Sreenan S, Caro JF & Reffetoff S. Thyroid dysfunction is not associated with alterations in serum leptin. Thyroid 1997 7 407–419.
8 Bornstein SR, Torpy DJ & Chrousos GP. Leptin levels are elevated despite low thyroid hormone levels in the ‘Euthyroid Sick’ syndrome. Journal of Clinical Endocrinology and Metabolism 1997 82 4278–4279.