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ORIGINAL ARTICLE

Thyroid hormone levels predict the change in body weight: a prospective study

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ABSTRACT

Background Different studies, mostly cross-sectional, have found an association between low levels of thyroid hormones, even within the normal range, and a greater body mass index. The aim of this study was to determine the association between thyroid function and the risk for obesity.

Materials and methods In this population-based prospective study, measurements were made of anthropometric parameters, thyroid hormone function and urinary iodine in a cohort of the Pizarra Study (n = 937), and repeated 6 years later (n = 784). At the second point, measurements were also made of leptin and adiponectin.

Results Among the persons who were not obese at the start of the study, the odds ratio (OR) of becoming obese for those in the fourth quartile (Q_4) for free triiodothyronine (FT3) (versus those in Q_1) was 2·94 (1·46–5·90) (P = 0·005). The OR of becoming obese in persons in Q_4 of FT4 (versus those in Q_1) was 3·06 (1·23–7·43) (P = 0·01). Those persons in Q_4 of weight gain had a higher FT3 at the 6-year follow-up than those whose weight gain was in Q_1 (P < 0·001). Leptin correlated with thyrotropin (β = 0·58, P = 0·001) and the FT4 (β = −1·12, P = 0·005). Adiponectin correlated with FT3 (r = −0·24, P < 0·001). The urinary iodine correlated negatively with both the BMI (β = −0·08, P = 0·01) and the increase in weight (β = −0·08, P = 0·04).

Conclusions The changes in the thyroid hormones could be the consequence, rather than the cause, of the increase in weight. The same pathophysiological mechanisms that induce obesity might also be modifying the thyroid hormone pattern.

Keywords Adiponectin, insulin resistance, leptin, obesity, thyroid hormone.

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Introduction

The effects of the thyroid hormones on resting energy expenditure are well known, even within the range of normality, and small variations in the levels of the thyroid hormones may influence body weight [1].

In recent years, there has been an increasing focus on the relationship between thyroid function and weight status. Different studies, mostly cross-sectional in design, have found an association between low levels of thyroid hormones, even within the normal range, and a greater body mass index (BMI), in both the general population [1] and obese persons [2], as well as with insulin resistance [3]. However, little is known about the relationship between insulin resistance and thyroid function [3,4]. An association has also been seen between the thyroid hormones and the BMI, both during weight loss [5] and during periods of dynamic weight gain [6].

The physiological pathways connecting obesity with thyroid hormone status are not clear. Adipose tissue secretes multiple factors, including leptin, adiponectin, inflammatory cytokines and others, which control feeding, thermogenesis, inflammatory response, neuroendocrine function and glucose and lipid metabolism [7–9]. Data have shown a possible relationship between adipocytokines and thyroid status [10]. Several studies

indicate that leptin may be a promising link between weight and thyroid function, at least in some animal studies [10,11]. An association between leptin and TSH has been reported in different studies [2,12]. Both adiponectin and resistin also appear to be related with the thyroid status [10]. However, when these associations are discussed, iodine intake and tobacco smoking should be taken into account, as they are well known to affect concentrations of thyroid hormones.

The aim of this study was to test in euthyroid subjects the hypothesis of an association between thyroid function and changes in weight and the risk for obesity in a prospective, population-based study in which the iodine intake was known.

Material and methods

Subjects

The study was carried out with a cohort of the Pizarra Study. The study population and the design of this survey have been described previously [13]. The Pizarra Study is a population-based prospective study undertaken in a population from Andalusia, southern Spain. The first phase of the study (1996–1998) included 937 individuals, aged 18–65 years, selected randomly from the municipal census of Pizarra. Of the original cohort, 784 (83·6%) were reassessed in 2002–2004 [13]. For the purposes of the present study, patients were excluded if they had a history of any intercurrent process during the 2 weeks prior to the evaluation, if they were receiving thyroid hormone therapy or if they had positive anti-thyroid peroxidase antibodies (TPO) (> 50 IU mL^{-1}) or thyrotropin (TSH) < 0·20 μIU mL^{-1} or TSH > 5 μIU mL^{-1}. All participants gave their informed consent, and the study was reviewed and approved by the Ethics and Research Committees of Carlos Haya University Hospital, Malaga. Reporting of the study conforms to the STROBE statement [14].

Measurements were made in all the participants of weight and height, and the BMI was calculated (weight/height^2). The subjects were classified into two groups according to their BMI: obese subjects with a BMI ≥ 30 kg m^{-2} and nonobese subjects with a BMI < 30 kg m^{-2} [15]. They also completed a standardized survey on health habits [16]. Measurements of TSH, free triiodothyronine (FT3), free tetraiodothyronine (FT4), urinary iodine excretion [17] and insulin resistance (HOMA-IR) were made at baseline and after 6 years. At the 6-year follow-up, leptin and adiponectin were measured.

Blood samples were collected after a 12-h fast. The serum was separated and immediately frozen at −80 °C. Serum biochemical parameters and thyroid hormones were analysed at the same time in an automated MODULAR ANALYTICS E170 analyzer (Roche Diagnostics GmbH, Mannheim, Germany). The TSH, FT3 and FT4 were measured by chemoluminescence (Roche Diagnostics GmbH). The anti-TPO antibodies were measured by a radioimmunometric assay (Biocode S.A., Liege, Belgium). The iodine concentration in the first urine of the morning was measured by the modified Benotti and Benotti technique [17]. Leptin was analysed by enzyme immunoassay kits (DSL, Webster, TX, USA). Adiponectin was analysed by enzyme immunoassay kits (DRG Diagnostics GmbH, Germany). The insulin was analysed by an immunoradiometric assay (BioSource International, Camarillo, CA, USA). The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated from fasting insulin and glucose.

Statistical study

The deviation of the continuous variables from a normal distribution was tested with the Kolmogorov–Smirnov *Z*-test. The hypothesis contrast of the qualitative variables (%) was made with the chi-square test. For the multivariate statistical analysis, the variable that failed to adjust to a normal distribution (urinary iodine) received a log-normal transformation. The hypothesis contrast of the continuous variables was made with the Student's *t*-test or an ANOVA of two or more ways. The association between variables was measured by calculating the Spearman *r* correlation coefficient and different models of multiple linear regression. In logistic regression models, the dependent variable was the absence or presence of obesity (BMI < 30 vs. BMI ≥ 30). In all cases, the level of rejection of a null hypothesis was $\alpha = 0{\cdot}05$ for two tails. The statistical analysis was carried out with SPSS (Version 11.5 for Windows; SPSS, Chicago, IL, USA).

Results

Most (61·1%) of the population were women. In the study population, the levels at the start of the study of TSH (obese: 1·81 ± 0·91 μIU mL^{-1} vs. nonobese: 1·97 ± 0·94 μIU mL^{-1}), FT3 (obese: 5·01 ± 0·55 pM vs. nonobese: 5·03 ± 0·75 pM) and FT4 (obese: 14·9 ± 2·2 pM vs. nonobese: 14·8 ± 2·3 pM) did not differ significantly between the obese persons and the nonobese persons (obese, $n = 263$; nonobese, $n = 674$). At the 6-year follow-up, there was a significant increase in weight and anthropometric measurements (Table 1). The incidence of obesity (persons who were not obese at the start of the study who became obese by the 6-year follow-up point) was 14·4%.

The chi-square test showed that the likelihood that those persons who were not obese at the start of the study would become obese was greater with the increase in levels of FT4 ($P = 0{\cdot}03$) and FT3 ($P = 0{\cdot}009$) (Fig. 1). Using a logistic regression model, the OR of becoming obese, adjusted for age and sex, of the persons with FT3 > 5·4 pM [> third quartile (> Q_3)] versus those with FT3 ≤ 4·6 pM [≤ first quartile (≤ Q_1)] was 2·94 (1·46–5·90) ($P = 0{\cdot}005$). The OR of becoming obese in persons with

Table 1 General characteristics of the study population. Both baseline and 6-year follow-up data are given for the Pizarra Study

	Baseline	6 years later	Change*	Paired *P**
Age	39·6 ± 13·8	46·4 ± 14·0	6·2 ± 1·9	< 0·0001
Weight (kg)	71·6 ± 13·8	74·5 ± 14·2	2·7 ± 6·2	< 0·0001
BMI (kg m^{-2})	27·4 ± 5·1	28·7 ± 5·2	1·0 ± 2·5	< 0·0001
Waist circumference (cm)	85·2 ± 13·4	93·8 ± 14·2	8·1 ± 6·9	< 0·0001
Waist to hip ratio	0·84 ± 0·10	0·90 ± 0·11	0·05 ± 0·06	< 0·0001
Thyrotropin (TSH) (μIU mL^{-1})	1·93 ± 0·93	2·05 ± 1·79	0·12 ± 1·67	0·03
Free tetraiodothyronine (FT4) (pM)	14·8 ± 2·2	15·4 ± 2·1	0·59 ± 2·51	< 0·0001
Free triiodothyronine (FT3) (pM)	5·02 ± 0·70	4·95 ± 0·61	−0·07 ± 0·69	0·003
FT3:FT4	0·34 ± 0·06	0·32 ± 0·04	0·02 ± 0·05	< 0·0001
Urinary iodine (μg L^{-1})	100·5 ± 70·0	128·1 ± 98·3	27·9 ± 113	< 0·0001
Prevalence of obesity (BMI ≥ 30)	28·0%	29·1%		

The results are expressed as mean ± SD.
*Who completed the study.

FT4 > 16·2 pM (> Q_3) versus those with FT4 ≤ 13·2 pM (≤ Q_1) was 3·06 (1·23–7·43) (P = 0·01).

The persons who were not obese at the start but who became obese by the end of the study had significantly higher levels of FT4 (15·7 ± 2·4 pM vs. 15·3 ± 1·9 pM, P = 0·04) and FT3 (5·15 ± 1·06 pM vs. 4·97 ± 0·54 pM, P = 0·038) at the 6-year follow-up than those who remained nonobese, after adjusting the ANOVA model for age and sex.

At the 6-year follow-up, the increase in weight (weight at the 6-year follow-up minus baseline weight) in those persons who were not obese at the start of the study was significantly greater in those with a higher FT4 at the start (P = 0·01, adjusted in a ANOVA model for age and sex) (Fig. 2a). This difference was already significant with effect from FT4 levels of 14·7 pM (Q2). In the persons who were obese at the start of the study, however, an increase in weight was not associated with baseline FT4 levels.

In the whole study population, the increase in weight correlated positively with FT3 at the 6-year follow-up (r = 0·19, P = 0·002), adjusted for age and sex. Those who experienced a weight gain > 5·8 kg (> Q_3) had a higher FT3 at the 6-year follow-up than those whose weight increased less than −1·0 kg (≤ Q_1) (P < 0·001), after adjusting the ANOVA model for age and sex (Fig. 2b).

At the start of the study, the nonobese persons with an FT3:FT4 ratio > 0·37 (> Q_3) experienced a significantly lower weight gain (2·50 ± 5·35 kg) than those with an FT3:FT4 ratio ≤ 0·30 (≤ Q_1) (3·93 ± 5·69 kg), an FT3:FT4 ratio between > 0·30 (> Q_1) and ≤ 0·34 (≤ Q_2) (3·15 ± 5·63 kg) or an FT3:FT4 ratio between > 0·34 (> Q_2) and ≤ 0·37 (≤ Q_3) (4·19 ± 5·17 kg), after adjusting the ANOVA model for age, sex and BMI (P = 0·02).

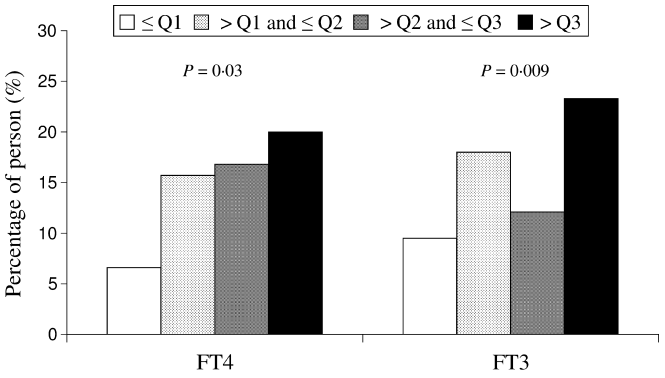

Figure 1 Percentage of normal-weight persons who became obese according to their free triiodothyronine (FT3) and FT4 quartiles at the start of the study. FT4 quartiles: ≤ Q1 (≤ 13·2 pM), > Q1 and ≤ Q2 (> 13·2 and ≤ 14·7 pM), > Q2 and ≤ Q3 (> 14·7 and ≤ 16·2 pM), > Q3 (> 16·2 pM). FT3 quartiles: ≤ Q1 (≤ 4·6 pM), > Q1 and ≤ Q2 (> 4·6 and ≤ 5·0 pM), > Q2 and ≤ Q3 (> 5·0 and ≤ 5·4 pM), > Q3 (> 5·4pM).

At the 6-year follow-up, leptin was significantly higher in obese persons than nonobese persons (18·9 ± 13·4 ng mL^{-1} vs. 10·4 ± 8·5 ng mL^{-1}, P < 0·0001), adjusted for age and sex. Leptin correlated significantly with the BMI, in both men (r = 0·70, P < 0·0001) and women (r = 0·67, P < 00001), and with weight gain (r = 0·28, P < 0·001, adjusted for age, sex and the presence of obesity). The FT4 at the 6-year follow-up correlated negatively with leptin (β = −1·12, P = 0·005) after adjusting the model for the BMI, age and sex. The model explained 3·6% of the variance, with leptin contributing 1·1% to the explanation of the variance in FT4. The TSH at the 6-year follow-up correlated

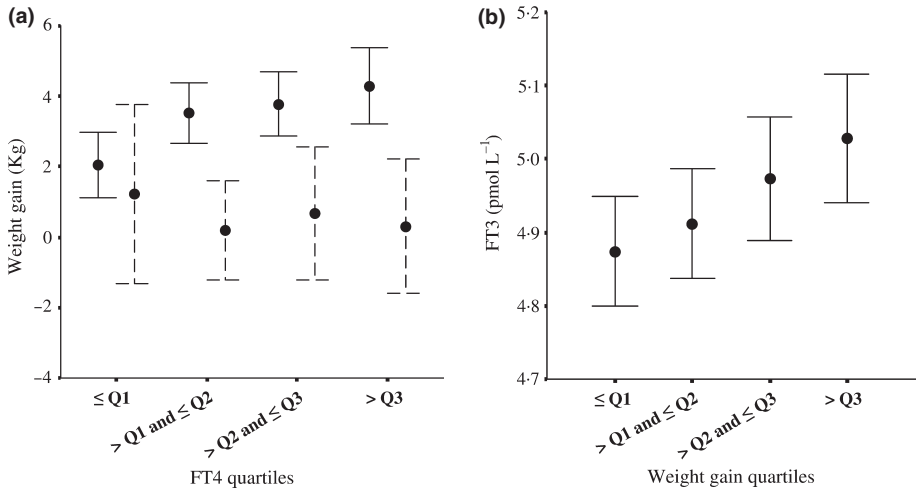

Figure 2 (a) Weight gain (mean ± 95% confidence interval) according to the FT4 quartiles at the start of the study (P = 0·01, adjusted for age, BMI, sex and urinary iodine): ≤ Q1 (≤ 13·2 pM), > Q1 and ≤ Q2 (> 13·2 and ≤ 14·7 pM), > Q2 and ≤ Q3 (> 14·7 and ≤ 16·2 pM), > Q3 (> 16·2 pM). (—) Persons with BMI < 30 kg m^{-2}. (- -) Persons with BMI ≥ 30 kg m^{-2}. (b) free triiodothyronine levels (mean ± 95% confidence interval) at the six-year follow-up according to weight gain (P < 0·001): ≤ Q1 (less than or equal to −1·0 kg), > Q1 and ≤ Q2 (greater than −1 and less than or equal to +2·0 kg), > Q2 and ≤ Q3 (greater than +2·0 and less than or equal to +5·8 kg), > Q3 (greater than +5·8 kg).

Table 2 Serum levels of TSH, FT4, FT3 and the FT3:FT4 ratio according to the presence or absence of smoking

	Baseline study			6-year follow-up study		
	Smokers	Nonsmokers	$P_{adjusted*}$	Smokers	Nonsmokers	$P_{adjusted*}$
Thyrotropin (TSH) (μIU mL^{-1})	1·82 ± 0·90	1·99 ± 0·96	0·001	1·85 ± 0·98	1·91 ± 0·91	0·30
Free tetraiodothyronine (FT4) (pM)	14·8 ± 2·5	14·8 ± 2·1	0·87	15·3 ± 2·1	15·9 ± 1·9	0·20[†]
Free triiodothyronine (FT3) (pM)	5·08 ± 0·61	4·99 ± 0·75	0·44	5·03 ± 0·55	4·89 ± 0·53	0·02
FT3:FT4	0·35 ± 0·05	0·34 ± 0·06	0·09[‡]	0·33 ± 0·04	0·31 ± 0·04	0·004[§]

*Adjusted for age, sex and the presence of obesity (BMI ≥ 30).
[†]Interaction obesity*smoker: P = 0·02.
[‡]Interaction obesity*smoker: P = 0·09.
[§]Interaction obesity*smoker: P = 0·01.

positively with the levels of leptin (β = 0·58, P = 0·001), after adjusting for BMI, age and sex. The model accounted for 6·7% of the variance, with leptin contributing 3·6% to the explanation of the variance in TSH.

At the 6-year follow-up, the levels of adiponectin were significantly lower in the obese persons than the nonobese persons (11·4 ± 18·2 μg mL^{-1} vs. 12·6 ± 10·9 μg mL^{-1}, P = 0·005), adjusted for age and sex, correlating negatively with the HOMA-IR (r = −0·18, P < 0·0001) and the levels of FT3 (r = −0·24, P < 0·001) (β = −0,20, P = 0,01), after adjusting for age, sex and BMI. The model accounted for 24·3% of the variance in FT3, with adiponectin contributing 2% to the explanation of the variance in FT3.

The FT4 at the start of the study correlated positively and significantly with the HOMA-IR (r = 0·10, P = 0·001). This did not remain after adjusting for age and sex. At the 6-year follow-up, the FT4 still correlated with HOMA-IR (r = 0·09, P = 0·001), but again disappeared after adjusting for age and sex.

Those persons who smoked had lower TSH levels at the start of the study (P = 0·001). At the 6-year follow-up, they had higher levels of FT3 (P = 0·02) and a higher FT3:FT4 ratio (P = 0·001) (R^2 = 0·5%) (Table 2). A significant interaction was found between the presence of obesity and smoking in the explanation of the variance in the FT3:FT4 ratio at the start of the study (P = 0·05) and in the explanation of the variance in

the FT3 (P = 0·02) and FT3:FT4 ratio (P = 0·01) at the 6-year follow-up.

Persons who were obese consumed iodized salt less often than the nonobese persons, both at the start of the study (4·8% vs. 11·1%, P = 0·003) and 6 years later (50·0% vs. 60·7%, P = 0·01). In all those who consumed iodized salt at the start of the study, the FT4 was significantly higher (15·1 ± 2·8 pM vs. 14·8 ± 2·2 pM, P = 0·001), after adjusting for age and sex, whereas the FT3 (4·80 ± 0·57 pM vs. 5·05 ± 0·74 pM, P = 0·05) and the FT3:FT4 ratio (0·32 ± 0·05 vs. 0·36 ± 0·06, P = 0·030) were significantly lower. Six year later, the FT3 remained significantly lower in those who consumed iodized salt (4·74 ± 0·53 pM vs. 4·99 ± 0·55 pM, P < 0·006, after adjusting the model for age and sex).

The urinary iodine was significantly lower in the obese than the nonobese persons (117·6 ± 84·9 μg L^{-1} vs. 129·5 ± 110·8 μg L^{-1}; P = 0·050, after adjusting for age and sex). The urinary iodine correlated negatively with both the BMI (β = −0·08, P = 0·01), adjusted for age and sex, and the increase in weight (β = −0·08, P = 0·04), adjusted for age and sex. The model accounted for 17·2% and 6·4% of the variance of BMI and weight gain, respectively, with urinary iodine contributing 2·4% and 1·0%, respectively. Finally, a logistic regression model showed that the likelihood of becoming obese by the 6-year follow-up was significantly less in those who consumed iodized salt (OR = 0·33; 95% CI, 0·14–0·74) and in those who had levels of FT3 ≤ Q_3 (OR = 0·58; 95% CI, 0·35–0·95), after adjusting the model for age, sex, urinary iodine and weight gain over the 6-year study period. The variable formed by the interaction between iodized salt and FT3 did not contribute significantly to the explanation of the risk of being obese at the 6-year follow-up.

Discussion

Several studies over recent years have examined the influence of the biological variability of the thyroid hormones on weight [18]. However, the results are contradictory. Studies have reported positive [2,19], negative [1,20] and nonsignificant differences [21] in circulating concentration of FT3 and FT4 in lean versus obese individuals. Other studies show controversial results following bariatric surgery [19] or after weight loss [6,22]. In our study, although levels of TSH, FT4 and FT3 at the start of the study were comparable in normal weight and obese humans, the thyroid hormone levels were not independent of the dynamic state of weight gain or loss. As in other studies [6], the data suggest that high circulating concentrations of thyroid hormone are indicative of ongoing dynamic weight gain [18].

At a particular time in life, thyroid function and thyroid hormone levels can be considered either the cause or the consequence of weight gain and obesity. While hypothyroidism is usually associated with a modest weight gain and decreased thermogenesis and metabolic rate, hyperthyroidism is known to lead to weight loss despite increased appetite and elevated metabolic rate. However, the changes in thyroid hormones are controversial in obesity [18]. The results of most studies conclude that the alterations in thyroid function are the primary event, whereas the increase in BMI is the secondary event, probably as a consequence of an alteration in energy expenditure [23]. The results of our study, however, which was undertaken in a euthyroid population, suggest that the higher levels of FT4 found in the obese persons could be the consequence of the increase in weight rather than the cause of the increase. Similar conclusions, concerning FT3, have been reported in previous studies [24]. The moderate increase of FT3 in obesity, which is usually in the upper normal range or slightly above the normal range [25], leads to an increase in energy expenditure. The elevation of thyroid hormone concentrations in obesity increases energy expenditure to avoid accumulation of energy as fat. Therefore, one would predict that subjects with higher initial circulating concentrations of thyroid hormones were already gaining weight, compared to subjects with lower thyroid hormone levels at the start of the study.

Thyroid hormones and adipocytokines can influence or be influenced by several factors [10]. Leptin might be one of the mediators of the association seen between weight increase and thyroid hormone levels, via the ability of leptin to interfere in the normal thyrostat regulation [26]. Indeed, in our study, leptin and BMI were associated with thyroid hormone levels differently. While the thyroid hormones were associated positively with the BMI, they were associated negatively with leptin. A correlation between leptin and TSH has been reported in different studies [2,27]. Some authors have demonstrated that the leptin-induced increase in TSH secretion via hypothalamic effects leads to an increase in serum FT4 [26,27]. Conversely, animal studies have shown that TSH stimulates leptin secretion by a direct effect on adipocytes [12].

Studies on the relation between adiponectin and thyroid hormones are discordant [2,10]. In our study, the adiponectin levels correlated negatively with insulin resistance and FT3, independently of age, sex and BMI. A previous study showed that experimentally induced hyperthyroidism resulted in significant changes in adiponectin levels [28]. A more recent study showed the potential inhibitory effect of T3 on adiponectin mRNA expression, specifically on white adipose tissue from a subcutaneous depot [29]. Both adiponectin and thyroid hormones share certain physiological actions, such as reduction in body fat by increasing thermogenesis and lipid oxidation [30]. Although the association between new adipokines and obesity and insulin resistance is known [8], their relation with thyroid function remains to be studied.

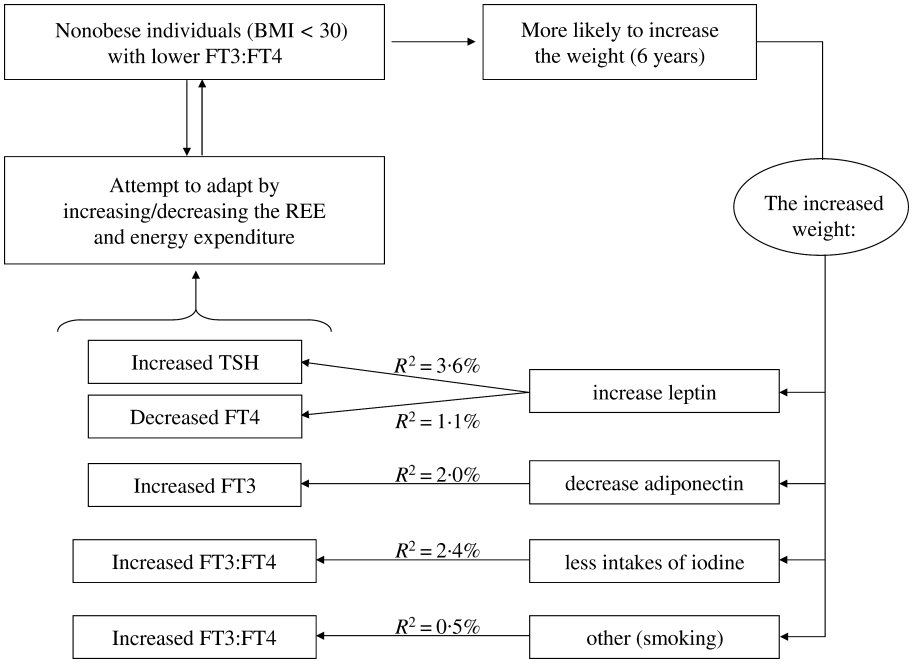

Figure 3 Nonobese persons (BMI < 30) with a lower free triiodothyronine (FT3):FT4 ratio are more likely to increase weight during their lifetime and become obese. During this process of weight gain, very important metabolic changes take place in the adipose tissue, such as an increase in leptin or reduction in adiponectin, as well as changes in other cytokines and adipokines. Conversely, the changes in peripheral thyroid hormone levels may be an adaptation process to increase resting energy expenditure (REE) and therefore energy expenditure. In real life, the influence of environmental factors is of great importance in the explanation of the variance in weight change (R^2). The response of the thyroid axis also probably varies depending on such factors as iodine intake or smoking. In our study, those persons who smoked had higher FT3:FT4 ratios, with an interaction between smoking and the presence of obesity in the explanation of the variance in the FT3:FT4 ratio. Finally, the obese persons consumed less iodine. Iodine intake may condition thyroid hormone levels and their association with weight gain. Admittedly, the contribution to weight gain and continued obesity of each of the variables related with thyroid function is small (R^2), but taken together and in the whole population, these contributions must nevertheless be taken into account.

A few cross-sectional studies have found an association in obese persons between levels of thyroid hormones and insulin resistance [2,3]. However, the results are contradictory [23]. In our study, the HOMA-IR seemed to correlate with the FT4. A reduction in thyroid hormones, especially FT3 [5], during active weight loss and an increase in FT3 and decrease in the FT3:FT4 ratio during active weight gain [6] have also been associated with the changes in insulin resistance [6,31]. Moreover, improvements in insulin sensitivity after exercise therapy were blunted by subclinical hypothyroidism [32]. Nevertheless, these correlations were weak, and we cannot rule out the possibility of interactions or confounding variables not contemplated in the analytical models.

Iodine is vital for the synthesis of the thyroid hormones. Of all the numerous studies that have examined the influence of small variations in the levels of the thyroid hormones in relation to body weight, only one considered iodine intake. However, unlike most studies [1], ours did assess iodine intake. The likelihood of being obese was lower in those persons who consumed iodized salt. At both the first and the second evaluation in the Pizarra Study, the levels of FT3 were significantly lower in those persons who did not consume iodized salt; at the second evaluation, we found a significant negative correlation between BMI, weight gain and urinary iodine concentration. The effect of iodized salt on the risk for obesity is probably mediated by the effect of the iodine on the thyroid hormone levels. Nevertheless, we were unable to demonstrate an interaction between iodized salt intake and FT3 levels in predicting the risk.

Tobacco smoking has complex effects on thyroid function. Like others [33], our study shows that the variation in thyroid hormone levels in obese persons is not independent of smoking. Different studies show that serum TSH concentrations are lower in smokers than nonsmokers, but the mechanism of this effect is unclear [34,35]. Smoking status is associated with differences in BMI, and in particular, smoking cessation is often followed by weight gain [36]. Also, Makepeace *et al.*

[37] have shown a significant association between FT4 concentrations and BMI in euthyroid subjects, which appears to be abolished by smoking. There are only limited data on whether smoking modifies any relationship that may exist between thyroid function and BMI in euthyroid subjects [1,38]. De Pergola *et al.* [39] showed that smoking increases FT3 levels independently of age, gender, obesity, body fat distribution and metabolic parameters. In the study by Nyrnes *et al.* [38], the relationship between TSH and BMI seen in nonsmokers was not evident in smokers, whereas Knudsen *et al.* [1] did not present data for smokers and nonsmokers separately.

This study has both strengths and limitations. On the one hand, a few of the associations found are weak. However, the contribution of the thyroid hormones to the explanation of the variance in basal metabolic rate in most studies is very low [23]. Furthermore, this study cannot determine cause and effect. On the other hand, the research method contemplated various nutritional aspects, such as iodine intake, that are of great importance in the regulation of the thyroid function [40], as well as health care habits, such as smoking. Some of the discrepancies found between the numerous earlier studies on the role of the thyroid hormones in the regulation of body weight in the general euthyroid population could be explained by the role played by iodine intake and smoking.

Obesity is a dynamic process that occurs as a result of weight increase over a person's lifetime. Taken together, the results of this study suggest that changes in the levels of the thyroid hormones could be the consequence, rather than the cause, of the increase in adipose mass and weight (Fig. 3). Therefore, these alterations of thyroid hormones seem to be an adaptation process to reduce the availability of energy for conversion into fat. The association found between weight gain, adipokines, urinary iodine and the levels of the thyroid hormones suggest that the associations between the thyroid hormones and body weight could be partly explained by the metabolic adjustments associated with weight gain.

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Conflict of interest statement

No conflicts of interest exit.

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