Effects of thyroid hormone and depression on common components of central obesity

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Abstract

Objective: We investigated the prevalence of abnormal thyroid function and depression in centrally obese participants, and to analyze the relationship of thyroid hormones and depression with components of central obesity.

Methods: We randomly selected 858 centrally obese participants and 500 non-obese controls in this study. For all participants, we measured serum free triiodothyronine (FT3), free thyroxine (FT4), thyroid-stimulating hormone (TSH), body mass index (BMI), waist–hip ratio (WHR), fasting blood glucose and insulin, homeostasis model assessment of insulin resistance (HOMA-IR), lipid concentrations, and blood pressure. Depression was assessed using the Center for Epidemiological Studies-Depression (CES-D) scale.

Results: Centrally obese participants had a higher prevalence of hypothyroidism and depression than non-obese controls. Serum FT4 levels negatively correlated with BMI and serum TSH levels and positively correlated with BMI, WHR, total triglycerides (TG), total cholesterol (TC), and low density lipoprotein cholesterol (LDL-C). After excluding participants with hypothyroidism and hyperthyroidism, serum FT4 levels showed negative correlation and serum TSH levels showed positive correlation with BMI in the remaining centrally obese participants. CES-D scores positively correlated with BMI.

Conclusion: We found high prevalences of hypothyroidism and depression among centrally obese participants. FT4 and TSH are important in weight regulation. Depression positively correlated with obesity.

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Introduction

Obesity is presenting a great challenge to developing countries worldwide. In China, previous studies have shown that the prevalence of obesity has been obviously increasing over the past two decades, especially in large cities.1,2 Thyroid hormones play an important role in the regulation of metabolism, including energy expenditure; thermogenesis; and protein, carbohydrate, and lipid metabolism.3–5 Thyroid dysfunction can lead to obesity or obesity-related diseases, such as metabolic syndrome, hypertension, hyperglycemia, and dyslipidemia.6–8 Modest alterations in thyroid hormone levels are common among obese people.9,10 Associations between thyroid hormones and related components of obesity have been reported in recent studies.11,12 Central accumulation of fat in obese people, called central obesity, causes a wide range of metabolic disorders.13 We aimed to investigate the morbidity of thyroid dysfunction, including modest thyroid function alterations within the normal range, among centrally obese people and to analyze the associations of thyroid hormone levels with common indices of obesity.

A systematic review and meta-analysis involving 41,344 outpatients showed the overall prevalence of depression or depressive symptoms was 27%.14 This suggests a high prevalence of depression among the general population. Obesity increases the occurrence of depressive symptoms, and depression seems to be a risk factor for obesity. Some studies have confirmed a bi-directional association between depression and obesity.15,16 In addition, extant evidence supports that the treatment of one condition (i.e., obesity or depressive disorders) appears to improve the course of the other condition.17 Research has revealed that depressive disorders increase unhealthy levels of physical activity, decrease energy expenditure, and promote biological changes in humans including inflammatory, endocrinological, and metabolic dysregulation.18–20 Therefore, we sought to investigate the prevalence of depression among people with central obesity and to determine the relationship between depression and components of obesity.

Participants and methods

Participants

From April 2017 to October 2018, we randomly selected centrally obese participants from among outpatients and inpatients of the Department of Endocrinology of Heilongjiang Provincial Hospital in Harbin, China. At the same time, we randomly selected non-obese individuals in the Physical Examination Center of the hospital. Non-obese controls were matched with obese patients for age and sex. We excluded participants with a history of heart failure, severe hepatic or renal disease, anemia, severe gastrointestinal diseases, malignant tumor, diabetes mellitus, or hypertension from this study. Participants diagnosed with thyroid diseases or receiving treatment for thyroid diseases (i.e., thyroid hormone drugs, anti-thyroid drugs, thyroid surgery, thyroid radiotherapy) or mental disorders were also excluded from this study.
Definitions

Participants with central obesity were defined as those with body mass index (BMI) ≥28 kg/m² and waist circumference (WC) >90 cm in men and >85 cm in women. Diabetes mellitus was diagnosed according to the following criteria: fasting plasma glucose (FPG) ≥7.0 mmol/L (no caloric intake for at least 8 hours) and/or casual plasma glucose ≥11.1 mmol/L and/or 2-hour plasma glucose ≥11.1 mmol/L in an oral glucose tolerance test. In the absence of typical clinical characteristics of hyperglycemia, these criteria were confirmed on a different day. Hypertension was categorized as average systolic blood pressure (SBP) ≥140 mmHg and/or diastolic BP (DBP) ≥90 mmHg, which was confirmed in measurements taken at least twice on a different day.

Anthropometric and biochemical measurements

Height and weight were measured using an ultrasonic height and weight measuring scale (OMRON, Beijing, China). WC was measured at the midpoint between the anterior superior iliac spine and the lower margin of the last rib. Hip circumference (HC) was measured with participants wearing light clothing at the level of the widest diameter around the buttocks. The waist–hip ratio (WHR) was then calculated according to the formula: WC (cm)/HC (cm). Blood samples were obtained from all participants after an 8-hour overnight fast. Levels of serum free triiodothyronine (FT3), free thyroxine (FT4), thyroid-stimulating hormone (TSH), and free thyroxine index (FI) were assayed using electrochemiluminescence immunoassays (Roche Diagnostics, Mannheim, Germany). FPG, total cholesterol (TC), total triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) were assayed with an automatic biochemical analyzer (Hitachi, Ltd., Tokyo, Japan). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated according to the formula: FI (mIU/L) × FPG (mmol/L)/22.5. Blood pressure was measured on the right arm using an electronic sphygmomanometer (OMRON, Beijing, China) with the participant in a seated position after resting for at least 30 minutes.

Assessment of depression

Depression was assessed using the Center for Epidemiological Studies-Depression (CES-D) scale by one professional physician (Bin-Hong Duan) on our research team. Participants were asked to report the frequency of each depressive symptom experienced in the previous week. This self-report measure includes 20 items and responses are given using a four-point Likert scale (0, less than 1 day per week; 1, 1–2 days a week; 2, 3–4 days a week; and 3, over 5–7 days a week). Among the 20 items, four (items 4, 8, 12 and 16) are reversed scores. The total CES-D score ranges from 0 to 60, with higher scores indicating higher levels of depression. A total score less than 16 indicates normality. A total score ≥16/60 indicates clinically significant depression.

Medical ethics approval

Ethical approval was obtained from the Medical Ethics Committee of Heilongjiang Provincial Hospital. We had access to identifying information of individual participants during and after data collection. Written informed consent was obtained from all participants; only those participants who signed the consent form were enrolled in the study. All study protocols were carried out in accordance with the principles laid down in the Declaration of Helsinki.
Statistical analysis

Statistical analysis was performed using IBM SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Categorical data were evaluated in terms of frequency and percentage and continuous data are presented as mean ± standard deviation. The chi-squared test was used to compare the prevalence of abnormal thyroid function, depression, and other obesity-related diseases between two groups. A two-sample \( t \)-test was used to compare continuous data between two groups. Pearson correlation analysis was used to estimate the association between variables. The odds ratios (ORs) and 95\% confidence intervals (CIs) for serum FT3, FT4, and TSH levels and CES-D scores, in association with components of central obesity, were analyzed using multivariate logistic regression analysis, after adjusting for age and sex. A \( P \)-value < 0.05 was considered statistically significant.

Results

Clinical and laboratory characteristics of the study groups
The study population included 858 centrally obese participants (460 males and 398 females) aged 57.2 ± 17.5 years, and 500 non-obese sex and age-matched controls (285 males and 215 females, age 53.4 ± 14.2 years). Descriptive statistics of participant characteristics are shown in Table 1. There were no significant differences with respect to age, sex ratio, serum FT3

| Parameters      | Centrally obese group (n = 858) | Control group (n = 500) | Statistical significance |
|-----------------|---------------------------------|-------------------------|--------------------------|
| BMI, kg/m\(^2\) | 28.92 ± 3.13*                   | 22.12 ± 2.04            | \( t = 43.49, P < 0.001 \) |
| WHR (male)      | 0.92 ± 0.21*                    | 0.85 ± 0.11             | \( t = 8.05, P < 0.001 \) |
| WHR (female)    | 0.85 ± 0.22*                    | 0.76 ± 0.10             | \( t = 10.30, P < 0.001 \) |
| FPG, mmol/L     | 5.13 ± 1.39                     | 5.06 ± 1.09             | \( t = 1.029, P = 0.303 \) |
| FI, \( \mu \)U/mL | 10.35 ± 5.62*                   | 9.76 ± 4.05             | \( t = 2.236, P = 0.025 \) |
| HOMA-IR         | 2.85 ± 1.61*                    | 2.63 ± 1.12             | \( t = 2.050, P = 0.040 \) |
| TC, mmol/L      | 4.97 ± 2.37*                    | 4.70 ± 1.59             | \( t = 2.507, P = 0.012 \) |
| TG, mmol/L      | 2.31 ± 1.59*                    | 2.13 ± 0.65             | \( t = 2.923, P = 0.003 \) |
| LDL-C, mmol/L   | 2.49 ± 1.23*                    | 2.25 ± 0.66             | \( t = 4.676, P < 0.001 \) |
| HDL-C, mmol/L   | 1.01 ± 0.30*                    | 1.05 ± 0.36             | \( t = 2.096, P = 0.036 \) |
| SBP, mmHg       | 121.95 ± 15.05*                 | 119.50 ± 13.50          | \( t = 3.090, P = 0.002 \) |
| DBP, mmHg       | 80.50 ± 12.25*                  | 78.50 ± 10.05           | \( t = 3.258, P = 0.001 \) |
| FT3, pmol/L     | 4.12 ± 1.23                     | 4.03 ± 1.17             | \( t = 1.341, P = 0.180 \) |
| FT4, pmol/L     | 12.08 ± 4.80*                   | 12.61 ± 4.46            | \( t = 2.053, P = 0.040 \) |
| TSH, miU/L      | 1.75 ± 1.05*                    | 1.63 ± 1.02             | \( t = 2.068, P = 0.039 \) |
| CES-D score     | 16.33 ± 5.35*                   | 15.75 ± 3.46            | \( t = 2.423, P = 0.015 \) |

Abbreviations: BMI, body mass index; WHR, waist–hip ratio; FPG, fasting plasma glucose; FI, fasting serum insulin; HOMA-IR, homeostatic model assessment of insulin resistance; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein; DBP, diastolic blood pressure; SBP, systolic blood pressure; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; CES-D, Center for Epidemiological Studies-Depression scale.

*Significantly different (\( P < 0.05 \)) from non-obese participants.
levels, and FPG levels between the centrally obese group and the control group. Levels of BMI, WHR (male and female), FI, HOMA-IR, TG, TC, LDL-C, SBP, DBP, serum TSH, and CES-D scores were higher and levels of serum FT4, HDL-C were lower in participants with central obesity than in controls.

**Prevalence of abnormal thyroid function, depression, and obesity-related diseases in participants**

The prevalence of hypothyroidism and depressive symptoms in the centrally obese group (8.74% and 17.83%, respectively) was higher than in the non-obese control group (5.80% and 12.60%, respectively); this was also the case for type 2 diabetes mellitus, and hypertension. There was no significant difference in the prevalence of hyperthyroidism between the two groups. The results of comparison for the prevalence of abnormal thyroid function, depression, and obesity-related diseases between the two groups are shown in Table 2.

**Relationship of serum thyroid hormone levels and CES-D scores with components of central obesity**

The results of correlation analysis between serum thyroid hormone levels, CES-D scores, and obesity-related indices in centrally obese participants are shown in Table 3. We found no obvious associations between serum thyroid hormone levels, CES-D scores, and BMI, WHR, FI, FPG, HOMA-IR, TG, TC, LDL-C, HDL-C, SBP, or DBP in these participants. Similarly, there were no significant associations between serum FT3 levels and the above obesity-related parameters in the centrally obese group. There was significantly a negative correlation of serum FT4 levels with BMI among participants with central obesity. Serum TSH levels were positively correlated with BMI, WHR, TG, TC, and

| Diseases                        | Centrally obese group (N = 858) | Non-obese control group (N = 500) | Statistical significance |
|---------------------------------|----------------------------------|------------------------------------|--------------------------|
| Hypothyroidism, n (%)           | 75 (8.74)                        | 29 (5.80)                          | $x^2 = 3.932, P = 0.047$  |
|                                 |                                  |                                    | OR = 1.562,              |
|                                 |                                  |                                    | 95% CI: 1.002–2.434      |
| Hyperthyroidism, n (%)          | 25 (2.91)                        | 21 (4.2)                           | $x^2 = 1.597, P = 0.206$  |
|                                 |                                  |                                    | OR = 0.685,              |
|                                 |                                  |                                    | 95% CI: 0.779–1.236      |
| Type 2 diabetes mellitus, n (%) | 94 (10.96)                       | 33 (6.60)                          | $x^2 = 7.070, P = 0.008$  |
|                                 |                                  |                                    | OR = 1.741,              |
|                                 |                                  |                                    | 95% CI: 1.152–2.631      |
| Hypertension, n (%)             | 109 (12.70)                      | 36 (7.20)                          | $x^2 = 10.034, P = 0.002$ |
|                                 |                                  |                                    | OR = 1.876,              |
|                                 |                                  |                                    | 95% CI: 1.265–2.782      |
| Depression, n (%)               | 153 (17.83)                      | 63 (12.60)                         | $x^2 = 6.465, P = 0.011$  |
|                                 |                                  |                                    | OR = 1.505,              |
|                                 |                                  |                                    | 95% CI: 1.097–2.066      |

Abbreviations: OR, odds ratio; CI, confidence interval.
LDL-C in centrally obese participants. CES-D scores were positively correlated with BMI in the centrally obese group. After excluding 75 patients with hypothyroidism and 25 patients with hyperthyroidism, we found that serum FT4 levels showed a negative correlation (r = -0.068, P = 0.046) and serum TSH levels showed a positive correlation (r = 0.074, P = 0.041) with BMI in the remaining centrally obese participants.

The results of multivariate logistic regression analysis for the associations of serum thyroid hormone levels with components of obesity among all participants are shown in Table 4. After adjusting for age and sex, serum TSH levels were positively correlated with BMI and WHR but not with FI, FPG, TG, TC, LDL-C, HDL-C, DBP and SBP. In all participants, serum FT3 and FT4 levels and CES-D scores were not correlated with any of components of obesity.

**Discussion**

In this study, we investigated the prevalence of hypothyroidism, hyperthyroidism, depression, and common obesity-related diseases, including hypertension and type
2 diabetes mellitus in participants with central obesity. We analyzed the relationship between thyroid hormones, depression, and components of central obesity including BMI, WHR, IR, blood glucose and lipid levels, and BP.

We found that the morbidity rate of hypothyroidism was 8.74% in participants with central obesity and 5.80% in non-obese participants. In addition, serum FT4 levels were lower and serum TSH levels were higher in centrally obese participants than in non-obese controls. Therefore, this finding suggests a higher prevalence of hypothyroidism among central obese people compared with non-obese people. Higher concentrations of serum TSH and lower levels of serum FT4 among obese individuals compared with non-obese ones has been similarly reported in some studies. The main mechanism related to this difference is thought to be increased activity of thyroxine 5-deiodinase in obese people. Local conversion of T4 to T3 by thyroxine 5-deiodinase is a key mechanism of thyroid hormone regulation. The high conversion rate of T4 to T3 in obese individuals has been interpreted as a defense mechanism, capable of burning fat by increasing the basal metabolic rate and stimulating the production of brown adipose tissue.

In our centrally obese participants, correlation analysis showed that serum FT4 levels were negatively correlated with BMI and serum TSH levels were positively correlated with BMI, WHR, TG, TC, and LDL-C. However, no significant associations were found between serum FT3 levels and components of central obesity. After excluding participants with abnormal thyroid function, we found that serum FT4 and TSH levels were still associated with BMI. These results further indicate that both FT4 and TSH have important roles in weight regulation as well as in people with normal thyroid function. We found associations between serum TSH levels and the degree of central obesity (WHR), blood glucose, blood lipids, and BP in all obese patients. However, these associations were not statistically significant in obese patients with normal thyroid function. Moreover, we analyzed the association of thyroid hormones with components of obesity using logistic regression and found that serum TSH levels were still positively associated with BMI.

Table 4. Association of serum TSH levels in association with components of obesity using multivariate logistic regression.

| Variables | P value | OR  | 95% CI |
|-----------|---------|-----|--------|
| *BMI      | 0.012   | 1.477 | 0.738–3.663 |
| *WHR     | 0.004   | 1.798 | 1.271–5.014 |
| FI        | 0.591   | 1.013 | 1.082–2.392 |
| FPG       | 0.738   | 1.006 | 0.998–10.421 |
| HOMA-IR  | 0.223   | 1.19  | 1.102–1.959 |
| TC        | 0.529   | 1.042 | 1.059–2.216 |
| TG        | 0.875   | 1.001 | 1.152–2.331 |
| LDL-C     | 0.172   | 1.232 | 1.282–10.054 |
| HDL-C     | 0.119   | 1.284 | 1.398–1.949 |
| SBP       | 0.264   | 1.108 | 1.093–12.32 |
| DBP       | 0.32    | 1.012 | 1.023–5.524 |

Abbreviations: BMI, body mass index; WHR, waist–hip ratio; FPG, fasting plasma glucose; FI, fasting serum insulin; HOMA-IR, homeostatic model assessment of insulin resistance; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein; DBP, diastolic blood pressure; SBP, systolic blood pressure; OR, odds ratio; CI, confidence interval.

*P < 0.05.
for the difference in study findings was owing to the different study populations. Of note, in studies among adults with normal thyroid function, few assessments of the relationship between thyroid hormones and blood lipids, BP, blood glucose, and IR have reached the same conclusions.6,28 Future longitudinal and large population-based studies should be performed, to better assess whether these relationships exist in adulthood. In the present study, we also observed a higher prevalence of hypertension and type 2 diabetes mellitus in participants with central obesity. This finding is consistent with the results of many other studies.29

Depression and obesity are both high-risk diseases that are becoming global public health problems. These diseases have enormous negative impacts on the physical and mental health of the population.30,31 In this study, we found that the prevalence of depression was 17.83% in centrally obese patients and 12.6% in non-obese participants; there was a significant difference in the prevalence of depression between the two study groups. We also found higher CES-D scores among people with central obesity and these scores were positively associated with BMI. We failed to find an association between depression and the evaluated components of central obesity, including WHR, blood glucose, IR, blood lipids, and BP. These results showed that the severity of depression is positively associated with the degree of obesity.

A previous study reported that obesity is significantly associated with increased likelihood of having depression; however, WC as an indicator of central obesity was not associated with depression.32 Another study differentiated depressive symptoms according to somatic–affective and cognitive–affective symptoms; a significantly positive association of BMI, WC, WHR was found with somatic–affective symptoms but not with cognitive–affective symptoms.33 A few clinical studies have reported that depression is significantly associated with blood glucose, IR, lipid profile, and BP.34,35 In the present study, we did not reach this conclusion.

The main strength of this study is that the sample size was relatively large. A total 1358 participants were randomly selected over a period of more than 1 year, such that reliable conclusions can be drawn. One limitation of our study is that we did not consider some additional biochemical variables that may also contribute to depression. Further investigation on the relationship of depression with central obesity should include measurement of additional variables associated with depression; visceral fat, which is a better way to evaluate central obesity; and different ways of evaluating depression symptoms, including somatic and cognitive symptoms.

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**Declaration of conflicting interest**

The authors declare that there is no conflict of interest.

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