Journal of Psychiatric Research 190 (2025) 216–224

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Thyroid antibodies and depression: Is the relationship overstated?

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ARTICLE INFO

Keywords:
Depression
Thyroid antibody
Hashimoto's thyroiditis
NHANES

ABSTRACT

Background: Depression has been associated with Hashimoto's thyroiditis (HT), with growing evidence suggesting that thyroid antibodies may play a role. This study aimed to explore this potential link.
Methods: Data from 2897 euthyroid adults in NHANES 2007–2012 were classified by thyroid antibody status (TPOAb/TgAb). Associations with depressive symptoms (PHQ-9 scores) were evaluated using survey-weighted linear regression and adjusted via propensity score matching (PSM).
Results: Although thyroid hormone levels (FT3, FT4, and TSH) significantly differed across antibody-defined groups, no significant differences in PHQ-9 depression scores or symptom severity were observed between antibody-positive individuals and controls. TPOAb and TgAb positivity were not significantly associated with depressive symptoms in either the unmatched or propensity score–matched analyses. TgAb levels showed a statistically significant but negligible association with PHQ-9 scores ($\beta = -0.002$, $P = 0.04$). In contrast, FT3 levels were inversely associated with PHQ-9 scores ($\beta = -0.758$, $P = 0.01$), indicating a modest relationship between lower FT3 concentrations (within the normal range) and more severe depressive symptoms.
Limitation: Cross-sectional design limits findings to single-time-point measurements, and results are based on a U. S. sample.
Conclusion: In this nationally representative sample of euthyroid individuals, thyroid autoantibody positivity, whether TPOAb, TgAb, or both, was not significantly associated with presence of depressive symptoms. Although lower FT3 levels within the normal range were inversely associated with PHQ-9 scores, the clinical significance of this finding warrants further investigation.

1. Introduction

Depression, one of the most common mental health conditions, ranks among the top 25 causes of global burden (Collaborators, 2020). The COVID-19 pandemic has exacerbated this issue, leading to a 27.6 % increase in cases of major depressive disorder worldwide (Collaborators, 2021). Emerging research suggests a link between Hashimoto's thyroiditis (HT) and depression (Siegmann et al., 2018). The most widely recognized reason for this association is hypothyroidism caused by HT (Weetman, 2013). Patients with hypothyroidism frequently experience depression due to hormonal changes (Bathla et al., 2016; Beydoun et al., 2013; Ge et al., 2014; Ittermann et al., 2015; Ritchie and Yeap, 2015).

Additionally, an increasing number of studies suggest that thyroid antibodies themselves may also be related to depression (van de Ven et al., 2012). This hypothesis is supported by clinical studies conducted in euthyroid patients (Giynas Ayhan et al., 2014; Kirim et al., 2012; Stanić et al., 2023; Yalcin et al., 2017), neuroimaging studies reveal cortical brain perfusion abnormalities and reduced grey matter density in the left inferior frontal gyrus in euthyroid patients with HT (Millan et al., 2016; Piga et al., 2004). Animal experiments on euthyroid mouse also confirmed it (Cai et al., 2018).

However, the relationship between thyroid antibodies and depression remains contentious, with some research suggesting that depression is not directly related to thyroid antibodies (Delitala et al., 2016; Engum et al., 2005). Based on these premises, we conducted a cross-sectional study using data from the National Health and Nutrition Examination Survey (NHANES), a nationally representative dataset curated by the National Center for Health Statistics (NCHS). By controlling for potential confounding variables such as thyroid function, age, gender, and

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https://doi.org/10.1016/j.jpsychires.2025.08.003
Received 3 November 2024; Received in revised form 21 July 2025; Accepted 6 August 2025
Available online 6 August 2025

socioeconomic status, we aimed to explore the potential association between thyroid antibodies (TPOAb and TgAb) and the presence of depression. The NHANES database provides a continuous and consistent set of health indicators, with particularly robust data on depression scoring, enabling us to derive more meaningful insights into the correlation between thyroid antibodies and depression.

2. Materials and methods

2.1. Study design and participants

The NHANES database, a publicly accessible national survey, evaluates the health and nutritional status of the non-institutionalized U.S. population. For this study, we analyzed data from the NHANES cycles 2007–2008, 2009–2010, and 2011–2012, which include information on depression and thyroid-related indicator, specifically antibody levels. Although NHANES was not specifically designed to study depression, relevant data were extracted using broad questions, particularly the Patient Health Questionnaire-9 (PHQ-9). Participants with incomplete data were excluded from the analysis. The NHANES study has been approved by the Ethics Review Board of the National Center for Health Statistics in the United States, and all survey participants provided written informed consent. Access to the NHANES database does not require ethical or administrative approval.

2.2. Definition of depression

The PHQ-9 was used to assess depressive symptoms experienced over the preceding two weeks. Participants rated the frequency of nine core symptoms on a 4-point scale: 0 ("Not at all"), 1 ("Several days"), 2 ("More than half the days"), and 3 ("Nearly every day"). The assessed symptoms included: (1) anhedonia, (2) depressed mood, (3) sleep disturbances, (4) fatigue, (5) appetite changes, (6) feelings of low self-esteem or failure, (7) concentration difficulties, (8) psychomotor disturbances, and (9) suicidal ideation. The total PHQ-9 score ranges from 0 to 27, with higher scores indicating greater depressive symptom burden. Although not a substitute for clinical diagnosis, a cutoff score of $\geq$10 has demonstrated strong diagnostic performance in previous validation studies, with both sensitivity and specificity of 88 % for identifying individuals likely to meet criteria for Major Depression (Kroenke et al., 2001). The PHQ-9 also exhibits high internal consistency and is widely recognized as a reliable and valid tool for measuring depressive symptom severity in both clinical and population-based settings. For descriptive purposes, depressive symptom severity was categorized as follows: no depression (0–4), mild (5–9), moderate (10–14), moderately severe (15–19), and severe (20–27). Further information on the PHQ-9 instrument is available at: https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Questionnaire1.

2.3. Thyroid-related indicator

Various thyroid-related indicators were collected, with the following reference ranges applied: TPOAb <9 IU/mL, TgAb <4 IU/mL, free triiodothyronine (FT3) 2.5–3.9 pg/mL, free thyroxine (FT4) 0.6–1.6 ng/dL, thyroid-stimulating hormone (TSH) 0.24–5.4 μIU/mL, and thyroglobulin (TG) < 35.0 ng/mL. To ensure rigorous comparisons within a physiologically stable population, only participants with normal levels of TSH, FT3, FT4, and TG were included and classified as having euthyroid status. Based on the reference cutoffs for TPOAb and TgAb, euthyroid participants were further categorized into four mutually exclusive groups: (1) Control (both antibodies negative), (2) TPOAb positive only (TPOAb(+)), (3) TgAb positive only (TgAb(+)), and (4) Both TPOAb and TgAb positive (TPOAb(+) + TgAb(+)). Antibody positivity was defined as serum levels exceeding the upper limit of the corresponding reference range. Detailed information regarding laboratory methods and reference values is available from the NHANES Laboratory Data website:
https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Laboratory.

2.4. Other variables

In addition to thyroid-related indicators and depressive symptoms, other variables were also collected and analyzed in this study. Demographic characteristics included age, sex, ethnicity, education level, and marital status. Behavioral and clinical characteristics covered smoking, alcohol use, and medical histories of diabetes mellitus and hypertension. Laboratory indicators were further grouped into two categories: (1) clinical and metabolic markers, including body mass index (BMI), triglycerides, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), total cholesterol, glycohemoglobin, fasting glucose, insulin, uric acid, and creatinine; and (2) nutritional and micronutrient status, represented by iodine, due to its known relevance to thyroid function (Sorrenti et al., 2021).

2.5. Survey-weighted multivariable linear regression analysis

To assess the independent association between thyroid autoantibody status and depressive symptoms, we conducted survey-weighted multivariable linear regression using data from participants with euthyroid status, defined by normal levels of FT3, FT4, TSH, and TG. The outcome variable was the PHQ-9 total score, a validated measure of depressive symptom severity. The regression model included 29 clinically relevant predictors, encompassing demographic factors (age, sex, ethnicity, marital status, education level, and survey year), lifestyle factors (smoking and alcohol use), and clinical variables such as diabetes mellitus, hypertension, BMI, triglycerides, LDL-c, HDL-c, total cholesterol, glycohemoglobin, iodine, creatinine, uric acid, fasting glucose, and insulin. In addition, thyroid-related biomarkers, TSH, FT3, FT4, TG, TPOAb, and TgAb, as well as the antibody group classification variable (HT Group) were incorporated into the model.

2.6. Propensity score matching (PSM)

To reduce potential confounding and improve comparability between groups defined by thyroid autoantibody status, propensity score matching was conducted between the control group and each of the three antibody-positive groups. Matching was implemented using the nearest-neighbor method with a caliper width of 0.01 on the logit scale of the propensity score. Covariates included in the propensity score model were selected based on their clinical relevance and potential associations with both autoimmune thyroid markers and depressive symptoms. These covariates included smoking, alcohol use, age, sex, ethnicity, marital status, education level, diabetes mellitus, hypertension, BMI, triglycerides, LDL-c, HDL-c, glycohemoglobin, total cholesterol, iodine, creatinine, uric acid, fasting glucose, and insulin. By matching both categorical and continuous variables, this procedure aimed to minimize bias related to comorbidities and other confounding factors. Covariate balance was evaluated post-matching to confirm the adequacy of the PSM procedure.

2.7. Statistical analysis

All statistical analyses were performed using R (version 4.5.0). Complex survey design features of NHANES, including sampling weights (wtmec2yr), stratification, and clustering, were accounted for using the survey package. Continuous variables were summarized as weighted means ± standard deviations (SD) and compared across groups using survey-weighted ANOVA with Bonferroni-adjusted post hoc tests. Categorical variables were expressed as weighted proportions and analyzed using survey-weighted Chi-square tests. To examine the association between thyroid antibodies and depressive symptoms, survey-weighted

linear regression was conducted using the svyglm function, with the survey design specified via svydesign using sampling weights, strata, and primary sampling units. Covariates were selected based on clinical relevance. Multicollinearity was assessed using the alias function in a standard linear model (lm), and aliased variables were excluded prior to model fitting. PSM was implemented using the MatchIt package with the nearest-neighbor method and a caliper width of 0.01 on the logit scale. After matching, group differences in baseline characteristics were reassessed using t-tests or Mann–Whitney U tests for continuous variables, and Chi-square or Fisher's exact tests for categorical variables. All p-values were two-sided, and values < 0.05 were considered statistically significant.

3. Results

3.1. Demographic and clinical characteristics

3.1.1. Categorical variables

The final weighted study sample consisted of 2897 euthyroid participants after excluding individuals with incomplete data, as illustrated in Fig. 1. Participants were categorized into four groups: Controls (n = 2530), TPOAb(+) (n = 171), TgAb(+) (n = 88), and TPOAb(+) + TgAb (+) (n = 108). The distribution of categorical variables across these groups is summarized in Table 1, which presents unweighted frequencies alongside weighted proportions, derived using NHANES sampling weights. All reported p-values are based on survey-weighted analyses accounting for stratification, clustering, and sampling weights.

Statistically significant group differences were observed in sex ($P < 0.0001$), ethnicity ($P = 0.004$), and smoking ($P = 0.02$). In contrast, no significant differences were found in other demographic or clinical variables, including survey year ($P = 0.25$), marital status ($P = 0.96$), education level ($P = 0.12$), alcohol use ($P = 0.05$), hypertension ($P = 0.81$), or diabetes mellitus ($P = 0.39$).

Our primary variable of interest was depressive symptom severity, as measured by the PHQ-9. When categorized into standard PHQ-9 score ranges, depression levels did not significantly differ among the four groups ($P = 0.25$). Further pairwise comparisons confirmed the absence of statistically significant differences in PHQ-9 category distributions between controls and TPOAb(+) individuals ($\chi^2 = 0.458$, $P = 0.735$), controls and TgAb(+) individuals ($\chi^2 = 2.522$, $P = 0.070$), and controls and TPOAb(+) + TgAb(+) individuals ($\chi^2 = 1.081$, $P = 0.355$).

3.1.2. Continuous variables

Table 2 presents the comparison of continuous variables, including thyroid-related biomarkers (FT3, FT4, TSH, Tg, TPOAb, TgAb), lipid indices, and demographic parameters. All values are presented as weighted means ± standard deviations (SD), and all p-values are derived from survey-weighted ANOVA.

Although all participants were euthyroid, statistically significant differences were observed among the groups in age ($F = 19.54$, $P < 0.0001$), HDL-c ($F = 7.62$, $P = 0.0003$), FT3 ($F = 9.75$, $P < 0.0001$), FT4 ($F = 3.47$, $P = 0.02$), TSH ($F = 11.14$, $P < 0.0001$), Tg ($F = 85.69$, $P < 0.0001$), TgAb ($F = 25.2$, $P < 0.0001$), and TPOAb ($F = 44.13$, $P < 0.0001$). Post hoc pairwise comparisons showed that age was

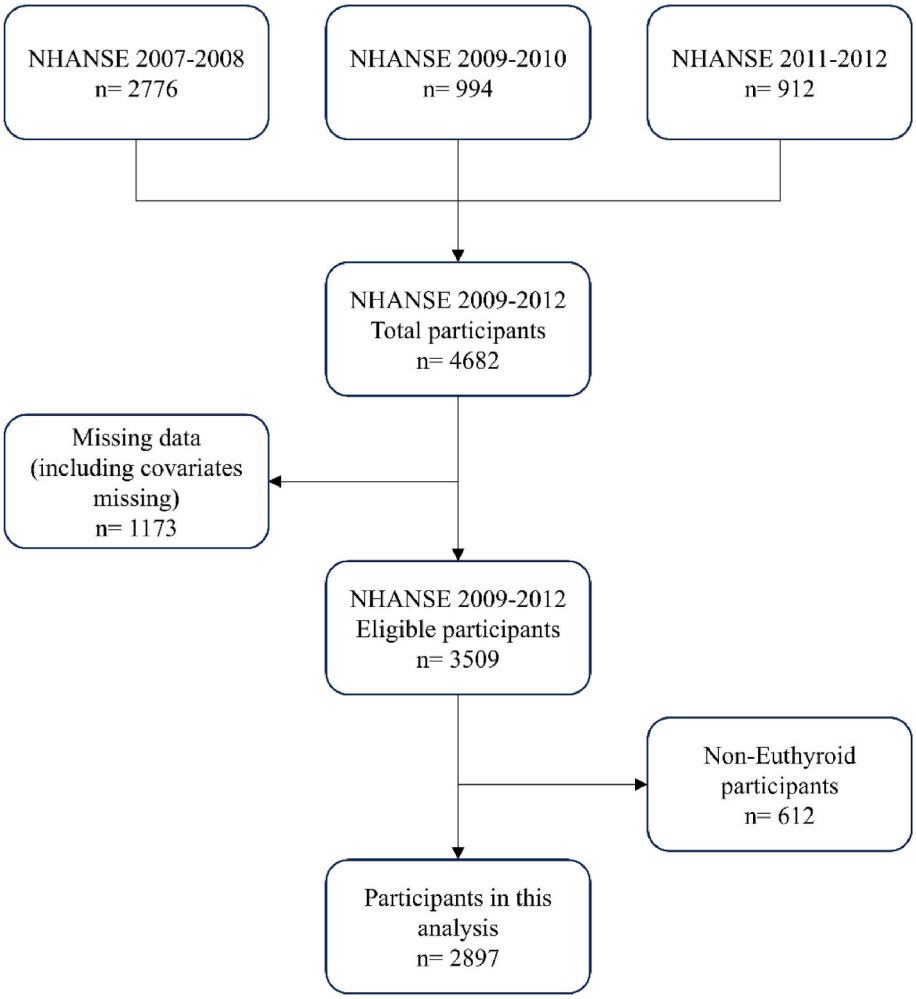

Fig. 1. Flow chart of the study.

Table 1
Distribution of categorical variables across four HT groups in the weighted NHANES sample.

Categorical Variables	HT Group				P
	Control (2530)	TPOAb(+) (171)	TgAb(+) (88)	TPOAb(+) + TgAb(+) (108)	
Year					
2007–2008	1544 (61.32)	97 (53.74)	54 (63.12)	63 (57.34)	0.25
2009–2010	542 (19.13)	44 (28.54)	15 (15.09)	29 (23.77)	
2011–2012	444 (19.55)	30 (17.72)	19 (21.79)	16 (18.89)	
Sex					
Female	1159 (46.52)	108 (70.14)	51 (68.54)	60 (56.7)	<0.0001
Male	1371 (53.48)	63 (29.86)	37 (31.46)	48 (43.3)	
Ethnicity					
Mexican American	420 (8.39)	28 (5.68)	16 (9.92)	26 (9.77)	0.004
Non-Hispanic Black	505 (10.47)	16 (3.78)	8 (5.26)	8 (3.90)	
Non-Hispanic White	1157 (69.89)	94 (80.99)	44 (72.09)	58 (79.26)	
Other Race	448 (11.24)	33 (9.54)	20 (12.73)	16 (7.07)	
Marital status					
Living alone	956 (34.45)	59 (32.42)	39 (34.7)	42 (34.05)	0.96
Married or living with partner	1574 (65.55)	112 (67.58)	49 (65.3)	66 (65.95)	
Education Level					
Less than 9th grade	40 (1.07)	2 (0.42)	3 (2.11)	0 (0)	0.12
9-11th grade	60 (1.75)	2 (0.19)	2 (1.58)	3 (4.41)	
Below high school	614 (15.13)	33 (9.97)	22 (14.75)	32 (15.81)	
High school	513 (19.64)	27 (15.22)	14 (20.89)	11 (10.56)	
Above high school	959 (45.68)	81 (57.09)	33 (42.58)	49 (54.74)	
High school graduate/GED or equivalent	79 (3.58)	10 (3.42)	2 (2.79)	2 (1.36)	
Some college or AA degree	141 (6.61)	5 (3.76)	3 (1.80)	5 (8.25)	
College graduate or above	124 (6.55)	11 (9.93)	9 (13.51)	6 (4.87)	
Smoking					
Never smoked	1354 (55.26)	92 (54.92)	53 (58.57)	69 (62.33)	0.02
Currently smoking	534 (20.16)	19 (10.05)	11 (12.87)	9 (6.95)	
Former	642 (24.58)	60 (35.03)	24 (28.55)	30 (30.72)	
Alcohol use					
Never drink alcohol	317 (9.69)	22 (7.86)	20 (16.48)	20 (16.53)	0.05
Former alcohol user	491 (16.36)	33 (13.11)	20 (17.67)	16 (9.75)	
Moderate alcohol user	353 (15.97)	32 (22.75)	7 (15.34)	11 (11.93)	
Mild alcohol user	809 (35.14)	59 (44.12)	29 (39.29)	48 (46.56)	
Heavy	560 (22.84)	25 (12.16)	12 (11.22)	13 (15.22)	
Hypertension					
No	1498 (64.63)	97 (62.64)	50 (59.71)	63 (61.74)	0.81
Yes	1032 (35.37)	74 (37.36)	38 (40.29)	45 (38.26)	
Diabetes Mellitus					
No	2145 (88.79)	141 (89.05)	67 (81.52)	94 (86.58)	0.39
Yes	385 (11.21)	30 (10.95)	21 (18.48)	14 (13.42)	
Depression symptom severity/PHQ9					
No Depression [0,4]	1941 (79.27)	132 (79.14)	67 (81.1)	84 (79.75)	0.25
Mild Depression [5,9]	370 (13.93)	25 (15.68)	11 (6.91)	17 (15.36)	
Moderate Depression [10,14]	145 (4.4)	11 (4.4)	7 (11.27)	4 (1.61)	
Moderately Severe Depression [15,19]	50 (1.52)	3 (0.77)	3 (0.73)	3 (3.28)	
Severe Depression [20,27]	24 (0.89)	0 (0)	0 (0)	0 (0)	

Abbreviation: HT, Hashimoto's thyroiditis; TPOAb, thyroid peroxidase antibody; TgAb, thyroglobulin antibody; Control (both antibodies negative); TPOAb(+), TPOAb positive only; TgAb(+), TgAb positive only; TPOAb(+) + TgAb(+), both TPOAb and TgAb positive; P, p-value. **Note:** Values are presented as unweighted frequencies and survey-weighted proportions, calculated using NHANES sampling weights.

significantly higher in the TPOAb(+), TgAb(+), and TPOAb(+) + TgAb (+) groups compared to controls (all $P < 0.05$). TSH levels were significantly elevated in the TPOAb(+) ($P = 0.0021$) and TPOAb(+) + TgAb(+) ($P = 0.0005$) groups relative to controls. FT3 was significantly lower in the TPOAb(+) group compared to controls ($P = 0.0027$), and FT4 also differed between these two groups ($P = 0.024$). HDL-c was higher in the TPOAb(+) group than in controls ($P = 0.0013$). Additionally, Tg, TPOAb, and TgAb levels were all markedly increased in antibody-positive groups versus controls (all $P < 0.001$). In contrast, no significant group differences were observed for BMI, triglycerides, LDL-c, glycohemoglobin, total cholesterol, fasting glucose, insulin, uric acid, creatinine, or iodine (all $P > 0.05$). Most critically, our primary outcome of interest, the PHQ-9 depression score, did not significantly differ among the four groups ($F = 0.05$, $P = 0.99$).

3.2. Association of thyroid antibodies with depression: a survey-weighted linear regression

For categorical variables (Table 3), the primary exposure variable, HT group, was not significantly associated with PHQ-9 scores. Compared to the control group, the TPOAb(+), TgAb(+), and TPOAb (+) + TgAb(+) groups yielded β-coefficients of −0.317 (95 % CI: 1.176 to 0.542, $P = 0.412$), 0.008 (95 % CI: 1.378 to 1.395, $P = 0.989$), and 0.151 (95 % CI: 1.155 to 1.457, $P = 0.793$), respectively.

In contrast, several other categorical covariates showed statistically significant associations with depressive symptoms. Male participants had significantly lower PHQ-9 scores compared to females ($\beta = -0.994$, 95 % CI: 1.639 to −0.350, $P = 0.008$). Being married or living with a partner was also associated with reduced depressive symptoms ($\beta = -0.787$, $P = 0.002$). Conversely, current smoking was linked to higher depression scores ($\beta = 1.279$, $P = 0.009$). Among ethnic groups, individuals categorized as "Other Race" had significantly higher PHQ-9 scores compared to Mexican Americans ($\beta = 0.964$, $P = 0.019$).

Table 2
Distribution of Continuous variables across four HT groups in the weighted NHANES sample.

Continuous Variables	HT Group				F	P
	Control	TPOAb(+)	TgAb(+)	TPOAb(+) + TgAb(+)		
Age (years)	46.33 ± 15.95[a,b,c]	51.20 ± 14.10	55.08 ± 17.85	52.35 ± 16.29	19.54	<0.0001
BMI (kg/m^2)	28.58 ± 6.27	28.44 ± 6.16	28.32 ± 5.60	28.00 ± 5.64	0.27	0.85
Triglyceride (mg/dL)	123.89 ± 65.35	119.41 ± 59.85	115.02 ± 63.06	125.40 ± 68.75	0.65	0.59
LDL-c (mg/dL)	116.58 ± 34.18	118.37 ± 31.50	117.18 ± 34.56	120.06 ± 33.91	0.42	0.74
HDL-c (mg/dL)	53.19 ± 15.05[a]	60.47 ± 17.69	57.59 ± 15.73	54.21 ± 15.16	7.62	0.0003
Glycohemoglobin (%)	5.58 ± 0.84	5.58 ± 0.76	5.82 ± 0.84	5.82 ± 1.12	2.64	0.06
Cholesterol (mg/dL)	194.56 ± 39.30[b]	202.73 ± 36.89	197.81 ± 42.84	199.27 ± 37.55	2.18	0.10
FastingGlucose (mg/dL)	105.33 ± 28.48	103.38 ± 27.47	106.95 ± 21.90	107.02 ± 24.08	0.42	0.74
Insulin (μU/mL)	12.39 ± 10.79	13.96 ± 39.61	10.68 ± 7.41	13.15 ± 10.61	1.22	0.31
Uric acid (mg/dL)	330.74 ± 81.21	314.32 ± 70.32	317.52 ± 73.31	331.46 ± 78.09	2.34	0.09
Creatinine (mg/dL)	121.22 ± 71.43	114.35 ± 66.84	107.88 ± 60.78	112.46 ± 71.20	1.78	0.16
Iodine (μg/L)	225.43 ± 986.61	190.05 ± 144.59	212.51 ± 303.05	198.56 ± 216.29	0.91	0.44
TSH (μIU/mL)	1.82 ± 0.94[a,c]	2.22 ± 1.09	1.95 ± 1.07	2.51 ± 1.23	11.14	<0.0001
FT3 (pg/mL)	3.21 ± 0.30[a]	3.12 ± 0.28	3.14 ± 0.35	3.13 ± 0.31	9.75	<0.0001
FT4 (ng/dL)	0.80 ± 0.12[b]	0.80 ± 0.15	0.86 ± 0.15	0.83 ± 0.19	3.47	0.02
Tg (ng/mL)	11.60 ± 7.11[b,c]	13.04 ± 8.61	3.99 ± 5.34	3.76 ± 5.98	85.69	<0.0001
TgAb (IU/mL)	0.66 ± 0.33[a,b,c]	1.11 ± 0.82	71.27 ± 157.01	161.34 ± 352.95	25.2	<0.0001
TPOAb (IU/mL)	0.95 ± 1.19[a,b,c]	127.46 ± 180	2.14 ± 2.26	207.19 ± 213.16	44.13	<0.0001
Depression scores	2.85 ± 3.88	2.75 ± 3.39	2.68 ± 3.93	2.71 ± 3.81	0.05	0.99

Abbreviation: HT, Hashimoto's thyroiditis; TPOAb, thyroid peroxidase antibody; TgAb, thyroglobulin antibody; Control (both antibodies negative); TPOAb(+), TPOAb positive only; TgAb(+), TgAb positive only; TPOAb(+) + TgAb(+), both TPOAb and TgAb positive; F, one-way ANOVA F-statistic; P, p-value. **Notes:** a: Control vs TPOAb (+), P < 0.05; b: Control vs TgAb (+), P < 0.05; c: Control vs TPOAb (+) + TgAb (+), P < 0.05.

Additionally, diabetes mellitus was positively associated with PHQ-9 scores (β = 0.775, P = 0.044).

For continuous variables (Table 4), among thyroid-related indicators, TgAb was significantly negatively associated with PHQ-9 scores (β = −0.002, 95 % CI: 0.003 to −0.0001, *P* = 0.04), but the effect size was small. A significant inverse association was also observed for FT3 (β = −0.758, 95 % CI: 1.506 to −0.069, *P* = 0.01), suggesting that lower FT3 levels within the normal range were linked to more severe depressive symptoms. No significant association was found for TPOAb (P = 0.33). Other thyroid-related markers, including TSH (P = 0.33), FT4 (P = 0.74), and TG (P = 0.20), were not significantly associated with PHQ-9 scores.

In addition, several clinical and metabolic indicators showed significant associations. Age was negatively associated with PHQ-9 scores (β = −0.025, 95 % CI: 0.043 to −0.007, *P* = 0.02), while both BMI (β = 0.050, 95 % CI: 0.015 to 0.084, *P* = 0.01) and insulin levels (β = 0.010, 95 % CI: 0.001 to 0.018, *P* = 0.04) were positively associated with depressive symptom severity.

The remaining continuous variables, including triglycerides, LDL-c, HDL-c, glycohemoglobin, total cholesterol, fasting glucose, uric acid, creatinine, and iodine, were not significantly associated with PHQ-9 scores (all P > 0.05).

3.3. Demographic and clinical characteristics after PSM

A total of 157, 76, and 99 matched pairs were obtained for comparisons between controls and the TPOAb(+), TgAb(+), and TPOAb(+) + TgAb(+) groups, respectively. After matching, most covariates demonstrated adequate balance across all comparisons, with the majority of standardized mean differences (SMDs) falling below the conventional threshold of 0.1 **(see** Supplementary Table 1.2.3**)**. As shown in Table 5a, Tables 5b, and Table 5c, demographic, clinical, and biochemical characteristics were generally well balanced.

Importantly, no significant differences in depression scores were observed between any of the matched groups. Specifically, PHQ-9 total scores were comparable between Control and TPOAb(+) (2.78 ± 3.78 vs. 2.76 ± 3.66, P = 0.922), Control and TgAb(+) (3.62 ± 4.17 vs. 2.95 ± 3.73, P = 0.121), and Control and TPOAb(+) + TgAb(+) (2.98 ± 3.96 vs. 2.95 ± 3.95, P = 0.819).

4. Discussion

Depression represents one of the top 25 global health burdens (Collaborators, 2020). The COVID-19 pandemic has further complicated the landscape, precipitating a 27.6 % surge in major depressive disorder diagnoses (Collaborators, 2021). Numerous studies have suggested a potential link between HT and depression, commonly attributed to hypothyroidism caused by HT. Thyroid hormones play a pivotal role in the functionality of the central nervous system, influencing the production of neurotrophic factors, mechanisms of learning and memory, and the regulation of brain stem cell fate (Chen et al., 2012; Fernández-Lamo et al., 2009; Koibuchi et al., 1999; Monopoli et al., 2011; Neveu and Arenas, 1996; Singh et al., 2003; Sui et al., 2010). Moreover, it is integral to mood regulation (Beydoun et al., 2013). Several studies, such as those by Gulseren et al. (2006) and Manish Bathla et al. (2016), have confirmed the impact of hypothyroidism on depression.

Additionally, research into Hashimoto's encephalopathy has shown that antibodies can significantly impact the central nervous system (Churilov et al., 2019). In patients with unipolar depression, anti-thyroid peroxidase and anti-thyroglobulin autoantibodies have been detected in cerebrospinal fluid (Dersch et al., 2020). These findings raise the possibility that autoimmune mechanisms, beyond thyroid dysfunction, may play a direct role in the development of depression.

Emerging clinical observations support this concept (Aydin et al., 2023; Giynas Ayhan et al., 2014; Kirim et al., 2012; Yalcin et al., 2017), complemented by imaging studies and animal models that provide further validation. M. Piga et al. (2004). identified significant perfusion abnormalities in patients with euthyroid HT, akin to those seen in severe forms of Hashimoto's encephalopathy. Moreover, research by Yao-Jun Cai et al. (2018) using a euthyroid HT mouse model revealed that these mice exhibited more depressive-like behaviors in forced swim and tail suspension tests compared to control counterparts.

However, some researchers have reported contradictory findings. In a study conducted by Anne Engum involving 30,175 individuals aged 40–84 years, no associations were identified between thyroid antibodies and symptoms of depression or anxiety (Engum et al., 2005). Alessandro et al. (Delitala et al., 2016). included 3138 individuals from the Sardi-NIA project and observed no association between TPOAb levels and depressive symptoms, nor any linear association between TSH or FT4 levels and depressive symptoms.

To investigate the relationship between thyroid antibody and

Table 3
Survey-weighted linear regression analysis of categorical variables associated with PHQ-9 depression scores.

Variable	Estimate	95 % CI	p
Sex			
Female	Reference		
Male	−0.994	[-1.639, −0.350]	0.008
Ethnicity			
Mexican American	Reference		
Non-Hispanic Black	0.144	[-0.473, 0.763]	0.597
Non-Hispanic White	0.496	[-0.003, 1.023]	0.061
Other Race	0.964	[0.216, 1.712]	0.019
Marital status			
Living alone	Reference		
Married or living with partner	−0.787	[-1.176, −0.397]	0.002
Education Level			
Less than 9th grade	0.594	[-1.499, 2.688]	0.524
9-11th grade	Reference		
Below high school	0.692	[-0.676, 2.061]	0.271
High school	−0.126	[-1.534, 1.282]	0.838
Above high school	−0.408	[-1.704, 0.889]	0.482
High school graduate/GED or equivalent	0.260	[-1.239, 1.759]	0.694
Some college or AA degree	−0.281	[-1.938, 1.376]	0.700
College graduate or above	−0.780	[-2.150, 0.590]	0.220
Smoking			
Never smoked	−0.199	[-0.655, 0.257]	0.337
Currently smoking	1.279	[0.439, 2.118]	0.009
Former	Reference		
Alcohol user			
Never drink alcohol	−0.304	[-1.219, 0.611]	0.457
Former alcohol user	Reference		
Moderate alcohol user	−0.394	[-1.281, 0.492]	0.328
Mild alcohol user	−0.689	[-1.551, 0.172]	0.100
Heavy	−0.413	[-1.036, 0.211]	0.162
Diabetes Mellitus			
No	Reference		
Yes	0.775	[0.028, 1.522]	0.044
Hypertension			
No	Reference		
Yes	0.705	[-0.048, 1.458]	0.062
HT Group			
Control	Reference		
TPOAb (+)	−0.317	[-1.176, 0.542]	**0.412**
TgAb (+)	0.008	[-1.378, 1.395]	**0.989**
TPOAb (+) + TgAb (+)	0.151	[-1.155, 1.457]	**0.793**
Year			
2007–2008	Reference		
2009–2010	0.211	[-0.308, 0.729]	0.369

Abbreviation: HT, Hashimoto's thyroiditis; TPOAb, thyroid peroxidase antibody; TgAb, thyroglobulin antibody; Control (both antibodies negative); TPOAb (+), TPOAb positive only; TgAb(+), TgAb positive only; TPOAb(+) + TgAb(+), both TPOAb and TgAb positive; Estimate, point estimate; 95 % CI, 95 % confidence interval; P, p-value. **Note:** The 2011–2012 cycle was removed from the regression due to perfect collinearity (aliasing) with other variables.

depressive symptoms, we analyzed data from the NHANES database, focusing on a control group and euthyroid individuals with positive thyroid antibodies, including TPOAb(+), TgAb(+), and TPOAb(+) + TgAb(+). After adjusting for potential confounding variables, we found no significant association between TPOAb positivity and PHQ-9 depression scores. This finding was consistent across both unmatched and PSM analyses. Although TgAb levels were nominally associated with depression scores in the linear regression model, the effect size was negligible ($\beta = -0.002$), and no significant differences were observed between TgAb(+) individuals and controls in the matched sample. These results suggest that thyroid antibody positivity, in isolation, is unlikely to exert a meaningful influence on depressive symptom severity. Notably, among participants with biochemically confirmed euthyroidism, serum FT3 levels showed a statistically significant negative association with PHQ-9 scores ($\beta = -0.758$, $P = 0.01$).

This suggests that even in the absence of overt hypothyroidism,

Table 4
Survey-weighted linear regression analysis of continuous variables associated with PHQ-9 depression scores.

Variable	Estimate	95 % CI	p
Age	−0.025	[-0.043, −0.007]	0.02
BMI	0.050	[0.015, 0.084]	0.01
Triglyceride	−0.056	[-0.218, 0.105]	0.43
LDL-c	−0.305	[-1.116, 0.506]	0.40
HDL-c	−0.307	[-1.115, 0.502]	0.40
Glycohemoglobin	−0.028	[-0.350, 0.294]	0.84
Cholesterol	0.306	[-0.504, 1.115]	0.40
FastingGlucose	−0.003	[-0.013, 0.008]	0.55
Insulin	0.010	[0.001, 0.018]	0.04
Uricacid	−0.003	[-0.006, 0.0004]	0.08
Creatinine	0.002	[-0.002, 0.005]	0.40
Iodine	0.0002	[-0.0001, 0.005]	0.24
TSH	0.077	[-0.098, 0.252]	0.33
FT4	0.226	[-1.332, 1.784]	0.74
FT3	**−0.758**	**[-1.506, -0.069]**	**0.01**
TG	0.015	[-0.01, 0.048]	0.20
TPOAb	0.001	[-0.001, 0.005]	0.33
TgAb	**−0.002**	**[-0.003, -0.0001]**	**0.04**
2009–2010	0.211	[-0.308, 0.729]	0.369

Abbreviation: Estimate, point estimate; 95 % CI, 95 % confidence interval; P, p-value.

relatively lower FT3 concentrations, within the normal reference range, may be linked to greater depressive symptom severity. Unlike previous studies that focused on depression caused by frank thyroid hormone deficiency, our findings highlight a subtler hormonal influence that may operate independently of clinically defined hypothyroidism. One possible explanation is that inter-individual differences in thyroid hormone sensitivity or peripheral conversion efficiency may influence mood and cognitive function despite normal laboratory values. This highlights the potential clinical importance of subtle hormonal variation in patients with autoimmune thyroid disease.

Taken together, these findings suggest that thyroid autoantibody positivity, whether TPOAb, TgAb, or both, is not significantly associated with depressive symptom severity among euthyroid individuals. This reinforces prior evidence that autoantibodies, in the absence of overt thyroid dysfunction, are unlikely to serve as reliable markers of depression risk. While a statistically significant association was observed between lower FT3 levels and higher PHQ-9 scores, this may reflect a subtle hormonal influence rather than a direct effect of autoimmunity. Further studies are warranted to explore the clinical relevance of FT3 variations within the normal range. Nonetheless, in this population, psychological evaluation remains the cornerstone for assessing depression risk.

To our knowledge, this study represents the first large-scale investigation into depression among control individuals and euthyroid patients with HT, utilizing the NHANES dataset. The consistent and coherent depression scoring system within NHANES has lent increased rigor and credibility to our findings.

However, this study has several limitations. First, as a retrospective cross-sectional analysis, it captures only a single time point and cannot reflect temporal fluctuations in thyroid antibodies or depressive symptoms. The lack of longitudinal data precludes causal inference and limits the ability to assess dynamic changes over time. Second, while the study focused on the commonly measured thyroid antibodies TPOAb and TgAb, TRAb was not included in the NHANES dataset and therefore could not be analyzed. The potential role of TRAb in mood disorders remains to be explored in future studies. Third, all participants were from the United States, which may limit the generalizability of the findings to other populations. Future research using longitudinal data, including broader antibody profiles and more diverse international cohorts, is warranted to confirm and extend these findings.

Table 5a
Differences in demographic and clinical characteristics between control and TPOAb(+) group after propensity score matching (PSM).

Variable	Group		P
	Control (157)	TPOAb(+) (157)	
Age	53.03 ± 17.82	52.96 ± 14.91	0.903
BMI	29.2 ± 7.45	29.33 ± 6.36	0.460
Triglyceride	128.56 ± 68.55	127.94 ± 69.68	0.966
LDL-c	115.11 ± 35.01	116.23 ± 31.93	0.664
HDL-c	55.76 ± 17.01	55.87 ± 16.21	0.873
Glycohemoglobin	5.83 ± 1.05	5.74 ± 0.93	0.381
Cholesterol	196.66 ± 40.52	197.71 ± 37.01	0.508
FastingGlucose	112.17 ± 33.54	108.77 ± 34.14	0.312
Insulin	14.69 ± 15.46	13.61 ± 10.38	0.883
Uricacid	323.32 ± 88.1	323.12 ± 73.04	0.754
Creatinine	119.30 ± 70.68	119.31 ± 71.89	0.985
Iodine	213.32 ± 230.79	186.82 ± 141.53	0.684
Depression score	**2.78 ± 3.78**	**2.76 ± 3.66**	**0.922**
Sex			
Female	98	97	1
Male	59	60	
Ethnicity			
Mexican American	26	25	0.932
Non-Hispanic Black	18	16	
Non-Hispanic White	88	87	
Other Race	25	29	
Marital status			
Living alone	58	53	0.637
Married or living with partner	99	104	
Education Level			
Less than 9th grade	3	2	0.785
9-11th grade	5	2	
Below high school	25	33	
High school	27	27	
Above high school	74	74	
High school graduate/GED or equivalent	8	4	
Some college or AA degree	4	5	
College graduate or above	11	10	
Smoking			
Never smoked	56	50	0.286
Currently smoking	25	18	
Former	56	50	
Alcohol user			
Never drink alcohol	19	21	0.813
Former alcohol user	29	32	
Moderate alcohol user	23	26	
Mild alcohol user	54	54	
Heavy alcohol user	32	24	
Diabetes Mellitus			
No	125	130	0.563
Yes	32	27	
Hypertension			
No	91	89	0.909
Yes	66	68	

Abbreviation: P, p-value. $p < 0.05$ was considered statistically significant.

Table 5b
Differences in demographic and clinical characteristics between control and TgAb(+) group after propensity score matching (PSM).

Variable	Group		P
	Control (76)	TgAb(+) (76)	
Age	58.57 ± 16.48	55.68 ± 18.8	0.446
BMI	28.67 ± 6.05	28.99 ± 5.83	0.912
Triglyceride	130.79 ± 67.57	124.66 ± 68.7	0.514
LDL-c	119.62 ± 37.94	117.84 ± 35.85	0.548
HDL-c	55.8 ± 15.86	54.67 ± 15.66	0.632
Glycohemoglobin	5.91 ± 1.36	5.83 ± 0.7	0.411
Cholesterol	201.59 ± 43.79	197.46 ± 42.97	0.402
FastingGlucose	112.82 ± 39.2	108.74 ± 21.09	0.841
Insulin	12.87 ± 9.37	12.3 ± 7.93	0.996
Uricacid	334.73 ± 81.49	330.27 ± 76.39	0.728
Creatinine	103.55 ± 59.3	111.57 ± 56.52	0.428
Iodine	181.71 ± 181.94	220.14 ± 347.64	0.221
Depression Score	**3.62 ± 4.17**	**2.95 ± 3.73**	**0.121**
Sex			
Female	43	42	1
Male	33	34	
Ethnicity			
Mexican American	15	13	0.952
Non-Hispanic Black	9	8	
Non-Hispanic White	37	38	
Other Race	15	17	
Marital status			
Living alone	32	30	0.869
Married or living with partner	44	46	
Education Level			
Less than 9th grade	0	2	0.945
9-11th grade	2	2	
Below high school	17	19	
High school	15	14	
Above high school	31	29	
High school graduate/GED or equivalent	1	1	
Some college or AA degree	5	3	
College graduate or above	5	6	
Smoking			
Never smoked	40	44	0.751
Currently smoking	14	11	
Former	22	21	
Alcohol user			
Never drink alcohol	12	14	0.452
Former alcohol user	16	19	
Moderate alcohol user	4	7	
Mild alcohol user	23	24	
Heavy alcohol user	21	12	
Diabetes Mellitus			
No	59	62	0.687
Yes	17	14	
Hypertension			
No	39	43	0.625
Yes	37	33	

Abbreviation: P, p-value. $p < 0.05$ was considered statistically significant.

5. Conclusion

In summary, this study, based on a large nationally representative cohort, found no significant association between thyroid autoantibody positivity, including TPOAb and TgAb, and depressive symptoms among euthyroid individuals. These findings remained consistent after adjusting for potential confounders and applying propensity score matching. Although TgAb levels demonstrated a statistically significant association with PHQ-9 scores in regression models, the effect size was minimal and unlikely to be clinically meaningful. A secondary finding revealed that lower FT3 concentrations within the normal physiological range were moderately associated with increased depressive symptoms, suggesting a possible hormonal influence independent of overt hypothyroidism.

Overall, these results indicate that thyroid autoantibodies alone are not reliable markers for depression risk in the absence of thyroid dysfunction. Psychological assessment should remain the clinical priority in this population. Future studies should further explore the relevance of subtle thyroid hormone variation, particularly FT3, using longitudinal and mechanistic approaches.

Table 5c
Differences in demographic and clinical characteristics between control and TPOAb(+) + TgAb(+) group after propensity score matching (PSM).

Variable	Group		P
	Control (99)	TPOAb(+) + TgAb (+) (99)	
Age	56.56 ± 15.25	54.29 ± 16.25	0.329
BMI	28.42 ± 5.38	28.23 ± 5.62	0.681
Triglyceride	132.19 ± 67.38	133.25 ± 71.53	0.934
LDL-c	115.66 ± 28.55	119 ± 31.21	0.433
HDL-c	54.1 ± 13.96	53.2 ± 14.15	0.654
Glycohemoglobin	5.71 ± 0.71	5.76 ± 0.89	0.995
Cholesterol	196.13 ± 33.5	198.84 ± 37.38	0.592
FastingGlucose	105.72 ± 20.76	106.02 ± 21.16	0.753
Insulin	12.12 ± 7.91	13.37 ± 9.69	0.349
Uricacid	327.14 ± 76.51	329.73 ± 77.12	0.812
Creatinine	109.58 ± 60.82	112.62 ± 68.07	0.893
Iodine	197.3 ± 177.2	203.14 ± 218.32	0.816
Depression Score	**2.98 ± 3.96**	**2.95 ± 3.95**	**0.819**
Sex			
Female	49	53	0.670
Male	50	46	
Ethnicity			
Mexican American	24	25	0.442
Non-Hispanic Black	3	8	
Non-Hispanic White	58	51	
Other Race	14	15	
Marital status			
Living alone	32	37	0.551
Married or living with partner	67	62	
Education Level			
Less than 9th grade	0	0	0.997
9-11th grade	1	2	
Below high school	31	29	
High school	10	11	
Above high school	44	44	
High school graduate/GED or equivalent	1	2	
Some college or AA degree	5	5	
College graduate or above	7	6	
Smoking			
Never smoked	55	62	0.591
Currently smoking	10	9	
Former	34	28	
Alcohol user			
Never drink alcohol	13	16	0.926
Former alcohol user	16	16	
Moderate alcohol user	13	10	
Mild alcohol user	42	44	
Heavy alcohol user	15	13	
Diabetes Mellitus			
No	81	85	0.562
Yes	18	14	
Hypertension			
No	52	56	0.669
Yes	47	43	

Abbreviation: P, p-value. $p < 0.05$ was considered statistically significant.

CRediT authorship contribution statement

Zhigang Tian: Writing – review & editing, Writing – original draft, Investigation, Data curation. **Bo Wang:** Software, Methodology, Investigation. **Li Chen:** Writing – review & editing, Writing – original draft.

Funding

None.

Declaration of competing interest

All authors declare that they have no conflicts of interest.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2025.08.003.

References

Aydin, E., Bingöl Aydin, D., Çarkaxhiu Bulut, G., İşgüven Ş, P., 2023. Psychopathological analysis of adolescent girls with autoimmune thyroiditis. Cureus 15 (12), e50418.
Bathla, M., Singh, M., Relan, P., 2016. Prevalence of anxiety and depressive symptoms among patients with hypothyroidism. Indian J. Endocrinology Metabolism 20 (4), 468–474.
Beydoun, M.A., Beydoun, H.A., Kitner-Triolo, M.H., Kaufman, J.S., Evans, M.K., Zonderman, A.B., 2013. Thyroid hormones are associated with cognitive function: moderation by sex, race, and depressive symptoms. J. Clin. Endocrinol. Metabol. 98 (8), 3470–3481.
Cai, Y.J., Wang, F., Chen, Z.X., Li, L., Fan, H., Wu, Z.B., Ge, J.F., Hu, W., Wang, Q.N., Zhu, D.F., 2018. Hashimoto's thyroiditis induces neuroinflammation and emotional alterations in euthyroid mice. J. Neuroinflammation 15 (1), 299.
Chen, C., Zhou, Z., Zhong, M., Zhang, Y., Li, M., Zhang, L., Qu, M., Yang, J., Wang, Y., Yu, Z., 2012. Thyroid hormone promotes neuronal differentiation of embryonic neural stem cells by inhibiting STAT3 signaling through TRα1. Stem Cell. Dev. 21 (14), 2667–2681.
Churilov, L.P., Sobolevskaia, P.A., Stroev, Y.I., 2019. Thyroid gland and brain: enigma of Hashimoto's encephalopathy. Best Pract. Res. Clin. Endocrinol. Metabol. 33 (6), 101364.
Collaborators, C.-M.D., 2021. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. Lancet 398 (10312), 1700–1712.
Collaborators, G.M.D., 2020. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. Lancet 396 (10258), 1204–1222.
Delitala, A.P., Terracciano, A., Fiorillo, E., Orrù, V., Schlessinger, D., Cucca, F., 2016. Depressive symptoms, thyroid hormone and autoimmunity in a population-based cohort from Sardinia. J. Affect. Disord. 191, 82–87.
Dersch, R., Tebartz van Elst, L., Hochstuhl, B., Fiebich, B.L., Stich, O., Robinson, T., Matysik, M., Michel, M., Runge, K., Nickel, K., Domschke, K., Endres, D., 2020. Anti-Thyroid peroxidase and anti-thyroglobulin autoantibodies in the cerebrospinal fluid of patients with unipolar depression. J. Clin. Med. 9 (8).
Engum, A., Bjøro, T., Mykletun, A., Dahl, A.A., 2005. Thyroid autoimmunity, depression and anxiety; are there any connections? An epidemiological study of a large population. J. Psychosom. Res. 59 (5), 263–268.
Fernández-Lamo, I., Montero-Pedrazuela, A., Delgado-García, J.M., Guadaño-Ferraz, A., Gruart, A., 2009. Effects of thyroid hormone replacement on associative learning and hippocampal synaptic plasticity in adult hypothyroid rats. Eur. J. Neurosci. 30 (4), 679–692.
Ge, J.F., Peng, Y.Y., Qi, C.C., Chen, F.H., Zhou, J.N., 2014. Depression-like behavior in subclinical hypothyroidism rat induced by hemi-thyroid electrocauterization. Endocrine 45 (3), 430–438.
Giynas Ayhan, M., Uguz, F., Askin, R., Gonen, M.S., 2014. The prevalence of depression and anxiety disorders in patients with euthyroid Hashimoto's thyroiditis: a comparative study. Gen. Hosp. Psychiatry 36 (1), 95–98.
Gulseren, S., Gulseren, L., Hekimsoy, Z., Cetinay, P., Ozen, C., Tokatlioglu, B., 2006. Depression, anxiety, health-related quality of life, and disability in patients with overt and subclinical thyroid dysfunction. Arch. Med. Res. 37 (1), 133–139.
Ittermann, T., Völzke, H., Baumeister, S.E., Appel, K., Grabe, H.J., 2015. Diagnosed thyroid disorders are associated with depression and anxiety. Soc. Psychiatr. Psychiatr. Epidemiol. 50 (9), 1417–1425.
Kirim, S., Keskek, S.O., Köksal, F., Haydardedeoglu, F.E., Bozkirli, E., Toledano, Y., 2012. Depression in patients with euthyroid chronic autoimmune thyroiditis. Endocr. J. 59 (8), 705–708.
Koibuchi, N., Fukuda, H., Chin, W.W., 1999. Promoter-specific regulation of the brain-derived neurotropic factor gene by thyroid hormone in the developing rat cerebellum. Endocrinology 140 (9), 3955–3961.
Kroenke, K., Spitzer, R.L., Williams, J.B., 2001. The PHQ-9: validity of a brief depression severity measure. J. Gen. Intern. Med. 16 (9), 606–613.
Millan, M.J., Rivet, J.M., Gobert, A., 2016. The frontal cortex as a network hub controlling mood and cognition: probing its neurochemical substrates for improved therapy of psychiatric and neurological disorders. J. Psychopharmacol. 30 (11), 1099–1128.
Monopoli, M.P., Raghnaill, M.N., Loscher, J.S., O'Sullivan, N.C., Pangalos, M.N., Ring, R. H., von Schack, D., Dunn, M.J., Regan, C.M., Pennington, S., Murphy, K.J., 2011. Temporal proteomic profile of memory consolidation in the rat hippocampal dentate gyrus. Proteomics 11 (21), 4189–4201.

Neveu, I., Arenas, E., 1996. Neurotrophins promote the survival and development of neurons in the cerebellum of hypothyroid rats in vivo. J. Cell Biol. 133 (3), 631–646.
Piga, M., Serra, A., Deiana, L., Loi, G.L., Satta, L., Di Liberto, M., Mariotti, S., 2004. Brain perfusion abnormalities in patients with euthyroid autoimmune thyroiditis. Eur. J. Nucl. Med. Mol. Imag. 31 (12), 1639–1644.
Ritchie, M., Yeap, B.B., 2015. Thyroid hormone: influences on mood and cognition in adults. Maturitas 81 (2), 266–275.
Siegmann, E.M., Müller, H.H.O., Luecke, C., Philipsen, A., Kornhuber, J., Grömer, T.W., 2018. Association of depression and anxiety disorders with autoimmune thyroiditis: a systematic review and meta-analysis. JAMA Psychiatry 75 (6), 577–584.
Singh, R., Upadhyay, G., Kumar, S., Kapoor, A., Kumar, A., Tiwari, M., Godbole, M.M., 2003. Hypothyroidism alters the expression of Bcl-2 family genes to induce enhanced apoptosis in the developing cerebellum. J. Endocrinol. 176 (1), 39–46.
Sorrenti, S., Baldini, E., Pironi, D., Lauro, A., D'Orazi, V., Tartaglia, F., Tripodi, D., Lori, E., Gagliardi, F., Praticò, M., Illuminati, G., D'Andrea, V., Palumbo, P., Ulisse, S., 2021. Iodine: its role in thyroid hormone Biosynthesis and beyond. Nutrients 13 (12).
Stanić, G., Marinković, S., Milin Lazović, J., Ignjatović Ristić, D., 2023. Association between affective temperaments and psychosomatic symptoms in women with hashimoto's thyroiditis. PLoS One 18 (8), e0290066.
Sui, L., Ren, W.W., Li, B.M., 2010. Administration of thyroid hormone increases reelin and brain-derived neurotrophic factor expression in rat hippocampus in vivo. Brain Res. 1313, 9–24.
van de Ven, A.C., Muntjewerff, J.W., Netea-Maier, R.T., de Vegt, F., Ross, H.A., Sweep, F. C., Kiemeney, L.A., Vos, P.E., Buitelaar, J.K., Hermus, A.R., den Heijer, M., Janzing, J.G., 2012. Association between thyroid function, thyroid autoimmunity, and state and trait factors of depression. Acta Psychiatr. Scand. 126 (5), 377–384.
Weetman, A., 2013. A hundred years of Hashimoto's thyroiditis. Thyroid. Offic. J. Am. Thyroid Assoc. 23 (2), 135–136.
Yalcin, M.M., Altinova, A.E., Cavnar, B., Bolayir, B., Akturk, M., Arslan, E., Ozkan, C., Cakir, N., Balos Toruner, F., 2017. Is thyroid autoimmunity itself associated with psychological well-being in euthyroid Hashimoto's thyroiditis? Endocr. J. 64 (4), 425–429.