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Prevalence of Psychiatric Disorders in Thyroid Diseased Patients

Key Words

Thyroid diseases
 Psychiatric comorbidity
 Semistructured clinical interview
 Anxiety disorders
 Mood disorders

Abstract

Several studies have underlined the high prevalence of psychiatric symptoms and disorders in thyroid diseases. The aim of this study was to evaluate the prevalence of psychiatric disorders in 93 inpatients affected by different thyroid diseases during their lifetimes, by means of a standardized instrument, i.e., the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders-III-Revised, Upjohn Version (SCID-UP-R). The results showed higher rates of panic disorder, simple phobia, obsessive-compulsive disorder, major depressive disorder, bipolar disorder and cyclothymia in thyroid patients than in the general population. These findings would suggest that the co-occurrence of psychiatric and thyroid diseases may be the result of common biochemical abnormalities.

Introduction

The first descriptions of neuropsychiatric symptoms, in particular impairments of cognitive functions, behavioral and mood disturbances, increased or decreased appetite and motor activity, muscular weakness and tremors and palpitations in patients with thyroid diseases, date back to the 19th century [1, 2]. Subsequently, they were documented by different authors [3–9] and mainly interpreted as consequences of thyroid dysfunctions and, therefore, subject to improvement after specific treatments for thyroid.

Anxiety states with symptoms similar to those of panic disorder, have been observed in hyperthyroidism [1, 2]. Subjects with thyroid diseases and a positive family history of mood disorders [10, 11] have also been reported as suffering from mania and hypomania, depression, obses-

sive compulsive symptoms and organic mental disorders, such as delirium [12, 13].

Depression and impairment of attention and memory seem to be more common in hypothyroidism [14], while depression, paranoid ideation and auditory or visual hallucinations are more typical of acute conditions such as mixedema [15].

Recently, more attention has been devoted to the diagnostic assessment of mental disorders concomitant with thyroid diseases, the more frequently reported diagnoses being schizophrenia, anxiety states, mood disorders and paranoid syndromes [16–18]. Furthermore, some authors underline the problem of distinguishing thyrotoxicosis from panic disorder or generalized anxiety disorder, especially in the early stages of the disorder [19, 20].

Less information is available on the possible relationship between autoimmune thyroid disorders and psy-

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chiatric disorders: according to some authors, dysregulations in some components of the immune response may themselves produce abnormal behaviors, even in 'euthyroid' states [20–22]. Furthermore, the available studies in this field are limited to the evaluation of the psychiatric symptoms that are concomitant with the thyroid disease, without taking into consideration the familial or personal history of the individual.

Our study aimed, therefore, at evaluating the frequency and severity of anxiety and mood disorders during the lifetime of patients with Graves' disease. Patients with other thyroid diseases were also included for further comparisons.

Method

Ninety-three inpatients (72 female, 21 male, aged between 21 and 81 years, mean \pm SD 48.2 ± 13.7) consecutively recruited at the Endocrinology Department of Pisa University, were studied. The endocrinologists (E.F., L.C.) reviewed all thyroid function test abnormalities and classified the patients being treated in a naturalistic way: 47 (38 female, 9 male) were affected by Graves' disease, 30 (24 female, 6 male) by multinodular goiter, 10 (6 female, 4 male) by adenoma, 5 (3 female, 2 male) by thyroid cancer and 1 (female) by pharmacological hyperthyroidism (table 1).

The presence of psychiatric disorders was assessed by means of the Structured Clinical Interview for DSM-III-R Upjohn Version (SCID-UP-R [23]) for Anxiety and Mood Disorder, by two residents of the Institute of Psychiatry of Pisa University, each with at least 4 years of clinical experience, under the supervision of senior psychiatrists. Subjects were also interviewed according to the Akiskal and Mallya criteria for affective temperaments [24].

Statistical analyses

The data were loaded into a database and statistically analyzed by means of frequency distribution. Comparisons between groups on continuous variables were carried out using Student's *t* test and on categorical variables, using χ^2 analysis. To minimize the chance of type II errors with the multiple comparisons, the Bonferroni correction was used to calculate the level of probability considered statistically significant. Only those variables with a value of $p < 0.05$ were considered statistically significant. However, variables significant at $p < 0.01$ are also shown in the tables as representing a trend deserving attention.

Results

The percentage of patients with psychiatric diagnoses, out of the total of 93 thyroid patients, was 63.2% ($n = 68$). Panic disorder (PD) was the most commonly reported disorder (45.6%, $n = 31$), followed by generalized anxiety disorder (GAD) (41.2%, $n = 28$), past depressive episodes (32.4%, $n = 22$), simple phobia (SP) (17.9%, $n = 12$),

Table 1. Demographic features and thyroid diseases of the patients (72 females, 21 males)

		Mean \pm SD
Demographic features	Age	48.2 \pm 13.7
	Age at onset (thyroid disease)	41.1 \pm 14.1
	Duration of thyroid disease, months	52.0 \pm 35.5
Thyroid diseases	Graves' disease	47 (38 f, 9 m)
	Multinodular goiter	30 (24 f, 6 m)
	Adenoma	10 (6 f, 4 m)
	Thyroid cancer	5 (3 f, 2 m)
	Iatrogenic hyperthyroidism	1 (f)

Table 2. Psychiatric disorder in 68 out of 93 patients with thyroid diseases

Psychiatric disorder	n	%
Panic disorder	31 (26 f, 5 m)	45.6
Generalized anxiety disorder	28 (27 f, 1 m)	41.2
Major depressive episode (past)	22 (21 f, 1 m)	32.4
Simple phobia	12 (12 f, 0 m)	17.6
Obsessive compulsive disorder	5 (f)	7.4
Social phobia	5 (f)	7.4
Manic episode (past)	4 (f)	5.9
Major depressive episode (current)	3 (f)	4.4
Cyclothymia	2 (f)	2.9
Substance abuse	1 (f)	1.5

Comparison between females and males (only significant data are reported) SP: $\chi^2 = 4.019$, $p = 0.045$; GAD: $\chi^2 = 6.798$, $p = 0.004$, past MDE: $\chi^2 = 4.096$, $p = 0.043$.

social phobia and obsessive compulsive disorder (OCD) (7.4%, $n = 5$), current major depressive episodes (MDE) (4.4%, $n = 3$). A positive past history for a manic episode was found in 5.9% ($n = 4$) of the patients, cyclothymia in 2.9% ($n = 2$) and substance abuse in 1.5% ($n = 1$) (table 2). Most of the 68 patients had two or more psychiatric diagnoses: 14 (20.6%) patients had two diagnoses, 9 (13.2%) patients three, 5 (7.4%) patients four and 1 (1.5%) patient five diagnoses.

Significant differences between males and females were observed for SP (12 female, 0 male; $\chi^2 = 4.019$, $p = 0.045$), GAD (27 female, 1 male; $\chi^2 = 6.798$, $p = 0.009$), and MDE in the past (21 female, 1 male; $\chi^2 = 4.096$, $p = 0.043$). No difference between the autoimmune and non-autoimmune diseases was recorded except a trend for

Table 3. Psychiatric disorders in 93 patients with thyroid disease: autoimmune vs. nonautoimmune

Psychiatric disorder	Graves' disease (n = 47)		Others (n = 46)	
	n	%	n	%
Panic disorder	17	36.1	14	30.4
Generalized anxiety disorder	15	31.9	13	28.3
Major depressive episode (past)	11	23.4	11	23.9
Simple phobia	10	21.3	2	4.3
Obsessive compulsive disorder	5	10.6	0	0
Social phobia	4	8.5	1	2.2
Major depressive episode	3	6.4	0	0
Manic episode	2	4.3	4.3	2
Cyclothymia	2	4.3	0	0
Substance abuse	0	0	1	2.2

Table 4. Affective temperament in 93 patients with thyroid disease

Temperament	n	%
Depressive	30	27.9
Hyperthymic	7	6.51
Cyclothymic	7	6.51
Irritable	3	2.8

OCD ($\chi^2 = 6.32$; $p = 0.0119$) and SP ($\chi^2 = 5.172$; $p = 0.023$) being more common in Graves' disease (table 3).

With regard to affective temperament, a depressive temperament was observed in 27.9% ($n = 30$), a hyperthymic temperament in 6.51% ($n = 7$), a cyclothymic temperament in 6.51% ($n = 7$) and an irritable temperament in 2.8% ($n = 3$) of subjects (table 4).

Discussion

The results of our study showed that a number of patients affected by different thyroid diseases were suffering concomitantly from a major psychiatric disorder. The most frequently encountered was PD, followed by GAD, MDE, SP and OCD. The prevalence rate was significantly higher than that reported in the USA by Regier and Robins [25] and in Italy by Bellantuono et al. [26]. The comorbidity between PD and thyroid diseases, especially hyperthyroidism, has already been underlined [27–29].

In our sample, MDEs and manic episodes were mainly recorded in the past; this is in contrast with previous studies which have reported a high incidence of depressive symptoms in thyroid diseases. However, our study is one of the few employing a semistructured interview which takes into account not only the current, thyroid disease-related psychiatric symptoms, but also those present during the subjects' lifetime.

When the patients were analyzed according to sex, significant differences between males and females emerged: female patients, who outnumbered the males 3:1 times in the total sample (not surprisingly, since thyroid diseases are more prevalent in females), showed a significantly higher percentage of GAD (27 vs. 1), MDE in the past (21 vs. 1) and SP (12 vs. 0); this would suggest the possible existence of sex-related patterns of psychiatric disorders in patients with thyroid diseases.

On the other hand, no difference was observed between patients with and without autoimmune thyroid diseases; however, although some diseases were present in an insufficient number of subjects for a reliable statistical analysis to be carried out, there was a trend for OCD and SP to be more common in Graves' disease.

The presence of psychiatric disorders during the lifetime of thyroid diseased patients would indicate that they are not related only to the occurrence of a physical illness, or to a sudden alteration in hormone levels or to specific thyroid treatments [30–32], but rather to persistent neurochemical abnormalities, perhaps at the level of a generic vulnerability to psychopathology, that may be restricted to temperament pathology or may trigger 'full' psychiatric disorders.

Alternatively, both thyroid diseases and psychiatric disorders might be the expression of a common dysfunction yet to be identified, perhaps affecting the hypothalamus or at the level of interactions between the immune and the central nervous systems.

References

- 1 Parry CH: Collections from the unpublished writings of the late C.H. Parry, London, Underwoods, 1825, vol 2.
- 2 Graves RJ: Newly observed affection of the thyroid gland in females. *Lond Med Surg J* 1835;7:516.
- 3 Fava GA, Sonino N, Murphy MA: Major depression associated with endocrine disease. *Psychiatr Dev* 1987;4:321-348.
- 4 Walter-Ryan WG, Fahs JJ: The problem with parsimony: Mania and hyperthyroidism. *J Clin Psychiatry* 1987;48:289-290.
- 5 Gabrilove JL: Neurologic and psychiatric manifestations in the classic endocrine syndromes; in *Endocrine and the Central Nervous System*. Edited by the Association for Research in Nervous and Mental Disease. Baltimore, Williams & Wilkins, 1966, pp 419-441.
- 6 Davis AT: Psychotic states associated with disorders of thyroid function. *Int J Psychiatry* 1989;19:47-56.
- 7 Zach J, Ackerman SH: Thyroid function, metabolic regulation, and depression. *Psychosom Med* 1988;50:454-468.
- 8 Wilson H, Jefferson JW: Thyroid disease, behavior, and psychopharmacology. *Psychosomatics* 1985;26:481-492.
- 9 Burch EA, Masservy TW: Psychiatric symptoms in medical illness: Hyperthyroidism revisited. *Psychosomatics* 1978;19:71-75.
- 10 Checkley SA: Thyrotoxicosis and the course of manic-depressive illness. *Br J Psychiatry* 1978; 133:219.
- 11 Reus VI, Gold P, Post R: Lithium-induced thyrotoxicosis. *Am J Psychiatry* 1979;136:724.
- 12 Bursten A: Psychosis associated with thyrotoxicosis. *Arch Gen Psychiatry* 1961;6:267.
- 13 Whybrow PC, Prange AJ, Treadway CR: Mental changes accompanying thyroid gland dysfunction. *Arch Gen Psychiatry* 1969;20:48.
- 14 Jain V: A psychiatric study of hypothyroidism. *Psychiatr Clin* 1972;5:121.
- 15 Beck HG: The hallucinations of myxedema. *Med Times* 1926;54:201.
- 16 Folks DG, Petrie WM: Thyrotoxicosis presenting a secondary depression. *Br J Psychiatry* 1982;140:432.
- 17 Granet RA, Kalman JP: Hypothyroidism and psychosis: A case illustration of the diagnostic dilemma in psychiatry. *J Clin Psychiatry* 1978; 39:270.
- 18 Trzepacz PT, McCue M, Klein I, Levey GS, Greenhouse J: A psychiatric and neuropsychological study of patients with untreated Graves' disease. *Gen Hosp Psychiatry* 1988;10:49-55.
- 19 Greer S, Ramsey I, Bagley C: Neurotic and thyrotoxic anxiety: Clinical, psychological and physiological measurements. *Br J Psychiatry* 1973;122:549-553.
- 20 Reus VI: Psychiatric aspects of thyroid disease; in Joffe RT, Levitt AJ (eds): *The Thyroid Axis and Psychiatric Illness*. Washington, American Psychiatric Press Inc, 1993, pp 171-194.
- 21 Baker GHB: Psychological factors and immunity. *J Psychosom Res* 1987;31:1-10.
- 22 Reus VI, Freimer N: Antithyroid antibodies: Behavioral significance; in Bunney WE Jr, Hippus H, Laakmann G, et al (eds): *Neuropsychopharmacology*. Berlin, Springer 1990, pp 362-370.
- 23 Spitzer RL, Williams JBW: Structured Clinical Interview for DSM-III-R, Upjohn Version, Revised (SCID-UP-R). New York, New York State Psychiatric Institute, 1988.
- 24 Akiskal H, Mallya G: Criteria for the 'soft' bipolar spectrum: Treatment implications. *Psychopharmacol Bull* 1987;23:68-73.
- 25 Robins LN, Regier DA: *Psychiatric disorders in America*. New York, The Free Press, 1991, pp 111-132.
- 26 Bellantuono C, Fiorio R, Zanotelli R, Transella M: Psychiatric screening in general practice in Italy. *Soc Psychiatry* 1987;22:113-117.
- 27 Weller MPI: Agoraphobia and hyperthyroidism. *Br J Psychiatry* 1984; 144:553-554.
- 28 Orenstein H, Peskind A, Raskind MA: Thyroid disorders in female psychiatric patients with panic disorder or agoraphobia. *Am J Psychiatry* 1988;145:1428-1430.
- 29 Turner TH: Agoraphobia and hyperthyroidism. *Br J Psychiatry* 1984; 145:215-216.
- 30 Berrios GE, Leysen A, Samuel C: Psychiatric morbidity following total and partial thyroidectomy. *Acta Psychiatr Scand* 1985;72:369-373.
- 31 Brockman DD, Withman RM: Post-thyroidectomy psychosis. *J Nerv Ment Dis* 1952;116: 340-345.
- 32 Josephson AM, MacKenzie TB: Appearance of manic psychosis following rapid normalization of thyroid states. *Am J Psychiatry* 1979;136: 846-847.