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Short communication

Stress is not associated with thyroid peroxidase autoantibodies in euthyroid women

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Abstract

Objective. Multiple genes and environmental factors play a role in the etiology of autoimmune thyroid disease (AITD). In Graves' hyperthyroidism, stress is such an environmental factor, but whether it plays a role in Hashimoto's hypothyroidism is unknown. We used validated questionnaires to evaluate an association between TPO antibodies, an early marker for AITD, and self-reported stress.

Subjects and methods. Recently Experienced Stressful Life Events, Daily Hassles, and mood (tendency to report positive and negative affects) were assessed in 759 euthyroid subjects.

Results. TPO antibodies were found in 183/759 (24%) of subjects. The TPO-Ab positive subjects were older (39.7 ± 12 vs. 34.2 ± 12 years; $p < .001$) than the TPO-Ab negative subjects, but the number of daily hassles (24 ± 14 vs. 25 ± 14; $p = .24$), the number of stressful life events (10 ± 6 vs. 11 ± 6; $p = .09$), and the scores on the affect scales (22.1 ± 7.4 vs. 22.2 ± 7.3; $p = .89$ for negative affect and 38.2 ± 5.1 vs. 38.3 ± 5.3; $p = .91$ for positive affect) were similar in TPO-Ab positive and TPO- Ab negative subjects.

Conclusions. We found no association between recently experienced stressful life events, daily hassles or mood and the presence of TPO antibodies in these euthyroid women.

Keywords: Thyroid peroxidase autoantibodies; Stress; Life events; Daily hassles; Mood; Autoimmune thyroiditis; Euthyroidism

1. Introduction

The etiology of autoimmune thyroid disease (AITD), encompassing Graves' hyperthyroidism and Hashimoto's hypothyroidism is multifactorial. It has been estimated that 79% of the liability to develop Graves' disease can be attributed to genes (Brix et al., 2001). Therefore other risk factors must play a role (Weetman and McGregor, 1994). Among environmental factors, stress has been implicated as a risk factor for the development of Graves' disease (Dayan, 2001; Winsa et al., 1991). Stress has a profound effect on the immune system (reviewed by Elenkov and Chrousos, 2002) and we have reported previously that self-reported life stress influences the number of circulating T lymphocytes (Brosschot et al., 1994). We therefore wondered whether stress might also be associated with Hashimoto's thyroiditis. The earliest event in Hashimoto's thyroiditis is the occurrence of TPO antibodies and we therefore compared stress-levels between 183 women with TPO antibodies and 576 without.

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2. Subjects and methods

The study cohort consisted of the 759 female subjects (age 18–65 years at study entrance) from the Amsterdam AITD cohort who were biochemically euthyroid at study entrance (Strieder et al., 2003). All subjects were in self-proclaimed good health, without a history of thyroid disease. They were asked to complete three questionnaires. Blood samples were drawn and coded to ensure confidentiality and serum was stored at −20 °C until assay.

The Dutch questionnaire on Recently Experienced Stressful Life Events (Brosschot et al., 1994; van de Willige et al., 1985) counts the total number of major life events experienced in the past 12 months (checklist of 60 possible events). The respondent scores separately the amount of pleasantness and unpleasantness associated with each experienced life event, rated on a scale from zero (meaning no (un) pleasantness at all) to four (a huge amount of (un) pleasantness). From this scale, the total amount of pleasantness and unpleasantness is calculated (maximal score 240 for each). When the amount of pleasantness exceeds the amount of unpleasantness the event is categorized as being pleasant and vice versa, yielding the total number of (un) pleasant events (maximum 60).

The Dutch Everyday Problem Checklist, a validated version of the Daily Hassles Scale (Kanner et al., 1981; Vingerhoets et al., 1989, 1996), consists of 114 items concerning daily hassles experienced in the last 2 months. It also measures the intensity of each hassle on a scale from zero to three, yielding the number of hassles experienced and the total intensity of these hassles (maximum 342).

The Positive and Negative Affect Schedule (PANAS; Watson et al., 1988) measures the current mood, in terms of positive and negative affect. It consists of 22 mood states (11 positive, 11 negative) and the respondent is asked to report whether she is affected by each of these states on a scale from 1 (not at all) to 5 (a lot). This yields the tendency to report positive and negative affect states both on a scale from 11 to 55.

Information concerning the use of psychotropic medication, educational level (on a 4-point scale), and employment (having a paid job) status was also obtained. Blood samples were drawn and coded to ensure confidentiality and serum was stored at −20 °C until assay. The concentration of antibodies against TPO and thyroglobulin (Tg) was measured using a chemiluminescence immunoassay (LUMI-test, Brahms, Berlin, Germany), and a value of $\geqslant$100 kU/L was defined as positive. Concentration of free thyroxin was assayed by time-resolved fluoroimmunoassay (fT4, Delfia, Turku, Finland) and concentration of thyrotropin by immunoradiometric assay (TSH, Delfia). For this study, euthyroidism was defined as a TSH value between 0.40 and 5.70 mU/L (Strieder et al., 2003).

The study was approved by the local Medical Ethics committee and all subjects gave their written informed consent.

Statistical analysis was done using the SPSS 10.0 package. Mean values were compared between subjects with and those without TPO antibodies using two-sided, unpaired Student's t test, median values using Mann–Whitney U test; rates were compared using χ^2 (or if appropriate Fishers' exact) tests. Because age is a known risk factor for a positive TPO antibody status (Strieder et al., 2003) comparison between groups was adjusted for the age difference using linear regression analysis.

3. Results

Subjects with TPO antibodies as compared to those without were older and had higher TSH levels, whereas free T4 values were similar in both groups as reported previously (Strieder et al., 2003). There were no differences in educational levels, employment status, or the use of psychotropic drugs (Table 1). As for the stress

Table 1
Characteristics of 759 female euthyroid relatives of AITD patients

	TPO-Ab pos	TPO-Ab neg	p Value
N	183	576	
Age (mean + SD) in years	39.7 ± 12	34.2 ± 12	<.001
TSH (median + range) in mU/L	2.3 (0.51–5.70)	1.6 (0.42–5.70)	<.001
Free T4 (median + range) in pmol/L	12.5 (7.6–42.7)	12.9 (7.2–21.5)	.16
Highest obtained level of education			
Elementary school (low level of education)	6 (3%)	20 (3%)	.90
High school (medium level of education)	55 (30%)	139 (24%)	.11
High school (high level of education)	65 (36%)	246 (43%)	.09
University (very high level of education)	56 (31%)	170 (30%)	.78
Employed	123 (67%)	404 (70%)	.45
On psychotropic drugs	4 (2.2%)	12 (2.1%)	.9
On psychotropic drugs in the previous year	9 (5%)	20 (3.5%)	.4

p Value for age was obtained by Student's t test, p values for TSH and free T4 were obtained by Mann–Whitney U test, p values for the other variables were obtained by χ^2 test. TPO-Ab positive: TPOAb $\geqslant$ 100 kU/L.