Reviewer's report

Title: Thyroid Function in Clinical Subtypes of Major Depression

Version: 1 Date: 18 October 2003

Reviewer: mauro giovanni G carta

Reviewer's report:

General

Thyroid function in Clinical Subtypes of Major Depression

The paper deals with an interesting topic: the role of thyroid autoimmunity on psychopathological manifestations of symptoms of mood disorders and on the mood disorders outcome. Some methodological issues and the small sample size limit the relevance of the results. The authors should work on the style of the presentation.

Specific Remarks:

Introduction

The introduction seems not to clear or sufficiently focalized the importance of the topic, the starting hypothesis and its basis.

The introduction should point out the recent hypothesis of a down regulation of hypothalamic-pituitary adrenal axis and CRH deficiency in atypical depression (see Gold PW and Chrousos GP, Mol Psychiatry 2002 7:254-75). As the modification of balance between proinflammatory and antiinflammatory cytokines may be related to cortisol and norepinefrine levels (see Elenkov et al. J Clin Metab 2001 86:4933-8, Elenkov and Chrousos Ann Acd Sci 2002 966:290-303) it is possible that only subtypes of depression are correlated with the autoimmune response.

Besides, the comorbidity of other autoimmune syndromes as the celiac disease (Carta et al. J Psychosom Research 2002) with depressive episodes seems to be strictly correlated with the presence of thyroid autoimmunity.

Methods

The measures of outcome are unclear. Authors write “According to their course during that period, they were divided in two groups....” Which are the positive outcome indicators? Symptoms at the end of the follow-up? Numbers of relapses/recurrences during the observation? The free periods of pathology?

1) The study does not assess the anti-thyroid peroxidase autoantibodies (anti-TPO), why? They are considered the most sensitive and specific markers of thyroid autoimmunity (see Mariotti et al. J Clin Endocrinol Metab 1990;71:661-669).

2) Statistical analysis: the sample size is at the limit of parametric tests applicability. It is difficult to accept that all thyroid parameters considered have a gaussian distribution (in contradiction against the hypothesis).

Results

Table 3 and 4: data correctly identify subtypes at 62%, 60%, 58.3% and controls at 98.3% but results are not statistically significant. This is also true for the distinction between treatment responders and not treatment responders. Authors should clarify these points.
Discussion
The conclusion that “melancholics are a more clearly defined and a core group” should be express with caution because of the methodological limits of the study. Authors assumed that some depressive subtypes have a different autoimmune profile. In the study depressive episodes are treated with SSRIs and SNRIs but literature support the idea that SSRIs and SNRIs have a worse response on atypical depression. The non response of atypical depressions (50% vs 33%) might have an influence on the difference of outcome between autoimmune depressive subtypes. This is not statistically significant but the sample is not large enough to exclude a type B error. The discussion is verbose. The role of thyroid function in depression might be faced only in relation with the specific study hypothesis.

Discretionary Revisions (which the author can choose to ignore)

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes

Declaration of competing interests: none