Reviewer's report

Title: Low vitamin D levels are associated with cognitive impairment in patients with Hashimoto thyroiditis

Version: 1 Date: 10 Sep 2018

Reviewer: Rowan Hardy

Reviewer's report:

The authors report a correlation between reduced vitamin D (25(OH)D) and cognitive impairment measured by the Montreal Cognitive Assessment score (MoCA) in a Hashimoto's thyroiditis (HT) cohort. Whilst findings of this nature have been reported in healthy control patients and in disease states such as CKD and T2D the finding may be of importance where evidence of attenuated vitamin D in a HT cohort exists. Unfortunately, these data are not well reported and require additional clarification and analysis.

Major

Methods: more details on numbers of HT patients required in methods.

Were MoCA scores taken in control cohorts? This is not clear

Table 1: You have a significant difference in age between MCI + and - HT groups. How can you interpret data where age may be a factor in influencing cognitive function

Please provide details of the control healthy cohort in a new table compared to the HT cohort. Please report these data in more detail in a table. The authors state that the patients in this study did not differ from the controls in terms of age, sex, BMI, education, as well as levels of TSH, FT3, and FT4 (all P > 0.05). Please let us see this data. Also any data on MoCA between groups would be relevant if collected

Authors state that "Serum levels of 25(OH)D were markedly lower in patients with HT than in healthy controls". Please include all of this data as discussed above.

Authors state "there was a negative correlation between 25(OH)D levels and MoCA scores (r = 160 0.510, P < 0.001).". Please also show these key correlations in a figure and in a table so that we can fully assess their correlation. In addition, what are the correlations like in the control
cohort you collected? This data is essential to help us identify if HT differs meaningfully from healthy controls.

"25(OH)D levels were inversely correlated with TPOAbs levels (r = -0.316, P < 0.001)." This is an important correlation. Please add a figure showing the univariate analysis. A table of all the univariate analysis performed in control and HT cohorts would be helpful in interpreting the data as requested above.

Table 1: the breakdown of vitD data into quartiles is very confusing and poorly explained. This requires better explanation and rationale as to why this was done, what it adds and the rationale for basing you multivariate analysis on these parameters.

The multivariate analysis are not well reported and brief. The legend for this table is limited and uninformative.

Greater detail is required within tables 1 and 2 in regards to the legends. Statistical tests used, multivariate, univariate etc. Are these HT patients only. Why cant we see data on control cohort here?

In their current form, interpretation of the results is complicated. These need to be presented more clearly with a more complete data for a better informed discussion. The discussion should then be re-written following the inclusion of additional data.

Minor:

Poor structure of sentence. Suggest removal of extremely: "It is well known that vitamin D is extremely essential for human health"

Methods. Please include all data on ELISA kits. Manufacturer, cat no etc.

Line 78: vitamin D may have neuroprotective properties by suppressing inflammation and oxidative stress [6-8].

These references do not identify an association with compromised cognitive function but do refer to inflammatory and mortality actions of vit D. Please find better references or include a reference that links inflammation directly to cognitive impairment.
These data support a growing body of literature linking cognitive impairment with reduced vitamin D levels. Previous studies have been mixed with reports of both vit D deficiency and normal vit D in HT cohorts (ie, Yasmeh et al, Endocr Pract. 2016 Hashimoto Thyroiditis Not Associated with Vitamin D Deficiency). This should be considered in the discussion.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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Please indicate the quality of language in the manuscript:

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