Reviewer's report

Title: Multi-parametric neuroimaging evaluation of cerebrotendinous xanthomatosis and their correlation with the neuropsychological presentations

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Reviewer: eytan raz

Reviewer's report:

This is a report of various imaging features in five patients with cerebrotendinous xanthomatosis.

As a whole the article is of limited interest.

The most important issue is that the five patients, a very small population for a VBM-TBSS study, are taken from only two families, posing a great interpretation bias in the results: are the results related to those family or are them generalized to CTX patients?

Adding at least five more patients from different families would be of added value to the paper.

The authors performed a thorough imaging study, including T13D, DTI and SPECT. This is of value, but should be sustained by hypotheses that are not really clear from the introduction. What is the aim of the work? Just look everything and describe the findings?

In the introduction the authors describe TBSS and VBM but do not really give us an understandable background of imaging in CTX.

In the methods section, it would be important to write the mean age of patients (although can be calculated from the table) and the mean age of healthy controls, not given at all. The parameters of imaging protocol should be much more detailed as well: for FLAIR and T2, add TR TE TI, number of slices, matrix and FOV. For DTI the authors did not obtain b0 images.

In the VBM description the authors write that "comparisonss between aptietns and controls were performed using the total volume of each segmented image": this is not clear, please explain.

In the TBSS section, although in the title is written that you performed TBSS for the three eigenvalues as well, in the description it looks like you only performed the FA and MD voxelwise analysis. It is not clear also which version of TBSS was used (1.0 1.1 or 1.2?)

Morevoer, while in data preprocessing section you say you used FSL version 4.0, in the TBSS section you state to have used FSL version 3.3.

Why did you only correlate CASI scores with FA? What is the purpose of reporting all the other neuropsychological tests that you name before?
It is not clear how the authors performed this correlation of CASi with FA, with which software and which methodology.

In the results, you should give the p values with FWE of the VBM findings.

In the discussion there are many non justified assumptions; the authors should review the discussion almost completely. they should start from the pathological findings in CTX and discuss the correlation of their findings with pathology in a more clear way.

The discussion and conclusions are not well balanced and are not adequately supported by the data.

The limitations of the work are not clearly stated

The writing is acceptable although sometimes the authors use non proper words.

**Level of interest:** An article of limited interest

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

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests