Reviewer's report

**Title:** Early microstructural white matter changes in patients with HIV: a diffusion tensor imaging study

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**Reviewer:** Davide Laneri

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Early microstructural white matter changes in patients with HIV: a diffusion tensor imaging study

N.B. Considering that my knowledge and understanding of the disease discussed in this paper is really modest, I will limit comments for my review to the methodological content.

This paper reports a DTI study with HIV patients. The main focus of the study is on the value of the fractional anisotropy resulting from a DTI analysis, which is considered an indicator of white matter integrity. White matter alterations were correlated with neurocognitive deficits and depression.

The main contribution of this paper is the discovery that the significant FA alteration found in areas adjacent to brain lesions of HIV patients also seems to occur, in the same regions, in patients with no microstructural lesions.

Below you can find comments for possible minor revisions.

In section 2.1 it seems a bit atypical to use an entirely male patient sample and include 4 females in the control group considering that there are studies, such as [1,2] which suggest a gender difference in FA values. A brief explanation in the discussion may be sufficient to explain it?

In section 2.1 test scores for many of the examinations would be useful to the reader. Particularly interesting would be to present the reader with a table summing up details about neuropsychological and depression tests (and possibly their correlation with FA).

In section 2.2, for the MRI measurements, it would be interesting to know the number of slices and their orientation.

In section 2.2, it is not entirely clear to me the steps involved in the optimized registration technique. A more exhaustive and clear explanation would help the reader to understand the methodology.

In section 2.2, five regions of interest are taken into consideration. It would be interesting to know how these ROIs were chosen and on which basis. Are they based on the authors' previous findings? Are they based on previous papers? On
a pre-study?

In section 3.1, Table 2 refers to FA values with an atypical representation (x1000). I would prefer to stay in line with the journal style which seem to adopt the original FA value between 0 and 1.

In section 3.1, I would like to suggest the authors to include, as well as FA, also mean, axial, and radial diffusivity which give very useful and complementary information about white matter structure. This is especially useful when comparing results of other studies mentioned in this paper, in which mean diffusivity is taken into consideration (section 4.2).

Discretionary Revisions

In the abstract, the last line should probably read: “Furthermore, they suggest a biological rather *than* a reactive origin of depression in HIVpatients.”

In section 2.1 the age range “range 26 to 56 years” is repeated twice.

Although commonly used in neurology papers, the terms CNS (section 2.1), CSF (section 3.1) and MD (section 4.2) should be defined.

In section 4.1, I believe that in the phrase: “There are additionally differences in the nature of WM abnormalities, given that some studies have preferentially observed man diffusivity alterations whilst other studies report multiple FA changes.” man should be substituted with main.

In section 4.4, I believe that “unnatural courses” should read “unnatural causes”.

References:


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: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests