Reviewer's report

Title: MRI-negative PET-positive Temporal Lobe Epilepsy (TLE) and Mesial TLE differ with Quantitative MRI and PET: a case control study

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Reviewer: Patrick Dupont

Reviewer's report:

General

In this manuscript, the authors describe the comparison of temporal lobe epilepsy with hippocampal sclerosis (HS+ve) and non-lesional temporal lobe epilepsy without hippocampal sclerosis (HS-ve) using quantitative MRI and FDG-PET. This is an interesting issue which is already partially described in two previous publications by the same group and using the same patient data. In its current form, the added value of this manuscript is limited but it can be improved by some additional analyses.

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

The primary hypothesis was that the epileptogenic focus in HS-ve involves primarily lateral rather than mesial temporal structures, and that the quantitative structural and functional changes would reflect this. However, the volumetric analyses using quantitative MRI it too limited. The hippocampus, whole brain, hemispheric and lobar volumes were used but additionally, a voxel based morphometry study would be in place (and if possible including a group of normal matched controls). Indeed, the authors conclude that HS+ve patients showed more hippocampal, but also marginally more ipsilateral cerebral and cerebrocortical atrophy but this is based on small differences in volumes in large parts of the brain. In this respect, the primary hypothesis was not investigated fully. Also the use of FDG-PET is adding little additional value compared to what is reported in one of the previous publications of the authors. In this manuscript, the authors are discussing the asymmetry (instead of the actual uptake) in FDG-metabolism (again in larger structures) and given the fact that morphological changes are reported, the differences in metabolism might be due to partial volume effects (see also a recent study by our group: Nelissen et al. NeuroImage 32 (2006), 684-695).

Table 2: add the standard deviation. I would also add a graph indicating all individual ratios for the three areas since I find it difficult to understand that an average change of e.g. 2% is highly significant (cerebrum, ration 0.98, p<0.001) given the variability within humans.

Table 5: I don't understand why for the HS+ve only the data of 24 instead of 27 cases are reported and similar for the 27 instead of 30 HS-ve cases. I guess that the three cases (and their case control counterparts in the HS+ve group) in which visually no lateralized hypometabolism was found are left out. If this is the case, the exclusion of these three PET negative cases should be made in the beginning (and these should also not be included for the MRI analysis since the title suggest that the patient population is "MRI negative PET positive").

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

P9: The PET acquisition was 30-40 min but nowhere it is mentioned at what time post injection the acquisition started. Also the details of the reconstruction should be mentioned as well as the type of corrections performed.

P9: how was corrected for the FDG dose injected?

P10: a conversion of MRI and FDG-PET to binary volumes was performed in order to coregister the two datasets. If this step is done properly, the coregistration is working well but the authors should give more details about this binarization itself.

P11: the authors are using statistical tests without correction for multiple comparisons. In the discussion section (P19), they give as argument that in the situation of an a-priori hypothesis it is appropriate not to correct for the multiple comparisons. I agree with this argument if you test only the a-priory hypothesis but the authors look at more than this hypothesis only and therefore, a combination is the best. Correction for multiple comparison should be done except when directly testing the hypothesis.
Figure 1: figure caption should be extended, labels should be given to each panel and a colorscale representing the “FDG uptake” should be included.
Figure 2: can be omitted
Figure 3: can be omitted
Figure 4: I have the impression that there is a mismatch between the hippocampal region and the “segmented” GM. How will this affect the results? It would be helpful to indicate the orientation of the figure for readers less familiar with this type of analysis/figures.

Discretionary Revisions (which the author can choose to ignore)
Table 3: I notice that the lobar volume of the contralateral temporal and insular cortex is larger in HS+ve patients compared to HS-ve patients. Are the authors willing to speculate that there might be a some sort of compensatory mechanism taking place because of HS?

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

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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