

# Review of: "Coupling between Human Brain Cortical Thickness and Glucose Metabolism from Regional to Connective level: a PET/MRI study"

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Potential competing interests: No potential competing interests to declare.

This study investigated the relationship between brain cortical thickness (CTh) and glucose metabolism using 18F-FDG PET/MRI in the middle and old age groups. The results emphasise the importance of understanding the link between brain structure and function, as this may provide valuable insights into neurological and psychiatric disorders. My comments are given below:

1. The writing needs to be greatly improved. For instance, in the Methods section of the manuscript, it is stated that "In the network, the node was defined as a brain region..." As a matter of fact, a brain region is defined as a node in the network (or called the node represents a brain region ...)
2. In the section on Network Construction, the authors adopted Spearman's correlation as the measure of FC. However, Pearson's  $r$  is typically used in a majority of studies. What's the author's consideration in selecting the method? It should be clarified in the manuscript.
3. How did the authors handle the negative edges when constructing brain networks? It should be further clarified, as there remains little consensus for handling or interpreting negative edge weights in FC graph analyses. Besides, some graph metrics are either not defined or need to be adapted when negative edges are included without additional processing.
4. Please be careful with the terminology such as  $P(\text{inexistence}|\text{disconnected})$ , which should be represented as a formula in the context.
5. In the section on Network properties, the authors stated that "the networks were binarized using a set of connective densities from 0.01 to 0.17 with a step of 0.02." What criterion is used to determine the range of density? As declared in the manuscript, the networks were binarized. Why not calculate the properties of weighted networks? Are there any considerations for these points? Besides, I suggest the authors clarify what the implication of sparsity was, which will make it more accessible to readers.
6. In the section on Statistics, the relevant context should be reorganized. All procedures related to statistical analysis, especially the statistical tools used in this work, should be presented in this part.
7. The authors estimated the similarity between SC and FC. Meanwhile, the S-F coupling was investigated. What are the relationships between the two analytical frameworks? I suggest authors clarify it in the method section, which will benefit readers.

8. The sections on methods and results should be reorganized. In the results section there are elements related to methodology, while the relevant content in the methods section is not clear.