# Review of: "Prediction and Analysis of Structural Brain Health Indicators Using Deep Learning Models with Functional Brain Images as Input"

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Potential competing interests: No potential competing interests to declare.

This study attempts to predict the gray matter brain healthcare quotient (GM-BHQ), derived from gray matter volume measurements, using resting-state connectivity measures from functional MRI. For this purpose, the authors resort to using a deep learning approach, BrainGNN, which was previously introduced for extracting relevant network topology from a functional graph.

One main concern regarding the interpretability of the results: There was no consideration for the quality control of the original fMRI connectivity measurements, which can be confounded by several factors, such as motion. It is generally recommended to inspect relationships to motion for quality control, for instance by inspecting the relationship with framewise displacement (for example, consult Ciric et al. 2018, NeuroImage). In the context of this study, this could be a concern as the brain health coefficient of interest is closely related to age, which also relates to motion (see Power et al. 2020, Cerebral Cortex). Additionally, as mentioned by the authors, classical networks were not identified: “In addition, most clusters were not determined as a set of ROIs, as indicated by the default mode network (DMN) or other popular resting-state networks (RSNs), but rather as a complex set of ROIs simultaneously attributed to various RSNs.” Thus it remains unclear what source is driving the relationship between connectivity and the GM-BHQ. Overall, further details regarding the interpretability of connectivity measures and the mitigation of potential confounds would be desirable.

Here are a few additional recommendations with regards to clarity and organization:

1. “However, there is a need for an index to evaluate brain health from the viewpoint of brain function, and no such method has yet been established.” This is the main motivation found in the introduction. It is unclear why this is a need, the motivations would benefit from further details.
2. “The rs-fMRI images were preprocessed as follows: (1) slice timing correction, (2) functional-anatomical registration using the boundary-based registration method with AFNI 3dAutoMask, (3) registration to the MNI152 standard space, and (4) nuisance regression. The nuisance regression procedure was performed as follows: (4.1) temporal filtering, (4.2) cerebrospinal fluid regression, (4.3) global signal regression, (4.4) regression of motion parameters, (4.5) polynomial detrending, and (4.6) component-based noise reduction (aCompCor).” More details would be desirable. What software was used at each step? AFNI throughout? Are the nuisance regression procedures listed in order of their application? What is the frequency range for temporal filtering? Which motion parameters?

Best regards,

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