

Peer Review

# Review of: "Altered Brain-Ventricle Coupling Modes Over Alzheimer's Disease Progression Detected With fMRI"

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This study investigates altered brain-ventricle coupling modes using rs-fMRI across the Alzheimer's disease (AD) progression spectrum. The authors identified distinct coupling modes between brain areas and ventricles, showing significant differences in mode occupancy correlated with cognitive decline. The study also highlights the potential role of cerebrospinal fluid (CSF) dynamics in functional connectivity and raises the need to reconsider fMRI preprocessing methods that exclude CSF signals. The findings suggest that coupling changes may serve as early indicators of AD-related neurodegeneration.

Could you clarify how the selection of K (the number of clusters) affects the robustness of the identified coupling modes? Would different values of K significantly alter the main findings?

Since this study observed significant differences in coupling modes related to the Default Mode Network (DMN) and other functional networks, would additional analyses using higher temporal resolution fMRI scans improve the detection of transient coupling events?

Have you considered incorporating volumetric data on brain atrophy (e.g., hippocampal or ventricular volume) to explore whether structural changes directly influence coupling mode alterations?

Recommended Citation: The role of ventricular volume changes as an early biomarker for AD has been proposed in other studies. Incorporating these references may support the idea that ventricular dynamics, including changes in volume, are valuable for detecting early AD-related brain alterations. Please discuss this matter with reference to the following papers:

## **Declarations**

**Potential competing interests:** No potential competing interests to declare.