Multimodal imaging of microstructural cerebral changes and loss of synaptic density in Alzheimer's disease

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Introduction

Multiple neuropathological changes are involved in Alzheimer's disease (AD) progression. The hallmark biomarkers are amyloid-beta, tau pathology, neuronal and synaptic loss. Other potential biomarkers, such as the level of iron and myelin content in the brain, have not been thoroughly studied. Nevertheless, these can be estimated in vivo thanks to tissue magnetic resonance (MR) properties measured through quantitative MR imaging (qMRI) techniques. I this study, we aimed to assess the co-occurrence of neurodegeneration (as measured with synaptic density), increased iron content and decreased myelin content in Alzheimer's disease.

Method and participants

Participants	HC (n=19)	AD (n=24)
Age	71.5(4.5)	73.3(8.0)
Female/Male	9/10	11/13
Education(years)	13.0(3.4)	12.8(3.6)
MMSE	29.2(1.1)	23.7(3.9)

Univariate Analyses on AD vs HC:

MPM data: Z-scored → F-test

PET data: Z-scored → Co-registration → F-test

Data PreProcessing:

- All data are BIDSified.
- Quantitative maps are calculated using hMRI toolbox-MATLAB
- All data are in MNI space
- PET process are done in PMOD.

Multivariate Analyses on AD vs HC:

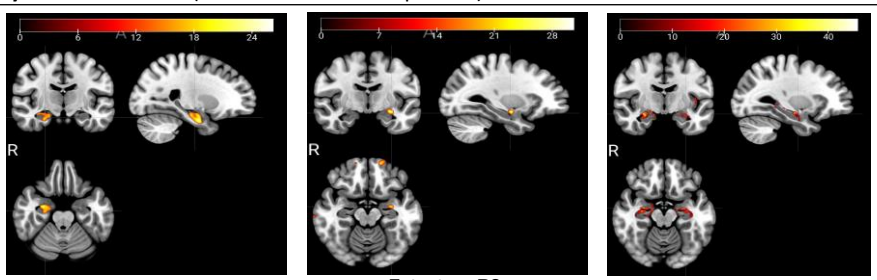
Between sub. parameter: $C = [0\ 1]_{2\times1}$

Within sub. parameter: $L = \begin{bmatrix}1 & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & 1\end{bmatrix}_{3\times3}$

Statistical test: $H_0: CBL = 0$, $H_1: CBL \neq 0$

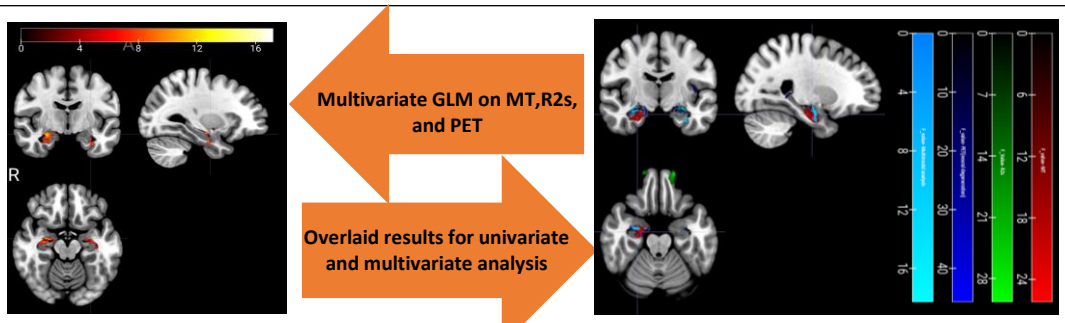
Results

Univariate Analyses on AD vs HC: (Statistical threshold: p< .001)



F_test on MT | F_test on R2s | F_test on PET

Multivariate Analyses on AD vs HC: (Statistical threshold: p< .05)



Discussion

- There is no significant difference between AD and HC groups in any map (at corrected statistical threshold).
- The multivariate analysis on GM, of MT, R2s, and synaptic density, provided significant group differences at FWEcorr p-value<0.05.
- Variations are observed in the R-amygdala (at voxel level) and in 5 distinct clusters covering the bilateral ant-hippocampal structures.
- There is a co-existence of different pathological mechanisms in areas known to harbor early-stage neuronal death.

1. Bastin et al., 2020. doi: 10.1007/s00259-019-04461-x
2. Braak et al., 1999. doi: 10.1007/pl00014168
3. Gyger et al., 2021. https://doi.org/10.1016/j.neuroimage.2021.117895

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