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

Soodeh Moallemian, Eric Salmon, Mohamed Ali Bahri, Nikita Beliy, Emma Delhaye, Evelyne Balteau, Christian Degueldre, Christophe Phillips* & Christine Bastin*

GIGA-Cyclotron Research Centre-in Vivo imaging, University of Liège, Allée du 6 Août, B30, 4000 Liège, Belgium

* These authors contributed equally to this work

Correspondence: Christine Bastin and Christophe Phillips, GIGA-Cyclotron Research Centre-in Vivo imaging, University of Liège, Allée du 6 Août, B30, 4000 Liège, Belgium, Phone: +32 4 366 23 16, Email: Christine.Bastin@uliege.be; c.phillips@uliege.be

Background:

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.

Aim:

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:

Data include 24 amyloid-positive Alzheimers patients (AD-11/13 males/females) and 19 healthy controls (HC-9/11 males/females). They underwent a multiparameter qMRI protocol used to generate quantitative maps sensitive to microstructural changes in myelin, iron deposits, and water content in grey matter (GM). Synaptic density was indexed by [18F]UCB-H-PET imaging using the distribution volume density (VT) maps. First, we applied univariate statistical analyses to investigate variation between AD and HC groups for each modality individually. Then, a multivariate GLM approach was used to compare the two groups pooling all modalities.

Results/Conclusions:

In GM univariate analyses, there was no significant difference between the AD and HC groups in any map at corrected statistical threshold. Conversely, the multivariate analysis on GM, combining MT, R2s, and synaptic density, provided significant group differences (FWEcorr P-value < 0.05) see figure 1. These variations are observed in the right amygdala (at voxel

level) and in 5 distinct clusters covering the bilateral anterior hippocampal structures. These show that patients with AD present convergence of neuropathological changes in the hippocampal area, suggesting that different pathological mechanisms co-exist in areas known to harbor early-stage neuronal death.

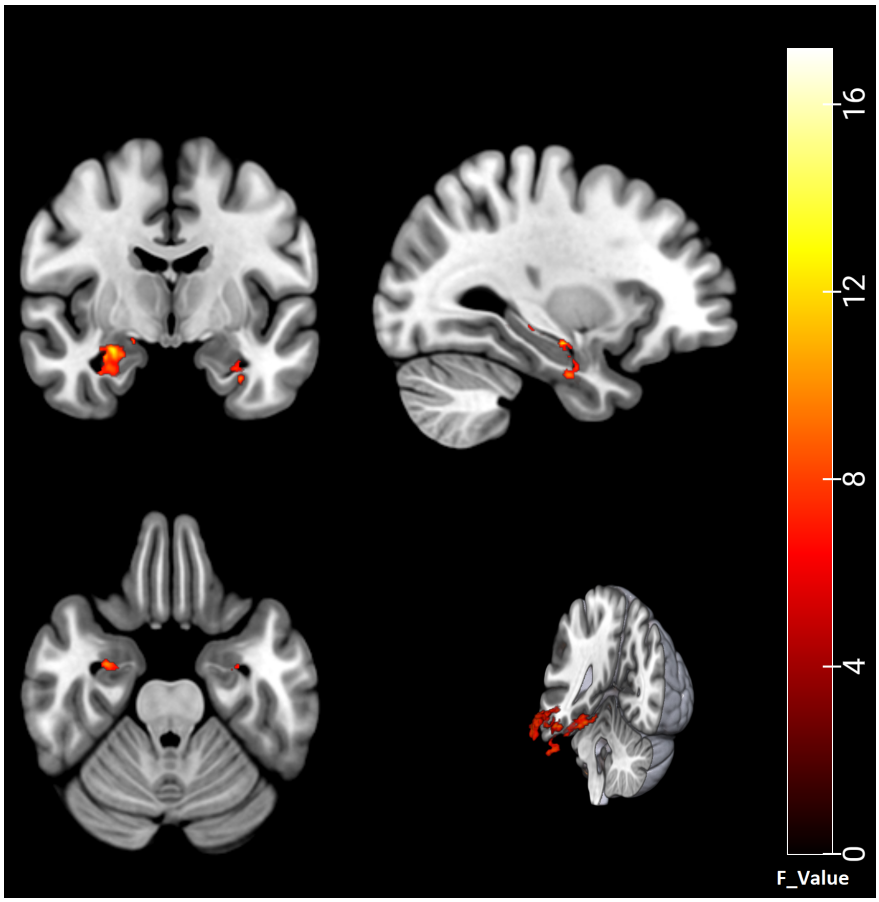

Fig. 1. The results of multivariate analysis on GM of AD and HC groups. It shows a significant bilateral difference in anterior hippocampal structures for AD in comparison to HC group when combining the information on combining MT, R2s, and synaptic density.