

## Neuroimaging / differential diagnosis

White matter hyperintensities in Alzheimer's disease:  
Topography of lesions and association with cognition

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## Abstract

**Background:** White matter hyperintensities (WMH) are frequent in the older adults and are associated to worse cognitive performances and to dementia. Alzheimer's disease is associated with greater brain WMH volume, particularly in posterior regions, compared to cognitively unimpaired older adults. The aim of this study was to assess in details the topography of brain WMH and their links with cognition in amyloid-positive cognitively impaired older adults, i.e. patients in the Alzheimer's continuum (ALZ), compared to amyloid-negative cognitively unimpaired adults (controls).

**Method:** Fifty-four ALZ and forty controls matched for age and cardiovascular risk factors were included in the IMAP cohort (Caen, France). Amyloid status was based on Florbetapir PET scans. In addition, each participant underwent 1) brain structural T1 and FLAIR MRI scans used for the automatic segmentation of WMH in the frontal, parietal, temporal, occipital lobes and in the corpus callosum (CC) region and subregions; 2) a comprehensive neuropsychological assessment of global cognition, episodic memory, working memory and executive functions. The regional volumes of WMH were compared between groups and the relationship of regional WMH to cognition was assessed within the ALZ patients.

**Result:** WMH volumes were significantly higher in ALZ patients than in controls in all brain regions, with highest differences in the splenium of the CC ( $p = 0.00005$ , size effect  $r = 0.42$ ) and lowest effects in the frontal lobe ( $p = 0.025$ , size effect  $r = 0.23$ ) (Figure 1). Within the ALZ patient group, WMH volumes of the CC, particularly in the splenium, were negatively associated with global cognition, working memory and executive functions (Figure 2). Total and frontal WMH volumes were also negatively associated with working memory, but this relationship did not survive correction for multiple comparisons.

**Conclusion:** WMH in the splenium of the CC most specifically characterize amyloid-positive patients in the Alzheimer's continuum and correlate to worse cognition especially in frontal cognitive functions. These specific ALZ-related WMH are probably not only due to small vessel disease and could be secondary to neurodegenerescence.

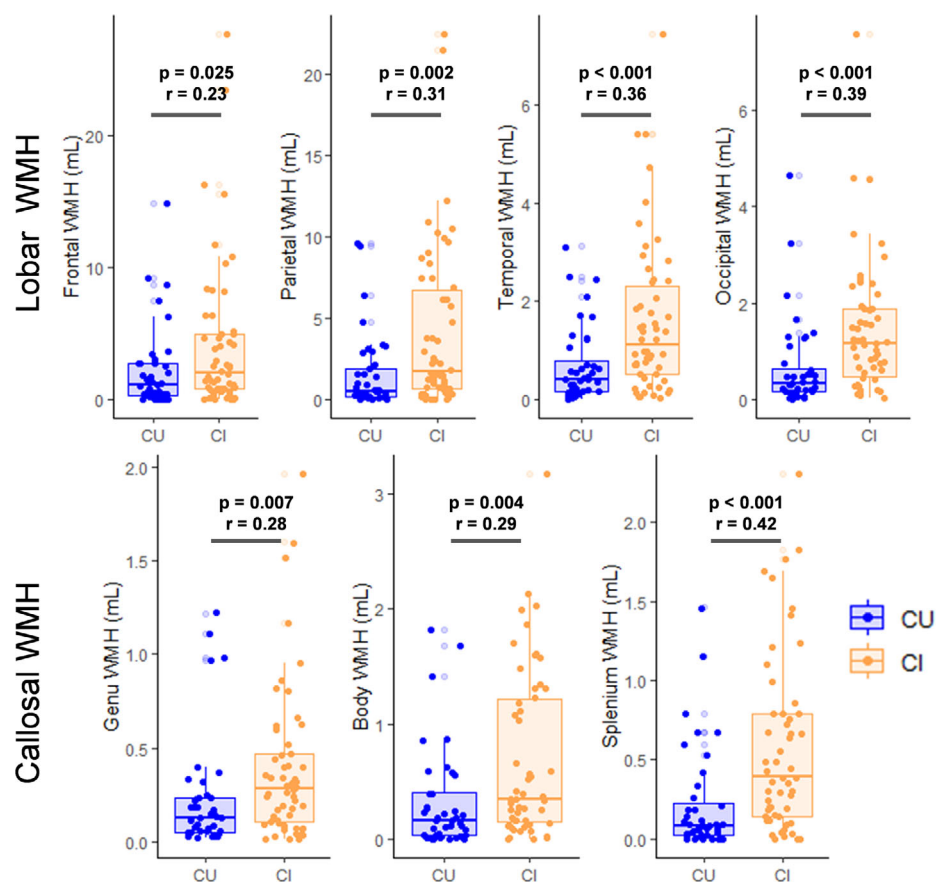


Figure 1: Boxplots comparing regional WMH volumes between amyloid-negative cognitively unimpaired adults (CU) and amyloid-positive cognitively impaired adults (CI).

**FIGURE 1**

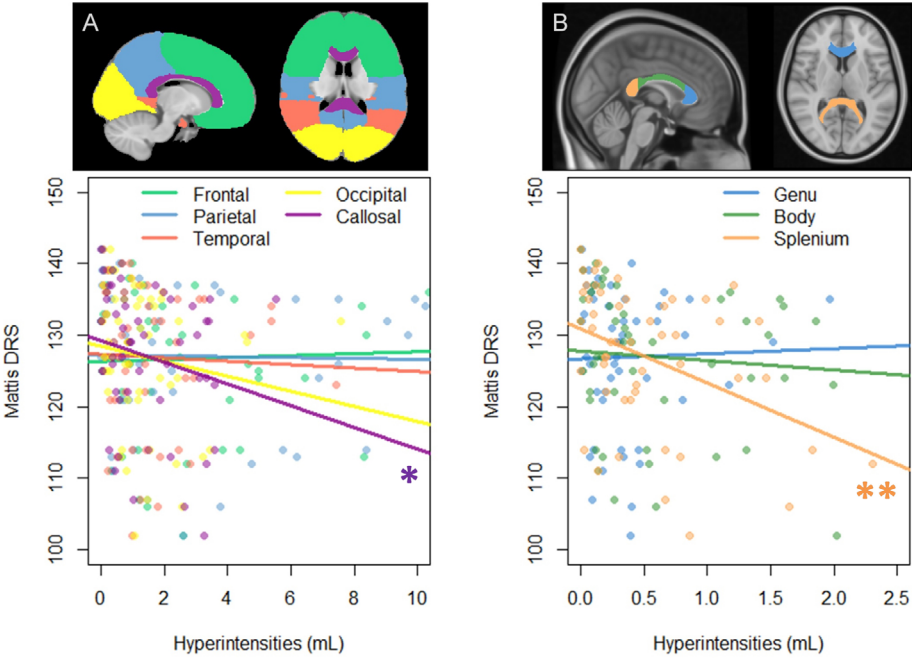


Figure 2: Mattis Dementia Rating Scale in association with regional white matter hyperintensities in amyloid-positive cognitively impaired adults. \* FDR corrected p-value < 0.05; \*\* FDR-corrected p-value <0.01, adjusted for age, sex, level of education, Florbetapir SUVR and Total Intracranial Volume

FIGURE 2