

O2-06-05 AVOXEL-BASED MORPHOMETRY STUDY OF
VOLUMETRIC MRI IN FAMILIAL ALZHEIMER'S
DISEASE

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Background: DIAN (Dominantly Inherited Alzheimer's Network) is an international longitudinal study of autosomal dominant Alzheimer's disease that involves serial clinical, imaging and biomarker studies of individuals at risk of disease and those already mildly affected. Understanding the patterns of atrophy associated with the disease will be important for studies and trials tracking atrophy progression in these cohorts. Methods: 158 participants from the DIAN cohort were included of whom 55 were non carriers (NC); 59 were asymptomatic carriers (aMut+) with a Clinical Dementia Rating (CDR) of 0; and 44 were symptomatic carriers (sMut+) with CDR >0. Voxel based morphometry (VBM) of baseline MR imaging was used to investigate differences in grey matter (GM) and white matter (WM) between the different groups. Tissue segmentation and spatial normalization of volumetric T1-weighted images were performed using the VBM8 toolbox of SPM8. One participant was excluded due to severe WM hyperintensities. Images were smoothed using a 6mm full-width-half-maximum Gaussian kernel. Statistical parametric maps were generated of the GM and WM differences between groups, controlling for total intracranial volume (TIV), gender, acquisition site, and APOE genotype. An interaction term between group and the expected age of onset (current age - parental age of onset) was included. Results: Significant clusters ($P < 0.05$ Family-Wise Error corrected) in the GM were observed between groups in the thalamus, precuneus, putamen, and amygdala. Most clusters were primarily driven by differences between the sMut+ and NC group (see Figure). No significant clusters were observed between the aMut+ and NC groups. There were also clusters in the parahippocampal/hippocampal regions. WM differences between groups were observed in the fornix superior to the thalamus, the cingulum inferiorly adjacent to the hippocampus, the splenium adjacent to the cingulate and areas adjacent to the precuneus. Conclusions: Symptomatic subjects show widespread differences in GM volume including deep grey structures (e.g. thalamus and putamen) and the precuneus; notable white matter changes included the fornix and the cingulum. The deep grey changes are of interest as PIB PET findings suggest early amyloid deposition in these structures.

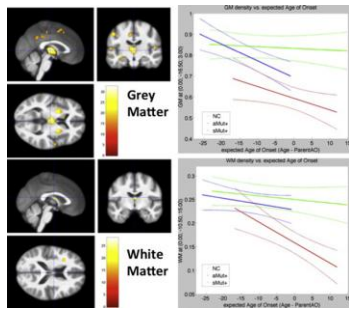


Figure. Summary of VBM study. Left column: centered on a significant cluster in the thalamus. A significant cluster in the putamen can also be seen. Right: significant cluster in the fornix. The plots below are the linear fit (with 95% confidence interval) of the tissue densities with respect to expected age at onset.