Focal thalamic degeneration is involved in PC/PCC dIsconnection and cognitive deficits of early Alzheimer's disease

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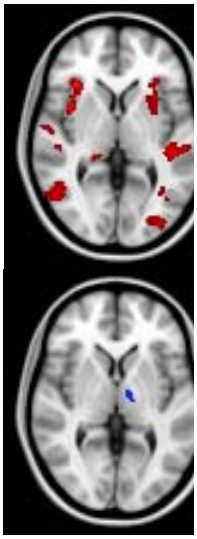
Target audience- Neurology, Cognitive Neuroscience

Purpose- In Alzheimer's disease (AD) a recent DTI-qMRI study demonstrated thalamic microstructural abnormalities (1), but its relevance compared to the temporomesial damage in early cognitive deficits is unknown. In the preclinical phase, Mild Cognitive Impairment (MCI), hypoperfusion of the precuneus/posterior cingulate cortex (PC/PCC), predicts conversion to AD (2). Hippocampal degeneration has been proposed to drive PC/PCC disconnection (3). The aim of this study was to test whether thalamic, other than hippocampal, degeneration is significant in early phases of Alzheimer's disease, and if it can also drive PC/PCC dysconnection and early cognitive deficits.

Methods- 12 AD (yrs = 70.3±6.2, M/F 5/7), 12 MCI (yrs = 70.6±5.6, M/F 2/10) and 18 healthy controls (CTRL, yrs = 69.1±5.5, M/F 5/13) were evaluated with neuropsychological tests (MMSE, story recall, Rey's figure, Trail making test, phonemic and semantic fluency). By a 1.5T Philips scanner, volumetric T1-FFE (TR 8.6 ms, TE 4 ms, flip angle 8 degrees, 170 slices, voxel 1.25x1.25x1.2 mm^3) and DTI data (TR 11.8 s, TE 70 ms, voxel 2.5x2.5x2.5 mm^3, 15 directions, b=0/900) were acquired .
Two main analysis were carried out on both volumetric and DTI parameters (MD, FA, DR, DA) data.
Voxel-wise analysis of volume and DTI parameters was carried out in whole brain by SPM8 with an optimized VBM protocol.
VOIs analysis of volume and DTI parameters were calculated by FSL in total GM, total WM (FAST), thalami, hippocampi (FIRST), PC/PCC (AAL template matching), and tracts connecting PC/PCC with hippocampi and thalami (FDT). The VOIs data were correlated with neuropsychological scores.



Results Voxel-wise analysis in AD vs CTRL revealed atrophy and ^MD of bilateral temporomesial areas, but only ^MD in the left posterior thalamus ($p<0.001$, fig 1a). In MCI vs CTRL, atrophy and ^MD in left temporomesial areas, but only decreased FA in right anterior thalamus ($p<0.001$, fig 1b).
VOI analysis in AD vs CTRL: atrophy and ^MD ($p<0.001$) of hippocampi and hippocampal-PC/PCC tracts, ^MD ($p<0.001$) of PC/PCC, ^MD ($p<0.05$) of thalami and right thalamic-PC/PCC tract. VOI analysis in MCI vs CTRL: atrophy ($p<0.05$) and ^MD (left $p<0.001$, right $p<0.01$) of hippocampi, only ^MD ($p<0.05$) of right hippocampal-PC/PCC and right thalamic-PC/PCC tracts. In AD, mild decreased FA ($p<0.05$) in hippocampi and hippocampal-PC/PCC tracts, while in MCI only in thalami, with increased radial diffusivity. About correlation with neuropsychological scores in AD, the most significant ($p<0.001$) were between between Rey's figure copy and radial diffusivity of right thalamic-PC/PCC tract.
Finally in AD, MD of left PC/PCC cortex was anticorrelated ($p<0.005$) only with volume of left thalamic-PC/PCC tract, but not with volume of left hippocampal-PC/PCC tract.

Discussion In this study, both voxel-wise and VOI analysis demonstrated in AD and MCI a significant diffuse macrostructural (atrophy) and microstructural (^MD) degeneration of hippocampi and hippocampal-PC/PCC tracts, but only focal mild degeneration of thalami and thalamic-PC/PCC tracts. However, the most significant neuropsychological correlation in AD and was found for the right thalamic-PC/PCC tract, and degeneration of left PC/PCC correlated with atrophy of the thalamic-PC/PCC tract.

Conclusion- As a whole, these results suggest that, although hippocampi and hippocampal-PC/PCC tracts are more significantly degenerated, focal thalamic degeneration could also drive PC/PCC disconnection and cognitive deficits in early phases of Alzheimer's disease.

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