Multimodal Brain Imaging to Reveal Abnormalities within and Between Default Mode Network Regions Related to Anosognosia for Memory Deficits in Alzheimer's Disease.

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Abstract Text:

Background: Anosognosia for memory deficits has major impact in Alzheimer's disease (AD). The neural mechanisms appear to rely on complex relationships between regions of the default mode network (DMN). Multimodal brain images were acquired, to search for brain regions that differ between AD patients and controls and to correlate anosognosia in AD and measures of brain activity within and between the regions. **Methods:** 31 patients with probable AD and 19 healthy volunteers underwent PET-FDG, T1-weighted structural MRI and resting functional MRI. Participant's awareness of memory functioning was assessed with the memory awareness rating scale (MARS)(Clare et al., 2004). Mattis Dementia Rating Scale was used to evaluate cognitive functioning. We used statistical parametric mapping (SPM12) to compare both groups in each neuroimaging modality and to correlate brain imaging measurements and anosognosia scores in AD patients, controlling for cognitive level, age, gender and education. For resting fMRI analysis, seed regions in the DMN were selected from the patients versus controls contrasts. **Results:** In the PET-FDG group comparison, we found a significant metabolic decrease in the posterior cingulate cortex (PCC), left temporo-parietal associative cortex and bilateral medial orbito-frontal cortex in AD. Additional structural MRI analysis with voxel based morphometry showed atrophy of the PCC and the medial temporal lobes (MTL) in AD. In AD patients, correlation between anosognosia scores and hypometabolism in the ventral PCC was evidenced. Using connectivity analyses of resting fMRI with selected parahippocampal (DMN) seed region, we essentially demonstrated that anosognosia for memory impairment was related with decreased intrinsic connectivity between the MTL region, the ventral PCC, the posterior inferior parietal lobules and the lateral temporal cortex (LTC). **Conclusions:** Regions involved in anosognosia for memory deficits are part of the MTL subsystem of the DMN, that contributes to autobiographical memory (Andrews-Hanna et al., 2010). Moreover, the vPCC is involved in self-referential processing (Leech and Sharp, 2014) and receives massive input from the lateral temporal gyrus, that contributes to mentalizing. These findings suggest that both vPCC dysfunction and disconnections in the MTL subsystem of the DMN participate to lack of awareness of memory deficits in AD.