

## Resting state functional patterns in AD and their correlation with regional amyloid- $\beta$ distribution.

E. Sanz-Arigit<sup>1</sup>, N. Tolboom<sup>2</sup>, J. Boverhoff<sup>2</sup>, A. Lammertsma<sup>2</sup>, R. Boellaard<sup>2</sup>, M. Yaqub<sup>2</sup>, A. Windhorst<sup>2</sup>, C. S. Stam<sup>3</sup>, P. Scheltens<sup>4</sup>, F. Barkhof<sup>6</sup>, and B. van Berckel<sup>2</sup>

<sup>1</sup>Radiology, VUmc, Amsterdam, North Holland, Netherlands, <sup>2</sup>Nuclear Medicine and PET Research, VUmc, Amsterdam, Netherlands, <sup>3</sup>Neurophysiology, VUmc, Amsterdam, Netherlands, <sup>4</sup>Neurology, VUmc, Amsterdam, Netherlands, <sup>5</sup>Radiology, VUmc, Amsterdam, Netherlands

### Introduction.

Brain networks characterized by low frequency BOLD fMRI fluctuations (dominant in rest condition) have been found to be different in Alzheimer disease (AD). The origin of these functional differences is likely be related to the regional distribution AD-related neuropathology.

To date, two networks have been found to display decreased activity in AD patients compared to age-matched controls: the default mode network (DMN) and the dorsal visuo-spatial attention system [1, 2]. In the DMN, recent reports demonstrate the co-localization of accumulation of amyloid- $\beta$  and functional changes [3, 4]. However, the neuropathological accumulation of amyloid- $\beta$  takes two forms with specific regional preferences: Amyloid plaques are more evenly distributed throughout the cortex while neurofibrillary tangles are thought to be present mainly in the medial temporal lobe. This study explores the relationship between the distribution of neurofibrillary tangles and amyloid plaques, demonstrated by 2 different amyloid- $\beta$  markers (11C-PIB and 18F-FDDNP) [5], and concurring functional changes observed in brain networks.

### Material and Methods.

Fourteen AD patients and thirteen healthy controls were included in this study. Parametric maps of the regional binding distribution of 2 amyloid markers were computed ([5] for details on subjects description, tracers, scanning and data processing). 11C-PIB binds to amyloid while 18F-FDDNP probably binds to neurofibrillary tangles. Brain scans of the same population were obtained in a MRI 1.5 T Siemens sonata MRI (200 volumes): structural T1 MPRAGE and functional T2 EPI resting state condition MRI (absence of stimuli, no goal-driven behavior; sequences described at [1]). Independent components analysis [6] was used to decompose group fMRI data into modes, identifying individual networks with coherent activity changes in BOLD response. The parametric maps of the functional networks displaying differences in power between AD patients and healthy controls were compared to the distribution maps of the binding corresponding to both amyloid tracers.

### Results.

The resting state analyses revealed the typical networks reported in previous studies [1], illustrating the robustness of the data-set. Most networks did not differ between age-matched controls and AD, except for two functional networks of interest. Significant group differences were found in:

- 1) A memory network split in 2 contralateral components, including the middle frontal and orbital and superior parietal cortices (Fig. A).
- 2) The DMN, including prefrontal, anterior cingulate, posterior cingulate, inferior temporal gyrus, and superior parietal region (Fig. B).

The amyloid-tracer parametric maps represent the distribution of 11C-PIB and 18F-FDDNP binding (Figures C and D respectively) showing their specific cortical or medio-temporal amyloid load.

Note that the memory network co-localizes with the accumulation of FDDNP (Figs. B and D), while the DMN changes co-localize with the PIB accumulation (Figs. A and C).

Fig. A

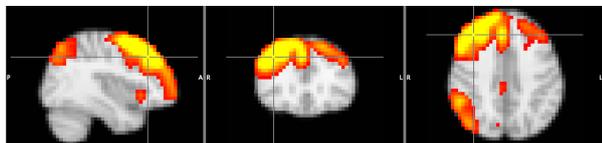


Fig. C

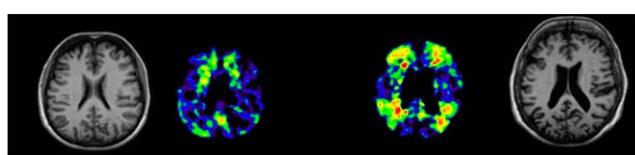
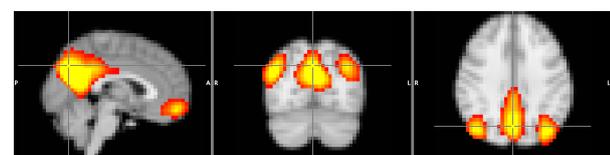
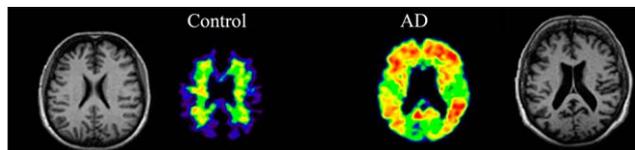


Fig. B

Fig. D

### Conclusions.

Within the same population of Alzheimer patients we demonstrate the co-localization between specific neuropathological changes determined by the regional binding an amyloid- $\beta$  and neurofibrillary tangle marker (11C-PIB and 18F-FDDNP respectively) and regional changes in low frequency BOLD signal functional networks in Alzheimer disease. Our results assist to establish the relationship between AD-related functional changes and structural pathology related to neurofibrillary tangles and amyloid plaques.

### References.

- [1] Damoiseaux et al., PNAS 2008
- [2] Greicius et al., PNAS 2003
- [3] Buckner et al., J. Neurosci. 2005
- [4] Buckner et al. J. Neurosci. 2009
- [5] Tolboom et al., J Nuc. Med. 2009
- [6] Beckmann et al., Phil. Trans. R. Soc. 2005