**Introduction**

Analysis of structural and functional brain networks has the potential to provide unique insight into the natural evolution of Alzheimer’s Disease, as well as facilitate the ability to assess the impact of therapeutic intervention. In order to elucidate the effect of β-amyloid deposition on brain networks at the early disease stage, we have performed a correlation density analysis of functional brain networks derived from FDG PET images of florbetapir-low and -high mild cognitive impairment (MCI) subjects in the Alzheimer’s Disease Neuroimaging Initiative (ADNI) study.

**Methods**

T1-weighted MRI, [18F]florbetapir PET, and [18F]FDG PET images were obtained from ADNI-GO/-2 study subjects classified with MCI. Standardized uptake value ratio (SUVR) images for florbetapir (full cerebellum as reference region) and FDG PET (pons as reference region) were generated using our fully-automated PIANO™ pipeline. All PET volumes were registered to a customized nonlinear MRI template in MNI stereotaxic space. Subjects were classified as florbetapir-low (n=84) and florbetapir-high (n=84) based on the mean [18F]florbetapir PET SUVR of several regions-of-interest (ROIs), including precuneus, posterior cingulate, and medial frontal cortex. For each group, correlation matrices were computed at both ROI and vertex-wise levels, and thresholded at each absolute correlation value in the range [0,1]. At each threshold, the correlation density was defined as the ratio of the number of significant correlations to the total number of possible correlations.

**Results**

- The florbetapir-high group showed regionally higher levels of β-amyloid deposition bilaterally in the cerebral cortex (Figure 1, top row).
- FDG SUVR levels were higher in the florbetapir-low group relative to the florbetapir-high group (Figure 1, middle row).
- The florbetapir-low group showed higher correlation density in a number of ROIs, especially default-mode network (DMN) regions (Figure 2, left panel).
- The global correlation density over all ROIs was higher in the florbetapir-low group compared to the florbetapir-high group (Figure 2, right panel).
- The vertex-wise integrated correlation density maps (Figure 1, bottom row) showed more densely correlated regions in the florbetapir-low group.

**Conclusions**

In MCI subjects, β-amyloid affects not only the FDG SUVR, but also the FDG correlation pattern as demonstrated by the ROI and vertex-wise correlation density analyses. While this study examined functional networks based on glucose utilization, future studies could evaluate correlation properties derived from resting-state BOLD and/or ASL perfusion MRI data.

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