

Resting-state fMRI Activity Profile in Prodromal Alzheimer's Disease and Older Adults with Cognitive Complaints

Yang Wang, John D. West, Tamiko R. Magee, Brenna C. McDonald, Shannon L. Risacher, Martin R. Farlow, Darren P O'Neill, Andrew J. Saykin

Departments of Radiology & Imaging Sciences and Neurology, Indiana University School of Medicine

Background: Resting-state functional MRI (RS-fMRI) has been proposed to detect neurodegenerative disease-related network alterations before brain atrophy has emerged. Disrupted resting-state connectivity in the posterior cingulate cortex (PCC) and hippocampus has been reported in AD (Greicius, 2004), yet results in prodromal AD including MCI vary. Other methods have suggested the feasibility of earlier detection in euthymic older adults with marked cognitive complaints (CC) but normal neuropsychological test performance (Saykin, 2006). The current study was designed to assess RS-fMRI patterns in CC compared with MCI, AD and healthy controls (HC).

Methods: To date, 13 CC, 9 HC, 4 MCI and 3 AD participants were scanned at rest with eyes closed on a Siemens 3T. RS-fMRI was analyzed using FSL, AFNI and SPM8. For each individual, the sum of amplitude of low frequency fluctuation (ALFF; 0.01–0.1 Hz) was calculated at each voxel (Biswal, 2010). Using PCC seed ROIs adapted from Fox et al (2005) voxel-wise cross-correlation maps were generated for each subject. Group comparisons and covariate analyses were performed using SPM8 with age as a covariate.

Results: Compared to HC, MCI/AD showed decreased ALFF in the PCC ($p < 0.01$, corrected), but increased ALFF in bilateral hippocampi ($p < 0.01$). The CC group consistently showed intermediate changes. ROI analyses indicated differences in ALFF of PCC (HC > CC > MCI/AD, $p < 0.05$, effect size: 0.61), and ALFF of hippocampus (HC < CC < MCI/AD, $p < 0.01$, effect size: 0.75). ALFF of PCC was positively correlated with neuropsychological performance (MMSE, DRS and CVLT; $r = 0.45$ to 0.56 , $p < 0.01$), while hippocampal ALFF was negatively correlated with performance ($r = -0.48$ to -0.67 , $p < 0.01$). PCC seeded crosscorrelation maps showed decreased hippocampal connectivity in MCI/AD compared to HC or CC ($p < 0.01$).

Conclusions: RS-fMRI appears sensitive to early prodromal neurodegenerative changes in regions associated with AD, notably including pre-MCI individuals with CC. While there is decreased functional connectivity between PCC and hippocampus, regionally increased ALFF in hippocampus may indicate a compensatory mechanism in early prodromal AD.

