Investigation of functional connectivity changes in Alzheimer disease using degree centrality

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Purpose: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline, often leading to dementia in later life [1]. Many studies used resting-state functional magnetic resonance imaging (fMRI) to investigate whether functional connectivity (FC) between different brain regions was altered in Alzheimer's disease [2]. But the choice of the seed regions and their accurate definitions raised numerous controversies. Degree centrality (DC), a novel resting-state fMRI parameter has been developed to reflect the number of functional connectivity of each voxel with all the other voxels in the brain to avoid subjectivity [3]. In this preliminary study, we used DC to perform a voxel-wise whole-brain FC analysis for AD patients as compared to normal controls.

Methods: The study was approved by the local ethical committee and written informed consent was obtained from all the participants. Six AD patients (aged 59.0±4.32 years, range 51-64 years) were recruited according to the criteria of NINCDS-ADRDA [4] and Mini-Mental State Examination (MMSE) scores. Nine gender- and age-matched healthy controls (aged 55.1±10.9 years, range 46-82 years) were selected for group comparison. All subjects were right-handed. Thirty-three axial slices covering the whole brain were acquired using a 3.0T GE Signa MR scanner (GE Healthcare, Milwaukee, WI) with an 8-channel phase array head coil (TR/TE 2000/30 ms, flip angle 90°, matrix 64 × 64, FOV 22 cm, thickness/gap 3.4/1mm, total 210 volumes). Data preprocessing included slice timing and realignment for temporal and spatial adjustment using SPM8, followed by spatial normalization to warp all the images into the same stereotactic space for group comparison. An in-house software REST was used for DC analysis (http://www.restfmri.net). All the time series were de-trended and band-pass filtered (0.01-0.08Hz). DC was calculated as the weighted sum of correlation coefficients between each pair of voxels and standardized by the global mean within the whole brain. The statistical analysis contained both of one-sample T test within the AD and control groups respectively and two-sample T test to reveal the group difference between two groups. The AlphaSim program implemented in AFNI was used for multiple comparison correction (corrected $p<0.05$).

Results: For one-sample T test, the control group showed decreased DC in the bilateral hippocampus, middle temporal lobe, superior frontal lobe and increased DC in the right insula, superior temporal gyrus as compared to the global mean across the brain (Fig. 1). In contrast, AD group only showed decreased DC in the bilateral frontal lobe, right putamen and insula (Fig. 2). For two-sample T test, the control group showed decreased DC in bilateral hippocampus and left middle temporal lobe as compared to the AD group (Fig. 3).

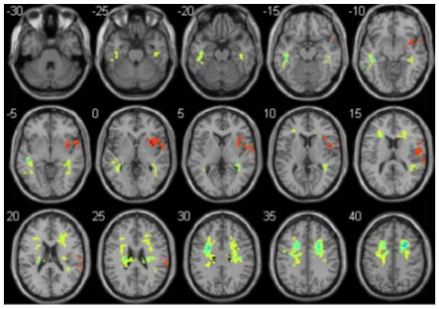

Fig. 1. Increased (red) and decreased (cyan) DC regions vs. the global mean for normal controls (corrected p<0.05)

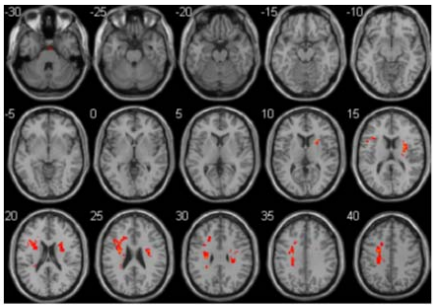

Fig. 2. Decreased DC regions against the global mean for AD patients (corrected p<0.05)

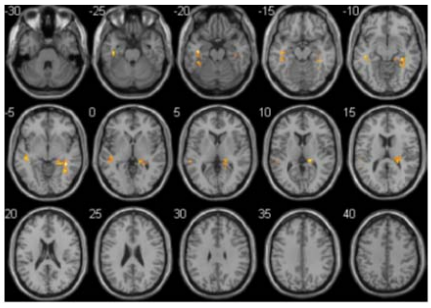

Fig. 3. Decreased DC regions for normal controls vs. AD patients (corrected p<0.05)

Discussion and Conclusion: In this preliminary study, we found deceased DC regions in bilateral hippocampus and frontal lobe for normal aging controls and AD patients, which was consistent with previous studies. The increased DC in the right insula for the control group might serve as a compensatory factor for normal aging and the decreased DC in this region for the AD group might provide interesting insight into the mechanism of the disease. More subjects are required for further study.

References:

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