Alteration of Integrity and Patterns of the Memory Modules in Mild Cognitive Impairment and Alzheimer's disease

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Introduction: Functional brain networks show small-world properties. As a disconnection syndrome, Alzheimer's disease (AD) shows the significant functional disconnection between brain regions. In addition, AD subjects also evidence different small-world properties when compared to normal subjects [1-2]. The small world is connected by many smaller modules. In the present study, we tested a hypothesis that the integrity and organization patterns of specific modules responsible for memory processing are altered in Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) subjects, in comparison with cognitively normal (CN) subjects.

Methods: Fifty-six participants, including 20 control subjects, 21 mild Alzheimer's disease subjects, and 15 mild cognitive impairment subjects, were recruited for this study. The detailed inclusion and exclusion criteria for those subjects have been described [3]. One of the AD subjects was excluded because of incomplete brain coverage. MRI protocol: Imaging was carried out on a 3T GE Signa whole-body scanner with a standard transmit-receive head coil. Thirty-six slices (sagittal-resting functional MRI data sets of the whole brain) were obtained in 6 minutes with a single-shot gradient echo-echo planar imaging (EPI) pulse sequence with TE/TR/flip angle/slice thickness, 25ms/2,000ms/90°/4mm, matrix size=64x64 and field of view=24x24 cm. High-resolution SPGR 3D images were acquired in axial direction for anatomical reference (TE=4ms, TR=10ms, TI=450ms, flip angle=12°,144 slices, slice thickness=1mm and matrix size=256x192). Data analysis: The data was processed with AFNI software. The preprocessing included motion corrections, removing Legendre polynomials of order up to 3, removing CSF, white matter and global signal, then band pass filtering to retain the signal between 0.01-0.15HZ. The high-resolution anatomical image for each subject was transformed and aligned with a reference template containing 116 anatomical ROIs [4]. The average time series of each ROI of functional data was extracted. Then, for each subject, the functional connectivity of any pair of ROIs was calculated by Pearson correlation coefficient (CC) to build a 116X116 matrix. The group CC matrix is the average matrix of all subjects in this group. Each group's average CC matrix was then thresholded in order to preserve the top 5% largest CC value, and then build a certain functional network. Then, Newman's modularity measurement [5] and greedy algorithm [6] were used to calculate the modules of each group's network. We extract the modules that have hippocampus and temporal lobe regions that involve memory processing to examine the different patterns of those modules among three groups.

Results and Discussion: We limited our observation to modules involving the hippocampus and temporal lobe modules (HIP-TP), which are most important for memory processing. HIP-TP modules in the CN group (Fig. 1) show that HIP-TP has two connected modules: one green module has the bilateral hippocampus, parahippcampal gyrus and amygdala regions; the second brown module covers the regions of the bilateral temporal lobes. These two modules are connected by the dark gray intermodule edges. The HIP-TP in the MCI (Fig. 2) and AD (Fig. 3) groups has 4 and 5 modules, respectively. HIP-TP in CN is very well organized and has highly directed connected bilateral symmetric regions, but the MCI and AD HIP-TP module have fewer directed left and right connections, and the modules are hardly symmetric and organized. Compared to the MCI group, the AD group has one large new module, which contains pathways that can connect left and right modules. Although this module in the AD group has more left and right connections than the MCI group, the path length seems too long, and not efficient. This may be a result of compensation effects. It is suggested the AD neurodegenerating processes may start from the left and right function disconnection, followed by the compensating connections by involving other regions in AD. There is a potential that patterns of the HIP-TP modules could be employed to distinguish MCI subjects from CN subjects.

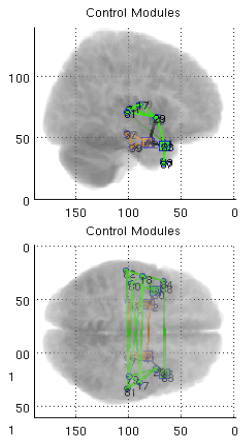

Figure 1. HIP-TP modules in CN.

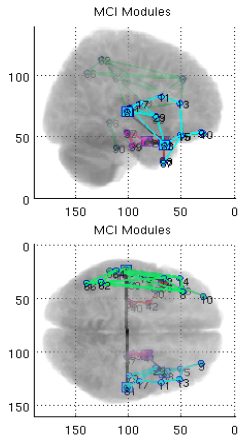

Figure 2. HIP-TP modules in MCI.

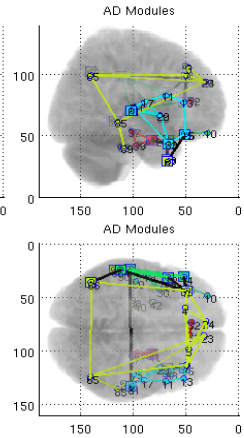

Figure 3. HIP-TP modules in AD.

Reference:

1. Bokde AL *et al.,* Prog Neurobiol. (2009). 2.Supekar K *et al.,* PLoS Comput Biol. 4(6) (2008). 3. Li *et al.,* Radiology 2251, 253-259(2002). 4. Tzourio-Mazoyer *et al.,* NeuroImage 15, 273-289 (2002). 5. Newman MEJ. Eur. Phys. J. B 38 321–330(2004). 6. Clauset A *et al,.* Phys. Rev. E 70, (2004).

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