Asymmetric Structural Connectivity of Default-mode Network : an integrated study of fMRI and probabilistic DTI

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Introduction

Default-mode network (DMN) of resting rhythm has been detected by utilizing BOLD-based fMRI at both 1.5T and 3T field strength (Gusnard et al, 2001; Yeh et al, 2005). And DMN spatial template of human brain has been constructed for the optimal solution for the automatic detection of default networks using brain fMRI studies (Lin et al 2008). DMN spatial template showed precuneus and posterior cingulate areas (labeled as PC) with the highest reproducibility, as indicated by previous deoxy-glucose positron emission tomography (FDG PET, Raichle et al 2001). The structural connectivity of DMN was characterized by probabilistic diffusion tensor imaging (pDTI) for illustrating the DMN asymmetry of bilateral cingulum.

Subjects and Methods

(1) Constructing spatial template of resting DMN

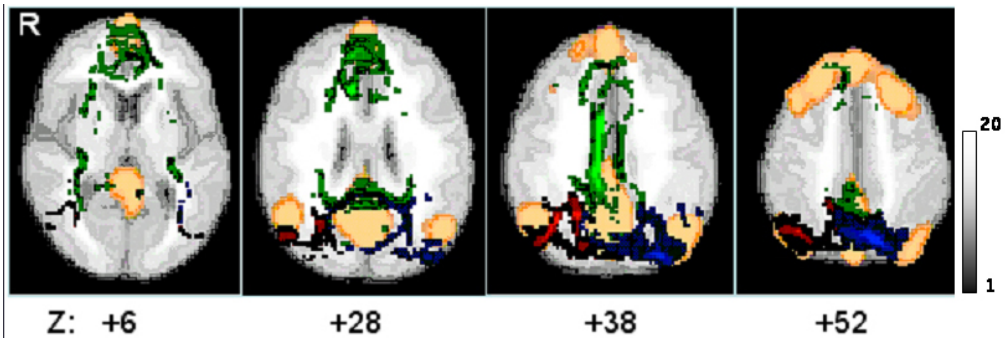
An fMRI database of sixty right-handed subjects (gender- and age-matched, age: 32 +/- 7 years old) was constructed for mapping the spatial template of DMN. Imaging studies of resting state were obtained with eye fixation. Images were acquired using a 3T Medspec S300 system (Bruker GmbH, Ettlingen, Germany) equipped with an actively shielded gradient coil and a quadrature transceiver of head. Image sequences included (1) single-shot echo planar images of fMRI (64x64 matrix, voxel size = 3.6x3.6x6 mm, 20 slices, TR/TE=2000/50 milliseconds, repetition number (NR) = 200) and structural image of MDEFT (256x256x128 matrix, voxel size = 0.98x0.98x1.5 mm). Processing of DMN spatial template included (1) preprocessing of individual data sets using SPM2 (Functional Imaging Laboratory, UCL, UK) was applied for spatial normalization; (2) Group ICA was applied to construct the spatial template of DMN using GIFT (Calhoun et al, 2001) of informax ICA (Computational Neurobiology Laboratory, The Salk Institute for Biological Studies, USA) with fixed component number of 50 by MDL (minimum description length); (3) temporal course of DMN was derived for each individual from GIFT as the regressor for GLM estimation after co-registration/normalization to MNI T1 template and smoothing of 8x8x8 mm in SPM2. Group analyses using two-level statistical evaluation of random-effect analysis was performed for DMN template of 60 subjects (DMN-60) with statistical criteria of $p<0.05$/voxel extension>0 for the second level with correction of false discovery rate (FDR).

(2) Probabilistic diffusion tensor imaging of DMN

The other 22 right-handed normal subjects (gender- and age-matched, age: 34 +/- 6 years old) received anatomical MRI [GE SignaExcite 1.5T system, T1-weighted, 3D spoiled gradient echo (SPGR) pulse sequence, TR=8.5ms, TE=1.8ms, matrix size=256x256x124, voxel size = 1.02 x 1.02 x1.5mm], and DTI [1.5T SignaExcite, spin-echo-based diffusion-weighted EPI sequence, TR=17000 ms, minimal TE, matrix size = 128x128, NEX= 6, b-value=1000sec/mm^2, 13 directions, voxel size = 2.0x2.0x2.2mm]. Five regions of interest (ROIs) were derived from DMN template as right PC, left PC, medial prefrontal area (MF), right parietal lobule (PL) and left PL for DTI probabilistic tractography. All tractographies applied FSL ProbTrack [FMRIB's Software Library, version 4.1.4, (Behrens, T.E. et al 2003), including eddy current correct, motion correction, parameter fitting of diffusion tensors and modeling of diffusion parameters with considering crossing fiber as eight. Exclusion masks, including corpus callosum and inter hemispheric plane, were applied to clarify structural asymmetry. Penetration maps of 22 subjects presented the reproducibility with the probabilistic cutoff of 0.16%.

Results

Spatial correlates of DMN mainly involved bilateral posterior medial parietal (Brodmann area 31, BA31), bilateral posterior lateral parietal, ventral medial prefrontal and dorsal medial prefrontal cortices (orange areas in **Figure 1**). Penetration maps showed the limited structural connectivity within each ROIs. For the structural connectivity between bilateral PC and MF, asymmetry of bilateral cingulum was noted as 2.4-fold higher reproducibility in right cingulum (the highest reproducibility as 86% and 36% for right and left cingulum cortices, respectively). Connectivity between right PC/right PL and left PC/left PL was demonstrated as red and blue labels with similar reproducibility (56%) in **Figure 1**.



◀ **Figure 1 :** Penetration maps of probabilistic DTI (N=22, probabilistic criteria of 0.16%) superimposed on the DMN template (N=60, corrected $p<0.05$ with FDR, orange areas). Structural connectivity was labeled as red, blue and green for right PC-right PL, left PC-left PL and bilateral PC-MF, respectively.

Discussion and Conclusion

With multimodal approaches using BOLD-based fMRI and pDTI, limited structural connectivity within each ROIs was observed as the diverse crossing fibers in associative cortices of parietal and prefrontal lobes. By penetration maps of twenty-two normal subjects, asymmetry of bilateral cingulum cortices implied preference of right posterior medial parietal regions for interpretation of internal/external environment with concert action of medial prefrontal areas, as one of the potential functions of DMN. But these hypotheses need future studies of refined pDTI methods and lesion brains for verification.

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