A combined DTI and resting state FMRI study of late aging

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PURPOSE

To examine associations of both functional and structural connectivity in resting state networks (RSNs) with late life depression (LLD) in otherwise healthy subjects.

Advanced aging is associated with a number of changes in brain structure and neurocognitive functionality. This study combines resting state FMRI (RS-FMRI), DTI and a set of neurocognitive test scores to investigate brain effects in a late aging (>65 years), high functioning population.

METHODS

Subjects: 68 healthy males (age 80.4±5.5 yrs; range 65-89 yrs) were scanned as part of an ongoing aging study.

Acquisition: Using a 3.0-T Siemens MRI scanner with 12-channel head coil (Siemens Magnetom Tim Trio, Erlangen, Germany) the following whole brain data were acquired:

- T1w: T1-weighted anatomical, 1x1x1 mm^3 (3D-MPRAGE);
- DTI: twice refocused SE-EPI, TR/TE=11000/104 ms, 2x2x2 mm^3 voxels, 3 reps of: 3 b_0 volumes and 30 directions with b=1000 s/mm^2;
- RS-FMRI: EPI sequence, TR/TE=2500/27 ms, 3.4 mm isotropic voxels.

Processing:

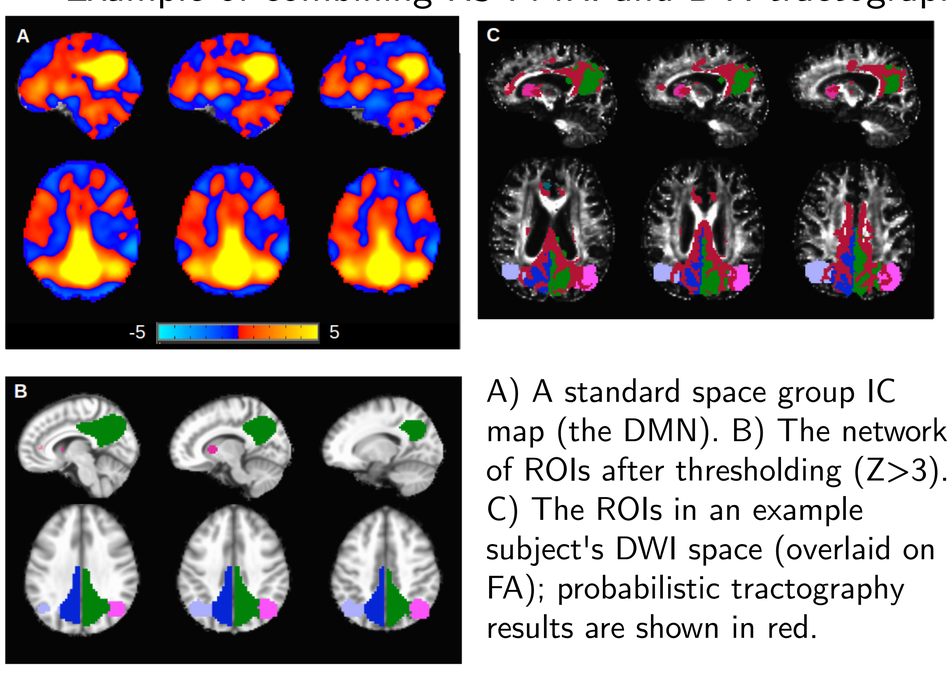
RS-FMRI data were pre-processed using SPM and AFNI following Gohel and Biswal[3], including temporal filtering between 0.01-0.1 Hz.

- Group ICA was performed using FSL-melodic[4], producing 20 IC maps;
- 12 ICs were identified as known resting state networks (RSNs), such as the default mode network (DMN) shown in Fig. 1A;
- These 12 ICs were thresholded at Z>3 to produce a set of functional ROIs (Fig. 1B), from whose average time series correlation (resting state functional connectivity; RSFC) matrices were calculated. The networks were also mapped to DTI space.

DWI volumes were aligned using FSL-eddy_correct.

- AFNI and FATCAT were used to calculate nonlinear tensor fits and FA and eigenvector uncertainty, as well as to inflate GM ROIs to WM;
- Probabilistic tractography was performed among all networks using standard parameters: 1000 iterations, 5 seeds/voxel, FA>0.2 and angle deflection <60° (Fig. 1C).

1. Example of combining RS-FMRI and DTI tractography



A) A standard space group IC map (the DMN). B) The network of ROIs after thresholding (Z>3). C) The ROIs in an example subject's DWI space (overlaid on FA); probabilistic tractography results are shown in red.

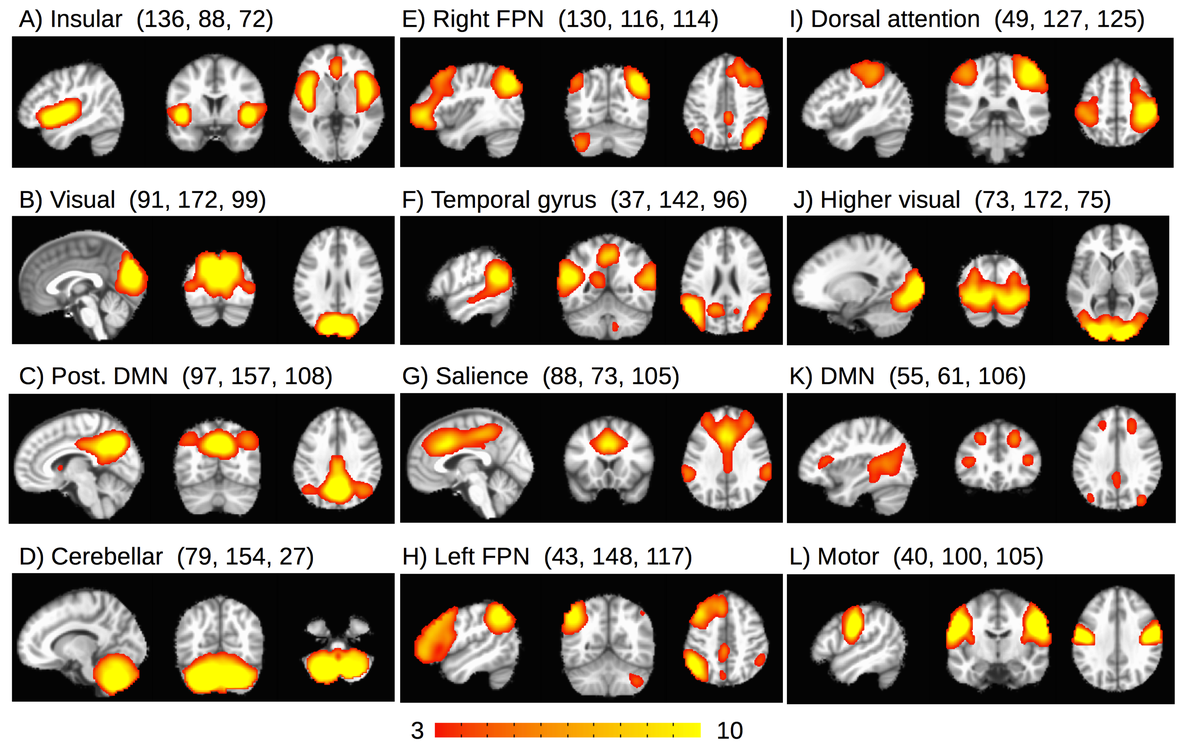
Additional subject data included brain tissue fractions and neurocognitive test scores indicating loneliness and depression level.

- Factor and parallel analyses were implemented in FATCAT to compute latent variables, of which two were used in further modeling:
  1) a variable with high factor scores of tissue fractions, and
  2) a variable with factors of the Geriatric Depression Scale (GDS) and loneliness scores, representing LLD;
- Multivariate modeling using FATCAT and AFNI's 3dMVM was performed to investigate associations of network functional connectivity with LLD, while controlling for age, education and tissue fractions;
- The same modeling was also applied to network structural connectivity matrices: fractional anisotropy (FA), first eigenvalue (L1), mean diffusivity (MD) and radial diffusivity (RD).

RESULTS

Fig. 2 shows the observed RSNs (thresholded at Z>3).

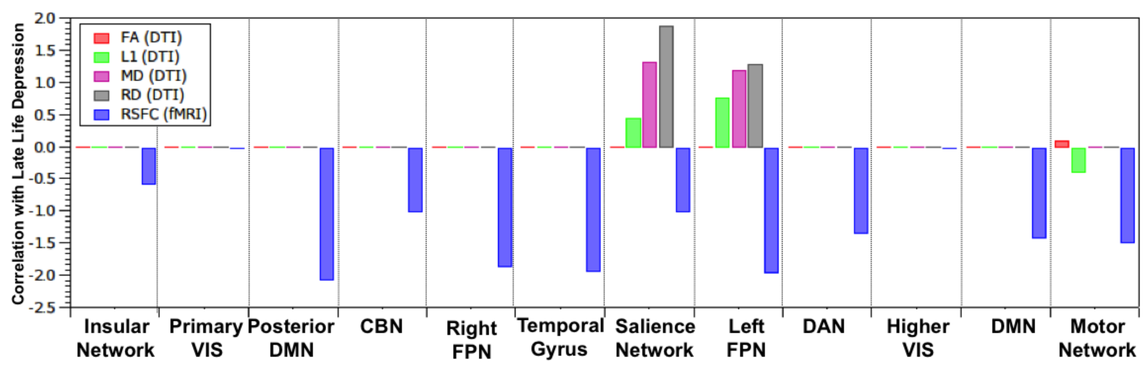
2. Resting state networks identified from group ICA



12 RSNs identified from group ICA results, shown in MNI space (slice number provides; left=left in coronal and sagittal views). DMN = default mode network; FPN = frontoparietal network.

Several networks exhibited significant associations (p<0.05, corrected for multiple networks and parameters) between network connectivity and LLD (Fig. 3). Most networks (except primary and higher visual) showed an inverse relation between depression and functional connectivity. The salience and left frontoparietal networks showed increased L1, MD and RD (but not FA) with increased LLD; the motor cortices showed increased FA but decreased L1 on average with increased LLD.

3. Group network results: LLD with RS-FMRI and DTI measures



Mean t-stat values across 12 observed RSNs for multivariate modeled associations between late life depression (LLD) and various connectivity measures: FA, L1, MD and RD (for DTI), and RSFC Z-scores (for RS-FMRI). VIS = visual; DMN = default mode network; CBN = cerebellar network; FPN = frontoparietal network; DMN = default mode network; DAN = dorsal attention network.

CONCLUSIONS

Increased values of LLD latent variables were strongly associated with functional connectivity decrease in networks across the brain, implying decrease in depression rating with increased functional connectivity.

Interestingly, significant structural association with LLD was mostly observed in a much smaller number of networks. These networks with structural effects were those which contained predominantly frontal components (left frontoparietal and salience), in agreement with locations of structural effects seen previously (see, e.g., studies[1,7]).

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FUNDING: Support for this study was provided by NRF/DST South African Research Chairs Initiative and NIH grants R01-AG032088 and R01-DA038895.

OHBM 2015: Poster #3603. Thurs, June 18: 12:45pm