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The Default Mode Network: Statistical Perspectives

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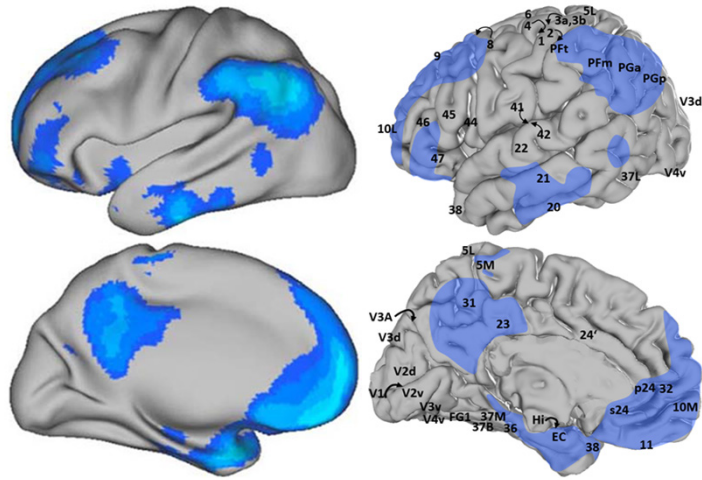
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Outline:

1. Resting-state networks
2. Resting-state fMRI experiment
3. Intraclass correlation (ICC) analysis
4. DMN and anti-DMN networks
5. Conclusion

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Zilles (2019). "Receptors and the DMN."



DMN areas defined by Buckner et al. (2008). Ann NY Acad Sci 1124, 1-38.

Cytoarchitectonic areas defined by Brodmann (1909) and JuBrain.

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Default mode areas (Buckner et al.,2008):

- * Posterior cingulate cortex (BA23)
- * Precuneus (BA31)
- * Anterior cingulate cortex (p24, s24)
- * Ventral medial prefrontal cortex (10m, BA32, BA11)
- * Dorsal medial prefrontal cortex (medial part of BA9)
- * Inferior parietal lobule (PGa, PGp, Pfm, Pft)
- * Lateral temporal cortex (BA20, BA21)
- * Anterior temporal pole (BA38)
- * Hippocampus, entorhinal (EC), and parahippocampal (BA36) cortex

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Resting State Networks (Greicius et al., 2003)

1. Sensorimotor network (SMN)
BA6, BA24, BA19, BA37, BA21, insula
 2. Default mode network (DMN)
BA9, BA10, BA32, BA7, BA39, BA23, BA31,
BA29, BA30, BA20.
 3. Executive network (ECN)
BA44, BA45, BA46, BA47, BA9, BA8, BA7,
BA39, BA40.
 4. Salience network (SLN)
BA32, BA24, BA46, BA47, BA12.
- Hippocampus, Entorhinal cortex, BA11, BA38, BA36
(Buckner et al., 2008).

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Resting States?



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NeuroImage: Eyes-closed or eyes-open rest

Resting-state refers to both (Raichle, 2015).

CBF is lower under eyes-closed than eyes-open conditions (Yuan et al. 2018).

EEG: Eyes-closed rest

Under eyes-closed, delta and theta pronounced in the midline, alpha and beta localized in the centro-parietal. Under eyes-open, beta increased in the frontal, other oscillatory activity decreased (Northoff et al., 2010).

HRV(ECG): Eyes-closed parasympathetic and eyes-open sympathetic

HRV is higher under eyes-closed than eyes-open conditions.

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fMRI Experiment:

No. of subjects: 55 (28 Females; Age 22.93 ± 3.078).

Task: 4-min eyes-closed followed by 4-min eyes-open
(with central eye-fixation).

fMRI parameters:

T2* (EPI): TR/TE 2000ms/30.0 ms; flip angle 84 deg;
35 slices; thickness 3.4mm; FOV 192mm.

T1 (anatomical images): TR/TE 2530.0ms/3.30ms;
flip angle=7 deg; 192 slices; FOV 256 mm.

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Intraclass Correlation Coefficient (ICC)

$$\widehat{ICC} = \frac{M}{M-1} \{1 - [\text{tr}(S)/(\underline{1}'S\underline{1})]\}$$

S is the sample cross-covariance with a zero-time shift,
and M is the number of subjects.

$-\infty < \widehat{ICC} \leq 1$: The conventional F-test may not work
well especially for neuroimaging applications.

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S has its population counterpart Σ and finite forth moments.

Number of scan volumes $n \rightarrow \infty$,

$\sqrt{n}(\text{vech}S - \text{vech}\Sigma)$ is asymptotically distributed as

$$\sqrt{n}(\text{vech}S - \text{vech}\Sigma) \rightarrow N(0, 2K_M(\Sigma \otimes \Sigma)K'_M)$$

$$\text{vech}\Sigma = K_M(\text{vec}\Sigma)$$

$\sqrt{n}(\text{vech}S - \text{vech}\Sigma)$ is valid if fMRI time courses are stationary and satisfy the ρ -mixing condition.

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$\widehat{ICC}$ (Kuo et al., 2019)

A scalar-valued function of S ;

Continuous with derivatives of 1st and 2nd order in the neighborhood of $S = \Sigma$.

Its asymptotic distributions can be expressed as:

$$\sqrt{n}(\widehat{ICC} - ICC) \rightarrow N(0, 2\eta'K_M(\Sigma \otimes \Sigma)K'_M\eta)$$

$$\eta' = \partial ICC / \partial \text{vech}'\Sigma, \text{ and } G_M(\text{vech}\Sigma) = \text{vec}\Sigma$$

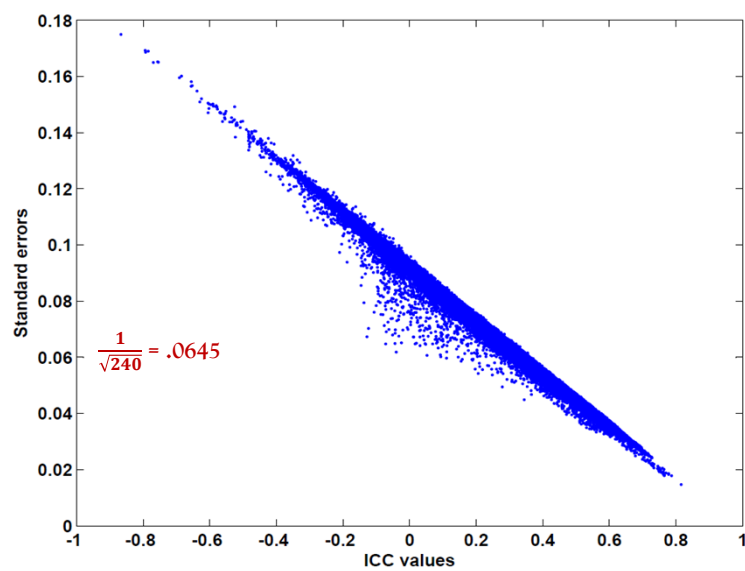
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$$\eta' = \frac{M}{(M-1)} (\underline{1}' \Sigma \underline{1})^{-2} [\text{tr}(\Sigma)(\underline{1}' \otimes \underline{1}') - (\underline{1}' \Sigma \underline{1}) \text{vec}' I_M] G_M$$

t-value of between-Subject $\widehat{ICC}$

$$t_{\widehat{ICC}} = \frac{\widehat{ICC}}{\sqrt{\text{Var}(\widehat{ICC})}}$$

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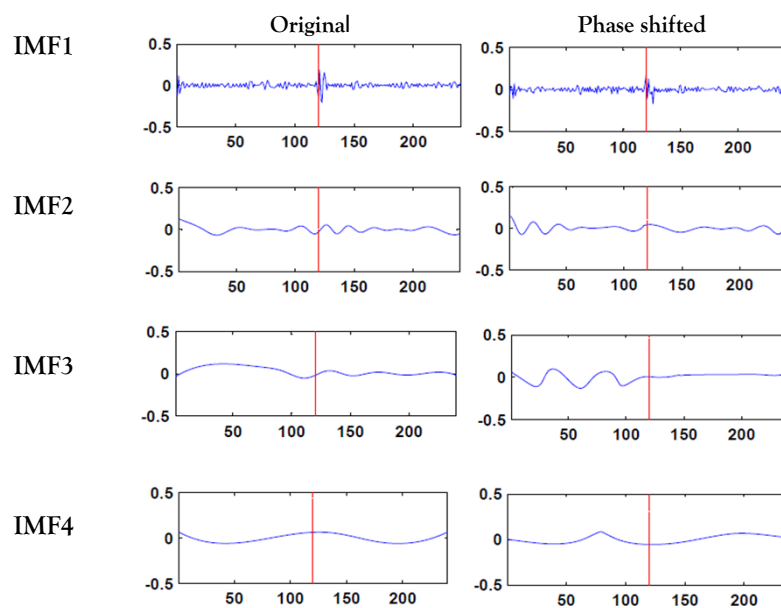
Empirical mode decomposition (EMD)

Analysis of non-stationary and nonlinear time courses.

Decomposition of the original signal into a set of intrinsic mode functions (IMFs).

Phase shifting applied to individual IMFs.

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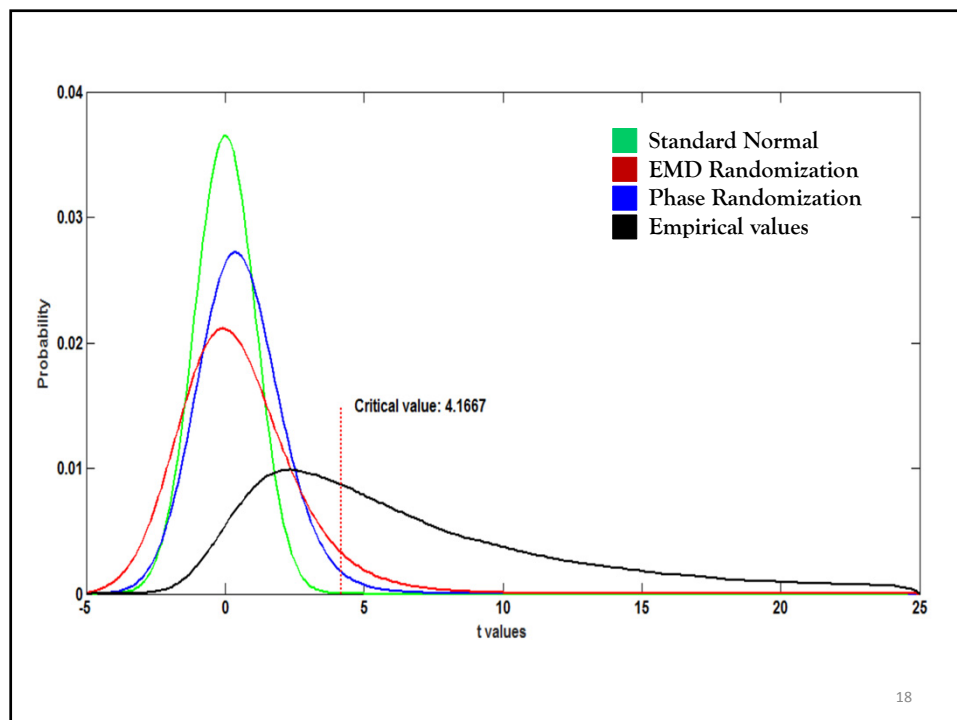


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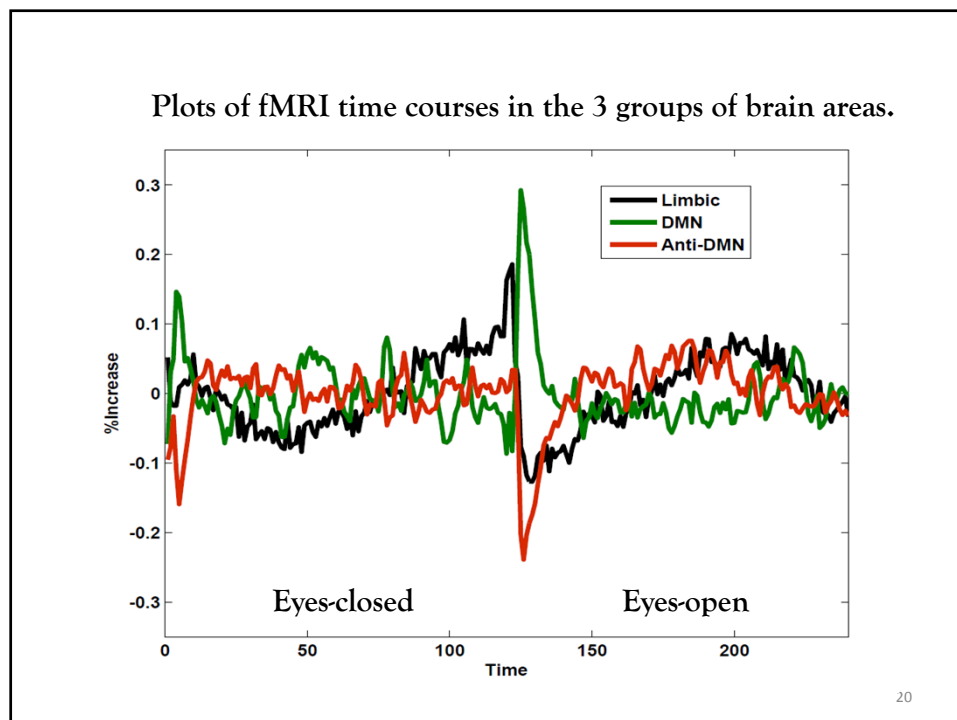
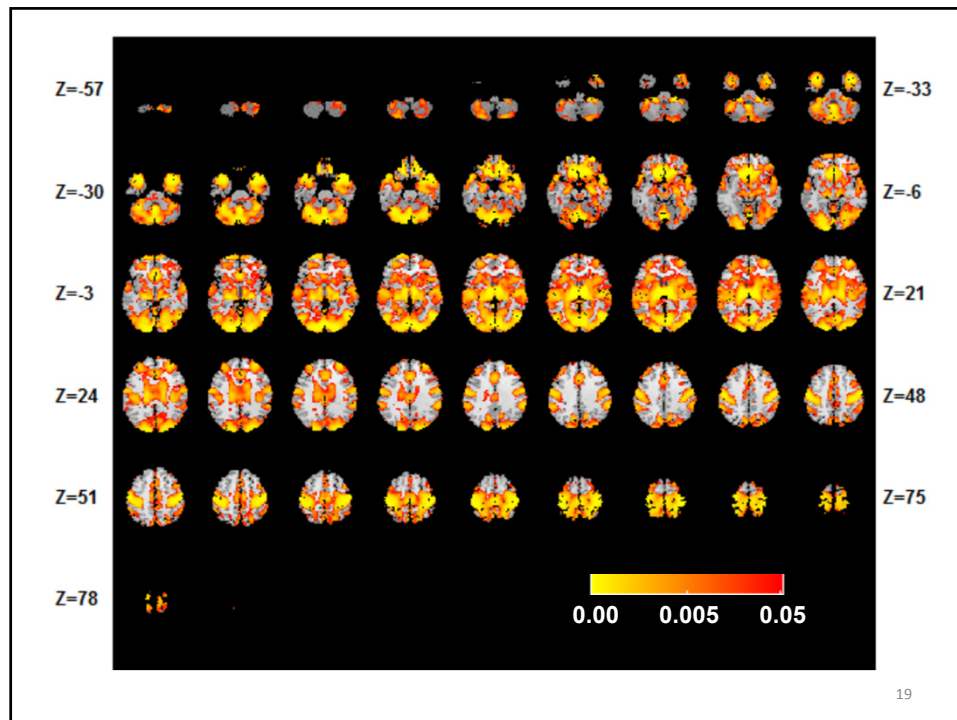
Thresholding the voxel-wise between-subject statistics

1. The ICC distribution under the null hypothesis $H_0: ICC = 0$ can be computed using the EMD randomization method.
2. The family-wise Type-I error can be controlled using the FDR procedure.

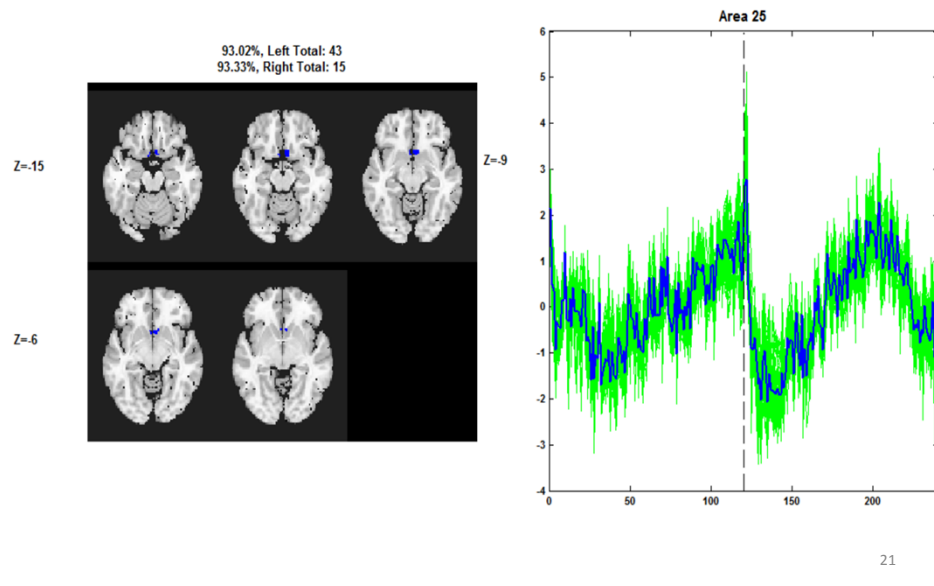
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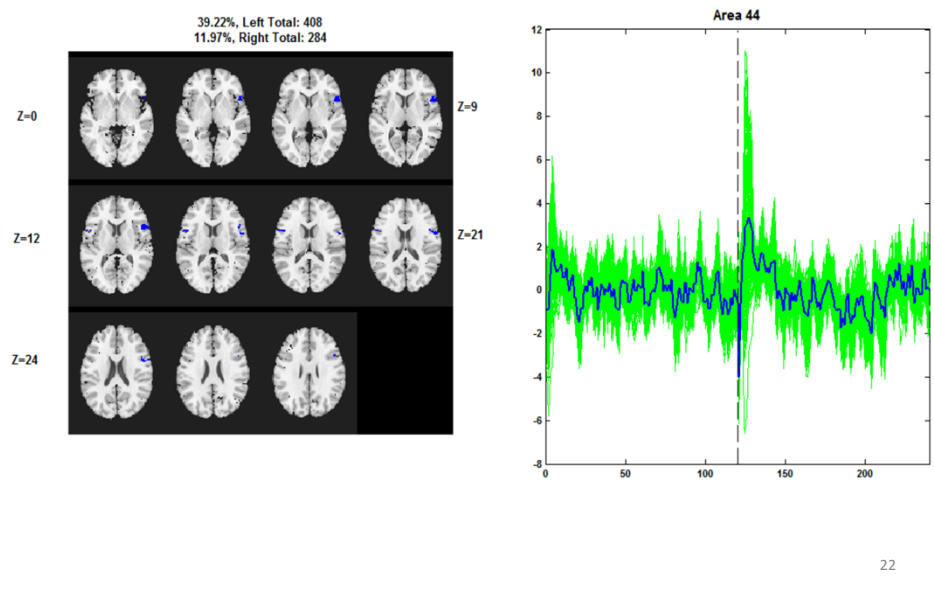
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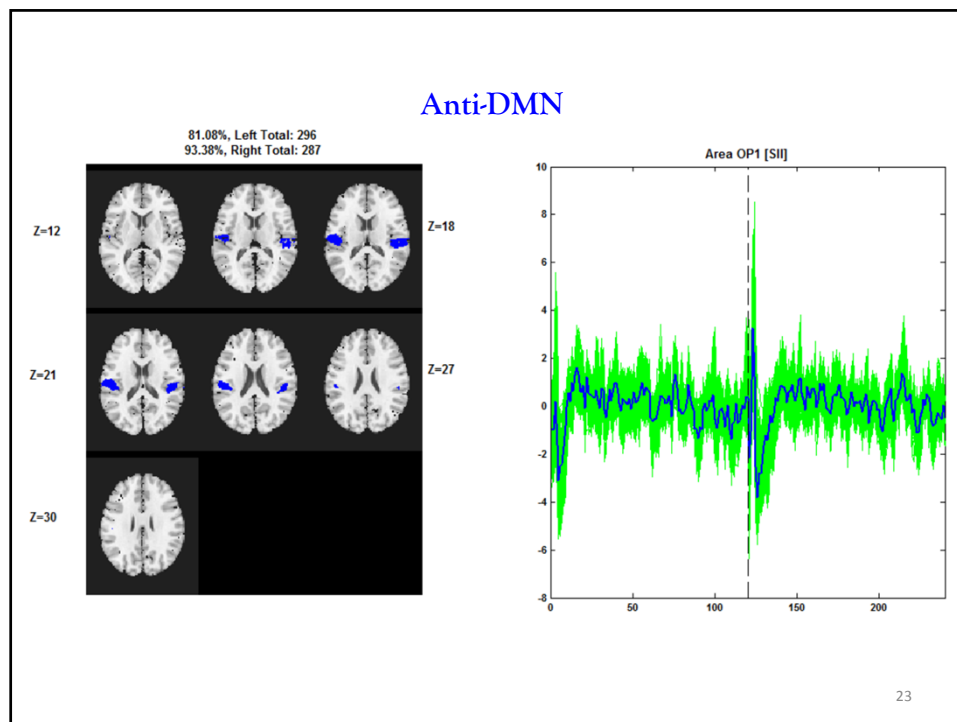


Limbic



DMN





Limbic & Related Structures:

Hypothalamus,
 Amygdala (CM, IF, LB, MF, SF, VTM, Astr);
 Orbitofrontal (Fo1, Fo2, Fo3);
 Frontal pole (Fp1, Fp2); (DMN)
 Basal forebrain (Ch1-3, Ch4);
 Hippocampal (CA1-3, DG, HATA, SC);
 Entorhinal cortex;
 Nucleus accumbens;
 Subgenual anterior cingulate (s24, s32, 25); (SMN, SLN)
 Visual association areas (BA20, BA21); (DMN, SMN)
 Anterior temporal pole (BA38);
 Parahippocampal (BA36);
 Pregenual anterior cingulate (BA33)

DMN:

Pregenua anterior cingulate (p24ab, p24c, p32); (SMN, DMN)

Posterior cingulate (BA23); (DMN)

Precuneus (BA31); (DMN)

Dorsal medial prefrontal cortex (BA9); (DMN)

Broca's region (BA44, BA45); (ECN)

Superior & posterior parietal (5Ci, 5M, 7M, 7P); (DMN)

Operculum parietal (OP8, OP9); (ECN)

Inferior & posterior parietal (PF, PFm, PGa); (ECN)

Intraparietal cortex (hIP1, hIP2, hIP6, hIP8) (DMN, ECN)

Angular gyrus (BA39)

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Anti-DMN:

Superior & posterior parietal (5L, 7A, 7PC); (DMN)

Operculum parietal (OP1, OP2, OP3); (ECN)

Inferior & posterior parietal (PFcm, PFop, PFt, PGp); (ECN)

Intraparietal (hIP3, hIP4, hIP5, hIP7, hPO1); (ECN, DMN)

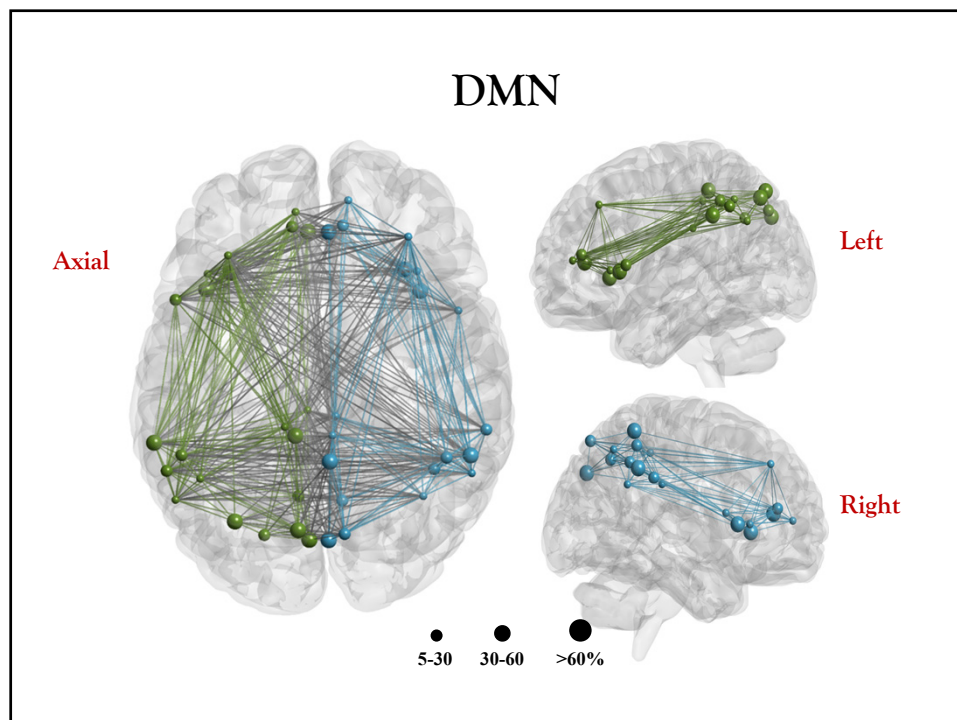
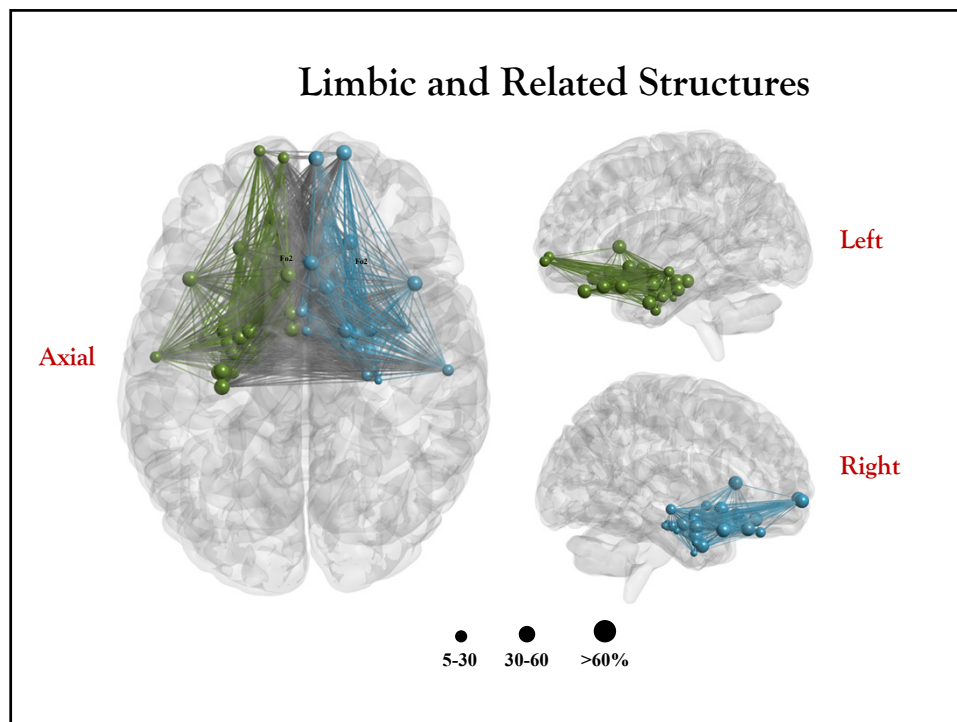
Superior temporal (Te1, Te1.1, Te1.2, Te3);

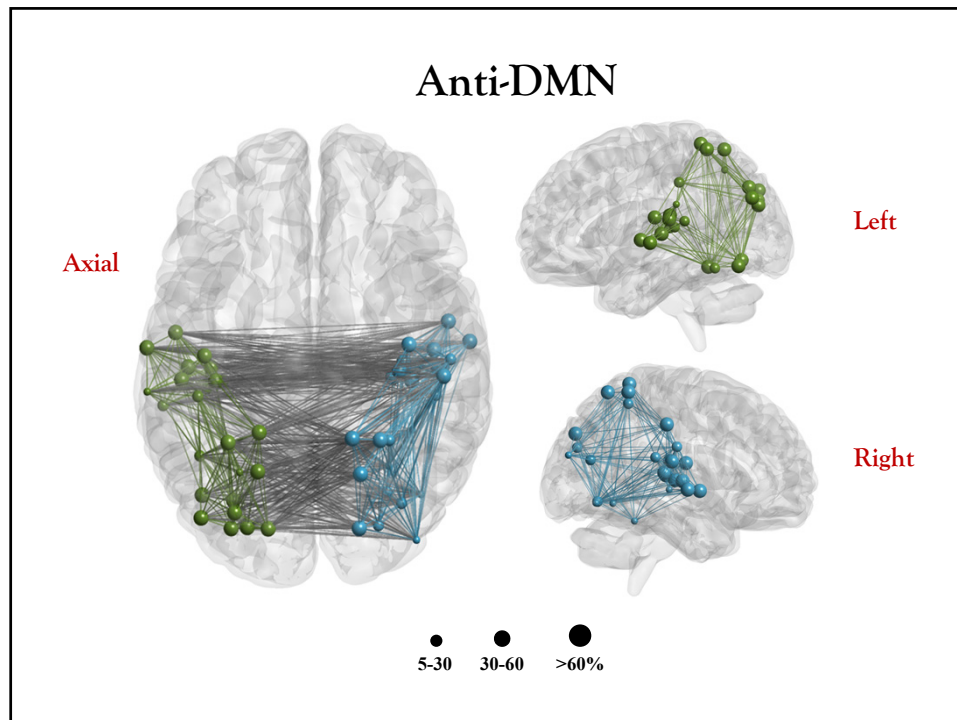
Posterior insula (Ig1, Ig2, Id1) (SMN)

Fusiform gyrus (FG1, FG2, FG3, FG4) (SMN)

Angular gyrus

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Conclusion

1. ICC defined ROIs give more stable estimates of connectivity networks.
2. Areas in the angular gyrus (PGa, PGp) belong to DMN and anti-DMN separately. It might not be precise to use a seed voxel for constructing connectivity.
3. The connectivity based on ICC defined ROIs may be correlated with other hormone or genetic measures.
4. JuBrain and ICC defined ROIs may be a new tool for investigating resting-state networks.

Brain Dynamics and Information Synthesis Lab

fMRI, EEG source localization,
feature selection in big data.

<http://www.stat.sinica.edu.tw/mliou>

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