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Whole-brain rs-fcMRI networks restructure over development, strengthening long-distance relationships and decreasing degree assortativity

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Introduction

fMRI can detect activity associated with task performance and has been used to define several functional systems, including control, default, and attention systems. rs-fcMRI correlations are purported to represent cumulative coactivation histories of brain regions, and have been used to recapitulate and extend networks identified with fMRI.

Here we examine the functional network structure of the brain, using a combination of fMRI and rs-fcMRI analyses. We begin by defining regions through meta-analyses of fMRI studies, and complement these regions with ones derived from rs-fcMRI analyses (fc-Mapping), to generate 259 regions of interest. We then examine the network structure of rs-fcMRI correlations between these regions by applying network community detection tools. In young adults the detected communities resemble several previously defined functional systems. In children, coarse versions of such communities are found, but network architecture also reflects local patterns.

Methods

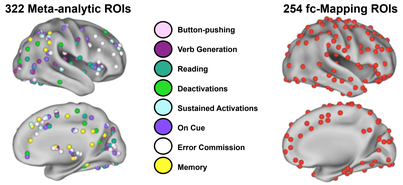
Identification of Regions of Interest (ROIs)

- Regions were defined by fMRI meta-analytic and rs-fcMRI-based (fc-Mapping) methods.
- Priority was given to fMRI-defined ROIs over fc-Mapping-defined ROIs.
- Task-based meta-analyses were conducted as shown in the table below.

Meta-analysis	# Studies	# Subjects	# ROIs
Button-pushing	12	310	46
Verb Generation	9	220	47
Reading	5	116	60
Sustained Task-Induced Deactivations	11	217	9
Transient Task-Induced Deactivations	11	217	8
Sustained Task Block Activations	11	217	17
On-Cue Task Block Activations	11	217	47
Error Commission	8	176	48
Memory	5	128	40

Total meta-analytic ROIs			322
fMRI ROI set (overlaps removed)			151
Total fc-Mapping ROIs			254
fc-Mapping ROI set (overlaps removed)			193
Combined ROI set (overlaps removed)			265

322 Meta-analytic ROIs **254 fc-Mapping ROIs**



- Regions were defined in a common stereotactic atlas, and by significant (typically z>=7) activity in a majority of studies examining a particular aspect of task performance.
- ROIs are modeled as 10mm diameter spheres.
- Meta-analytic ROIs were summed, smoothed, and a peak-finding algorithm determined final placement of fMRI ROIs, thus eliminating redundant ROIs.
- fMRI ROIs were complemented by ROIs defined in a separate group of 40 adults using fc-Mapping developed by Cohen et al (2008).
- fMRI and fc-Mapping ROI sets were examined singly, then merged into a combined set.

rs-fcMRI Data Collection

- Data were obtained from 250 subjects (age 7-35 years) at rest during crosshair fixation on a 3T Siemens Tim TRIO scanner. Results are reported on a cohort of 52 young adults (20-30 years old) and 15 children (7-9 years old).
- Images were preprocessed as normal fMRI data, then processed through a series of steps (Fox et al., 2005) with a bandpass filter of 0.009<f<0.08 Hz to obtain standard rs-fcMRI timecourses.
- Data were analyzed for motion artifacts, and frames displaying artifacts were ignored in network calculations. Only subjects with at least 125 usable frames were retained in network analyses.

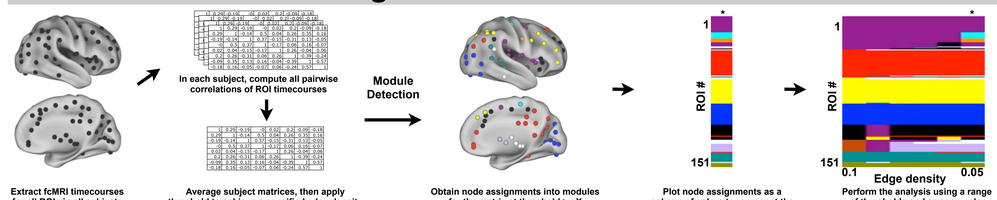
Network Construction & Characterization

- rs-fcMRI timecourses were extracted at all ROIs in every subject.
- For each subject, an NxN (e.g., 265x265 in the combined ROI set) correlation matrix was generated by calculating the pairwise correlation coefficients of the timecourses of all N ROIs.
- An average matrix was calculated from the subject matrices.
- We formed a network of nodes (ROIs) connected by edges (pairwise correlations)
- Correlation values range from -1 to 1, and one may apply a threshold to the matrix, setting all cells below a certain value to zero. Correlation distributions for large networks are typically Gaussian-like, centered around zero, with right tails.
- Here we examine threshold ranges that resulted in network with 10% edge density or less (a common regime for network analyses).

Community Detection

- The correlation matrix was subjected to community detection using the Infomap algorithm (Rosvall & Bergstrom, 2008).

Detecting modules within networks



Extract fcMRI timecourses for all ROIs in all subjects

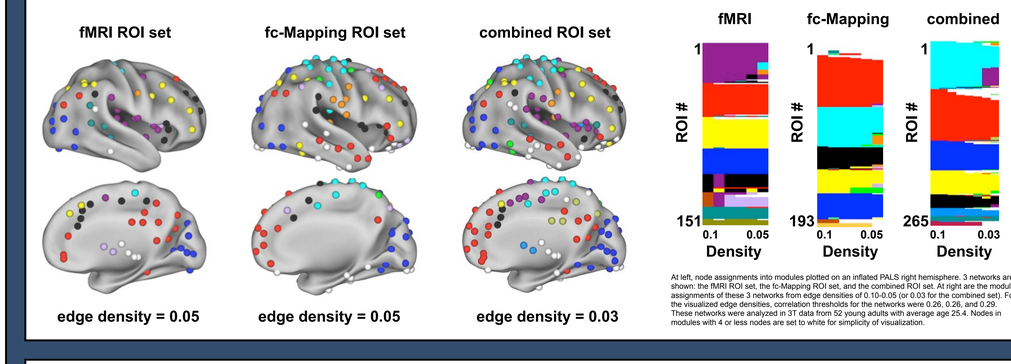
Average subject matrices, then apply threshold to achieve a specified edge density

Obtain node assignments into modules for the matrix at threshold >= X (here, edge density = 0.05)

Plot node assignments as a column of colors to represent the module assignment of each node

Perform the analysis using a range of thresholds and arrange color columns next to one another

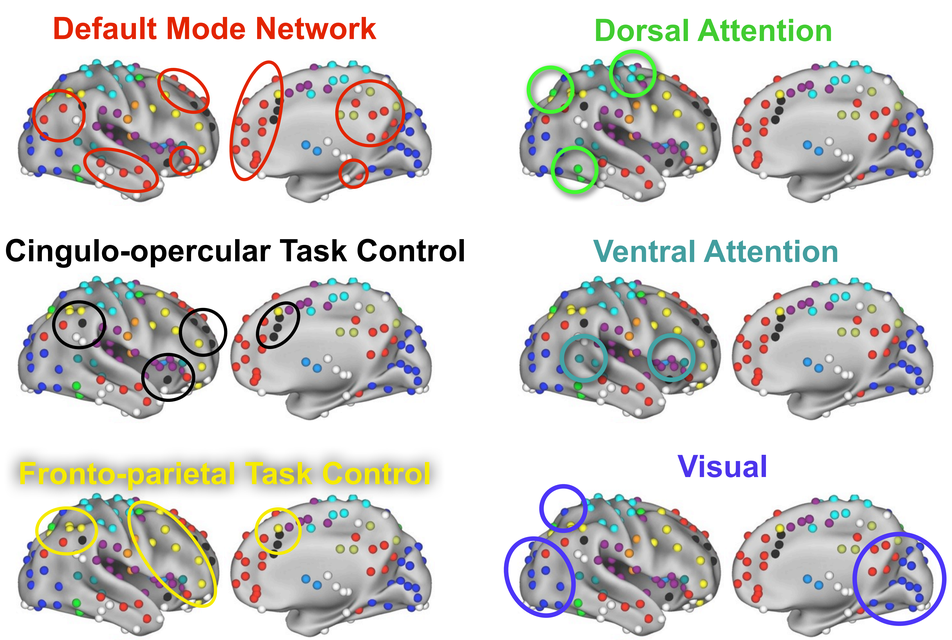
Areal networks in young adults display distributed modules



edge density = 0.05 edge density = 0.05 edge density = 0.03

At left, node assignments into modules plotted on an inflated PALS right hemisphere. 3 networks are shown: the fMRI ROI set, the fc-Mapping ROI set, and the combined ROI set. At right are the module assignments of these 3 networks from edge densities of 0.10-0.05 (or 0.03 for the combined set). For the visualized edge densities, correlation thresholds for the networks were 0.26, 0.26, and 0.29. These networks were analyzed in 3T data from 52 young adults with average age 25.4. Nodes in modules with 4 or less nodes are set to white for simplicity of visualization.

Young adult modules resemble functionally-defined brain systems



Combined ROI set from previous panel is used to display the correspondence between detected modules and various functionally-defined brain networks, such as default mode and task control networks (Raichle, et al., 2001; Dosenbach et al., 2006; Corbetta & Shulman, 2002).

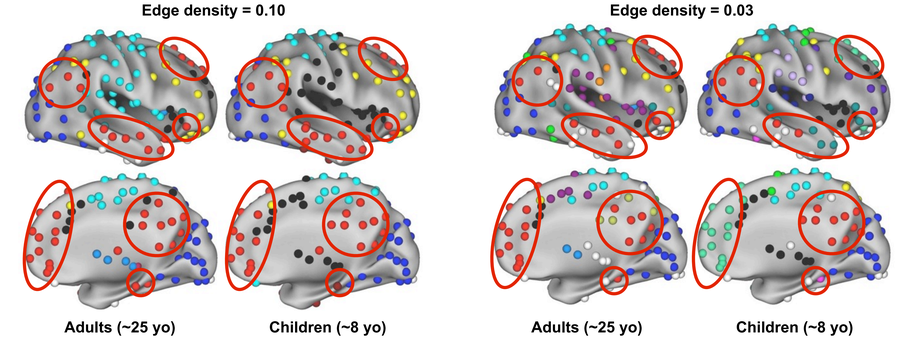
Child and adult networks display similarities and differences

Dense networks: similar structure

Edge density = 0.10

Sparse networks: different structure

Edge density = 0.03

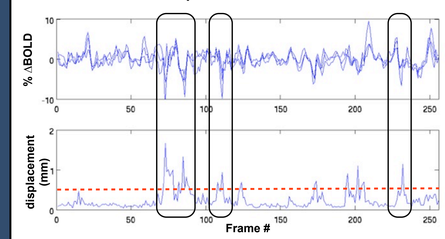


Adults (~25 yo) Children (~8 yo) Adults (~25 yo) Children (~8 yo)

The combined network from previous panels was applied to 15 children (RMS & frame-matched) aged 7-9 years old. On the left, modules in adults and children are displayed for the network at 10% edge density (dense). Note the evident correspondence in modular structure in children and adults. At the right, modules at 3% edge density (sparse), where clear differences between children and adults are seen. "Default" regions are circled in red ovals. From left to right, thresholds were 0.16, 0.15, 0.29, and 0.27.

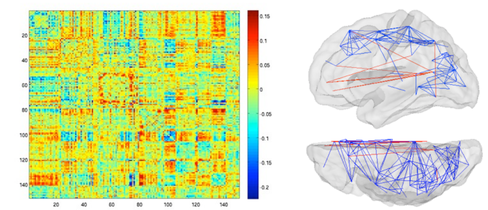
Studies of correlations are influenced by small movements

Timecourses of 3 occipital seeds with movement measures



At left, the timecourses of 3 occipital seeds (of the fMRI network) are plotted in a single subject, along with the subject's movement parameters across 2 runs of data (255 volumes, RMS=0.52). Note the large-amplitude displacements of the BOLD timecourse at points of movement. In the middle, the matrix shows the change in calculated correlations between nodes of the fMRI-defined ROI set (N=151, 29 subjects ages 7-9) when frames surpassing the red line in the left panel are ignored. At right, the changes in correlation with amplitude > 0.12 are plotted on a PALS surface. For simplicity, only edges in the left hemisphere are plotted. Note that "cleaning" the data tends to reduce short-range correlations, and increase long-distance correlations. Such changes impact the network structure.

Δr ('cleaned'-'uncleaned') |Δr| > 0.12



Conclusions

- Networks of putative functional areas in young adults possess modules that resemble known functional systems.
  - Distributed: default mode network, cingulo-opercular task control, fronto-parietal task control, dorsal and ventral attention networks.
  - Non-distributed: Visual, somatomotor cortex.
- The gross organization of networks in children is similar to that of adults, but strong short-distance correlations result in locally-organized modules as opposed to distributed modules when the network is sparse.
- Small, transient movements (sub-millimeter) can substantially impact BOLD signal, augmenting short-distance correlations and diminishing long-distance correlations. Such movements must be measured and addressed to accurately compare cohorts in rs-fcMRI studies.

References

Fox et al., (2005): PNAS 103:10046-10051; Cohen et al., (2008): Neuroimage 41: 45-57; Rosvall & Bergstrom, (2008): PNAS 105: 1118-1123; Raichle et al., (2001): PNAS 98: 676-682; Dosenbach et al. (2006): Neuron 50: 799-812; Corbetta & Shulman, (2002): Nat Rev Neurosci. 3: 201-215.

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