Detecting Cognitive States with Graph Theory Network Metrics

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INTRODUCTION

Background

* During resting scans, subjects continually engage and transition between different cognitive states such as visual imagery, inner speech, etc. [1].

* Whole-brain connectivity matrices contain sufficient information to classify similar cognitive states (e.g., silent signing, memory tasks, arithmetic computations, etc.) with high accuracy levels [2,3]. However, the dimensionality of the feature space associated with the whole-brain connectome makes classification and interpretation of results very challenging.

* Novel methods are needed to reduce the dimensionality of the data in a completely unsupervised fashion, without compromising accuracy. Such methods may allow understanding of which regions/connectivity patterns are most characteristic of each state.

* Graph theory metrics [4] are useful tools that provide compact descriptions of the functional organization of the brain at a given moment in time. However, it is not yet clear which graph theory metrics are most appropriate to describe the connectivity patterns associated with different cognitive states.

Objectives

* Find a minimal, yet optimal, set of graph theory metrics that help reduce the dimensionality of the data without compromising classification accuracy.

* Compare classification accuracy based on whole-brain connectivity vs. that based on network metrics.

* Evaluate variability in informative value of network metrics across subjects.

Experiment Overview

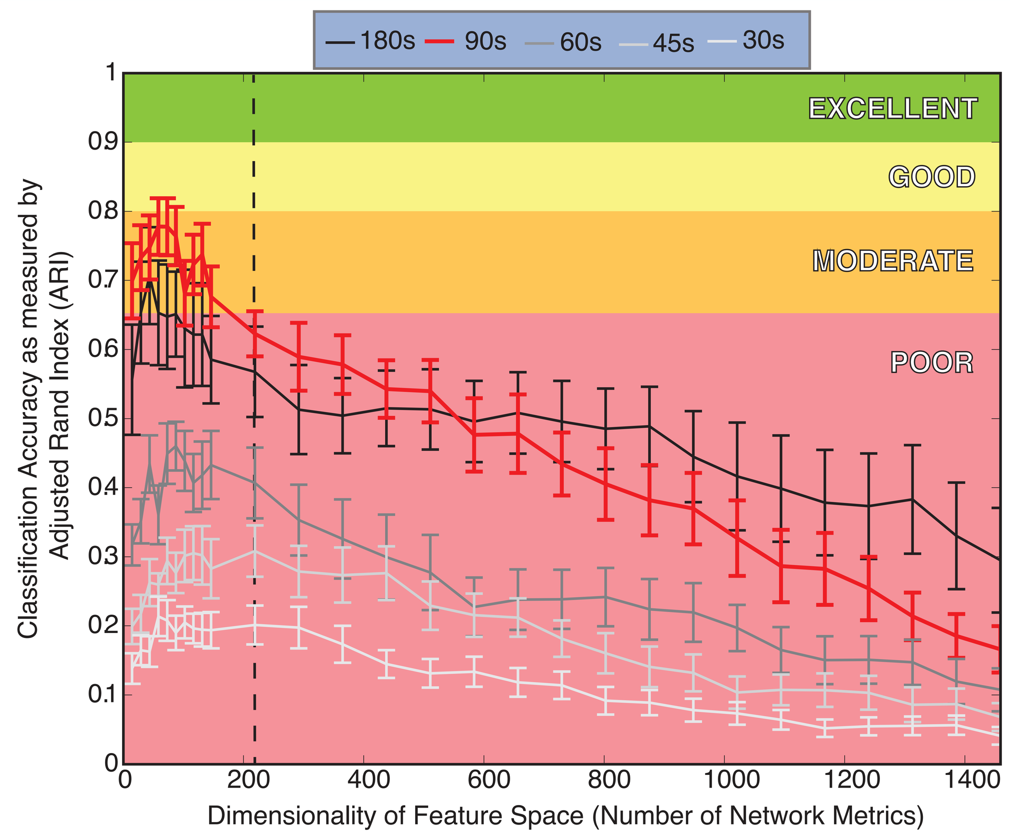
- Subjects continuously perform and transition between 4 distinct tasks throughout an fMRI scan
- The brain is parcellated into 132 functionally homogeneous ROIs

- Time-series are broken into non-overlapping windows aligned with the tasks
- Connectivity matrices are computed for each window
- Select network metrics are computed
- Metrics are ranked based on their discriminative ability
- Cognitive state classification is attempted using different sets of metrics
- Classification accuracy is measured using the Adjusted Rand Index [5]

- Identify most informative regions and metrics common across subjects

RESULTS

Classification Accuracy VS. Dimensionality of Feature Space



Classification accuracy as a function of number of metrics entering the clustering analysis for all window lengths

The figure to the left shows average classification accuracy (as measured by the ARI metric) versus the number of network metrics entering the analysis for all subjects and window lengths (WL).

* Highest accuracy levels were reached for WL=90s, the window length used for the sorting of metrics based on their discriminative value.

* Highest accuracy levels were reached using less than 10% of available metrics.

* Classification accuracy is worse than when classification was attempted based on whole-brain connectivity matrices:

TABLE 1. Classification for Different Analysis Methods	Window Length						Number of Subjects
	180s	90s	60s	45s	30s	15s	
Whole-brain ROI-to-ROI Connectivity [3]	1 ± 0	0.99 ± 0.01	0.97 ± 0.02	0.92 ± 0.03	0.86 ± 0.04	0.64 ± 0.05	22
Whole-brain ICA-to-ICA Connectivity [poster #1800]	1 ± 0	0.91 ± 0.04	0.84 ± 0.05	0.82 ± 0.05	0.68 ± 0.04	0.34 ± 0.04	11
Network Metrics Approach	0.71 ± 0.07	0.78 ± 0.05	0.44 ± 0.04	0.29 ± 0.03	0.21 ± 0.03	N/A	15

* Commonalities in ROIs and metrics across "half + 1" subjects were obtained for a dimensionality space of 218 metrics (15% of available metrics). These commonalities are shown below.

Most Informative Regions of Interest across Subjects

LEFT HEMISPHERE | RIGHT

Posterior Middle/Inferior Temporal Gyrus (BA37)	Supramarginal Gyrus (BA40)	Angular Gyrus/Posterior STG (BA39)	Inferior Frontal Gyrus (BA44)	Anterior Superior Temporal Sulcus (BA21)	Posterior Middle Temporal/Occipital Gyrus (BA39)
MNI -56, -54, -8	MNI -58, -32, 36	MNI -48, -68, 20	MNI -48, 10, 30	MNI -56, -6, -18	MNI 40, -80, 16
orthographic, concepts, phonology, writing, **thinking**, **arithmetic**, animals, **numerical**, **calculation**, chinese	simulation, nonpainful, heat, grasping, nonwords, scenarios, noxious, presentations, violations, **thinking**	avoidance, empathic, **mentalizing**, antipsychotic, phonology, feelings, text, theory of mind, confidence, names	orthographic, phonology, solving, **calculation**, **rehearsal**, **arithmetic**, character, writing, phonological, chinese	**autobiographical**, aphasia, **mentalizing**, text, scenarios, **thinking**, meaning, perspective, stories	**visual**, scene, houses, readers, distractors, orthographic, **character**, imagery, virtual, play
Degree	Degree, Betweenness Centrality, Eigenvector Centrality	Clustering Coefficient, Local Efficiency	Clustering Coefficient, Local Efficiency	Eigenvector Centrality	Eigenvector Centrality

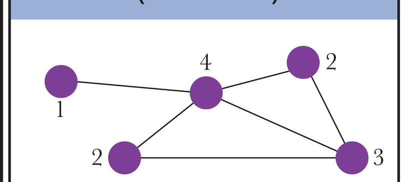
10 features with the highest probability of occurrence in the literature for each ROI according to the Neurosyth database [7].

Most Informative Network Metrics across Subjects

CENTRALITY METRICS
Relative importance of a node within a graph

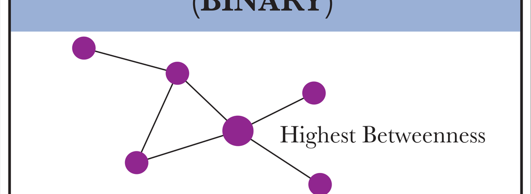
CLUSTERING METRICS
Degree to which nodes tend to cluster together

DEGREE (BINARY)



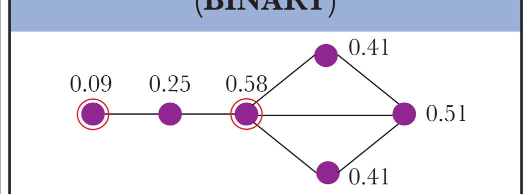
Number of edges emanating from a node.

BETWEENNESS CENTRALITY (BINARY)



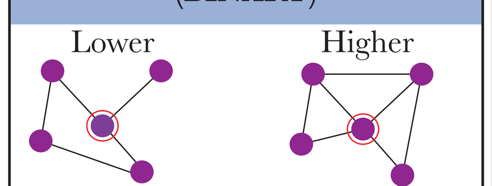
The fraction of all shortest paths in the network that contains given node.

EIGENVECTOR CENTRALITY (BINARY)



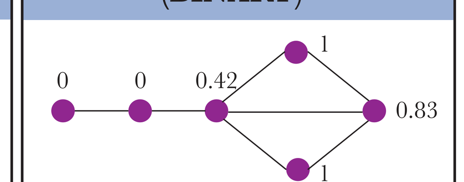
Normalized eigenvector for the principal eigenvalue of the adjacency matrix.

CLUSTERING COEFFICIENT (BINARY)



Fraction of a node's neighbors that are neighbors to each other.

LOCAL EFFICIENCY (BINARY)



Inverse of average shortest path length connecting all neighbors

METHODS

Data Acquisition and Preprocessing

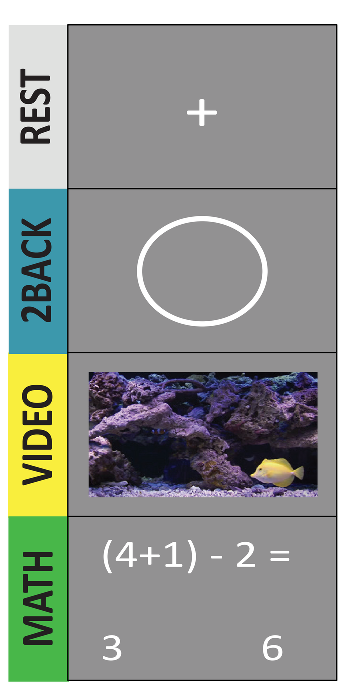
Data Collection Parameters

- 15 subjects (self reported right handed)
- 7T fMRI + 32Ch Coil

Anatomical:
- T1-weighted MP-RAGE

Functional:
- GR-EPI
- TR = 1.5s, TE = 25ms
- 2 x 2 x 2 mm
- 25 min & 24 sec task paradigm

Task Paradigm

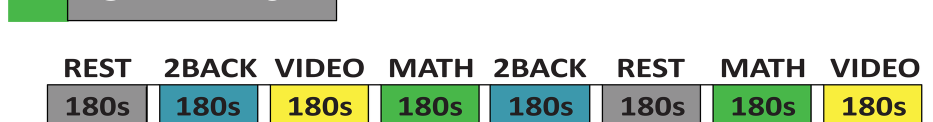


Rest: passively stare at crosshair and let mind wander.

2-Back: Press button when shape on screen is the same as the one two shapes before.

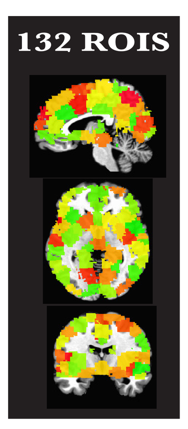
Video: Press a button to indicate appearance of red cross. Press left if cross covers clownfish, right if over any other fish.

Math: Press button to select correct answer (left/right) for the given operation.



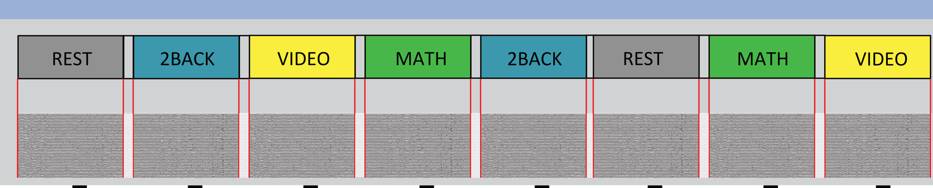
Data Preprocessing

(1) Despiking.
(2) Physiological noise correction.
(3) Slice-time correction.
(4) Head motion correction.
(5) Remove local WM & CSF signals, motion estimates and their 1st derivative
(6) Intensity normalization
(7) Bandpass filtering (0.001-0.2 Hz)
(8) Spatial smoothing (FWHM=4mm)
(9) Parcellate brain (150 ROI Craddock Atlas [6])
(10) Remove ROIs outside of field of view ➡ 132 ROIs



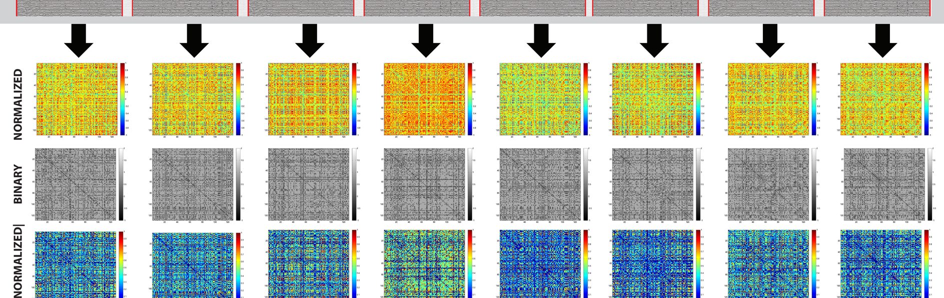
Data Analysis

Step 1:



Segment time-series into windows aligned with task
- Windows lengths of 180, 90, 60, 45, and 30 seconds analyzed

Step 2:



Compute 3 connectivity matrices for each window
- Binary and absolute normalized matrices are thresholded; the 70% strongest connections are kept

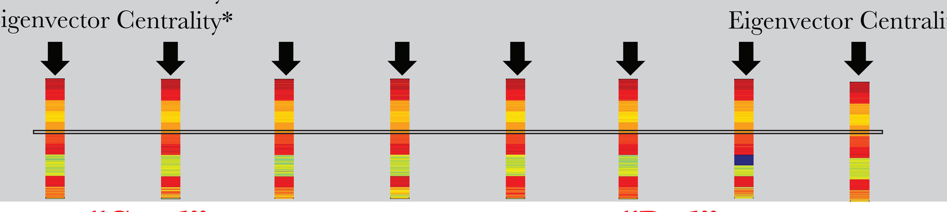
Step 3:

Graph Theory Network Metrics

BINARY	NORMALIZED	|NORMALIZED|
Degree*	Positive Node Strength*	Strength*
Density	Negative Node Strength*	Clustering Coefficient*
Clustering Coefficient*		Transitivity
Transitivity		Assortativity
Local Efficiency*		Global Efficiency
Assortativity		Eccentricity*
Path Length		Radius
Betweenness Centrality*		Betweenness Centrality*
Eigenvector Centrality*		Eigenvector Centrality*

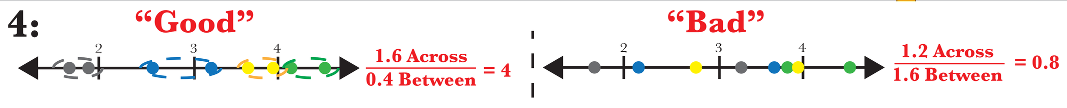
* Starred metrics compute a value for each ROI. The other metrics compute one value for the entire brain

Compute network metrics
- Whole brain and node based metrics from the Brain Connectivity Toolbox [4] were selected
- Several metrics were excluded due to excessive computation time



Evaluate metrics' discriminative capability
- The average distance between metric values for windows of different task types, over average distance between windows of the same task type, measures discriminative aptitude

Step 4:



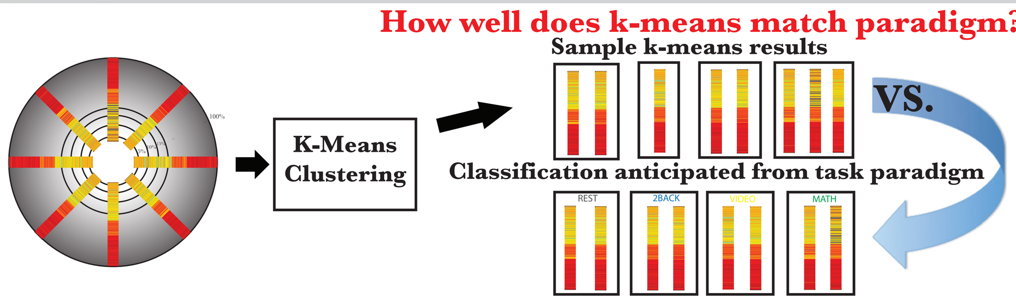
Step 5:

Discriminative metrics are those where windows of the same task type have similar values, and windows of different task types have dissimilar values. The sort index for the 90 sec windows was applied to metric vectors for all windows.

Sort the metrics from most to least discriminative

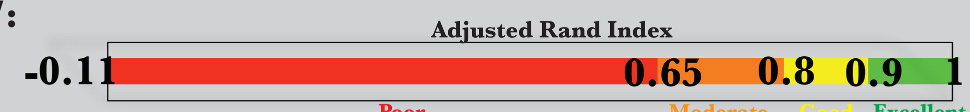
Step 6:

How well does k-means match paradigm?



Attempt classification with different sets of metrics
- An increasing number of metrics are entered into k-means, starting with the most discriminative, to determine optimal input

Step 7:



Evaluate classification accuracy against experimental paradigm
- ARI [5] is used to determine the accuracy of the k-means clustering output

CONCLUSIONS

* Metric-based classification did not reach the levels of accuracy previously obtained based on direct whole-brain connectivity matrices (see Table 1).

* Measures of centrality and local clustering are among the most informative, suggesting that such metrics best reflect the differences in connectivity patterns across cognitive states.

* Global brain measures (e.g., density, assortativity, etc.) did not provide any consistent discriminative value across states.

* We observed large across-subject variability regarding which metrics and regions are most discriminative. This may reflect across-subject differences in the strategies used to complete the tasks.

* Most discriminative ROIs concentrate in left lateralized, higher-order cognitive regions (for this group of self-reported right handed subjects), suggesting that most informative changes occur outside of primary sensory-motor regions.

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