Detecting Cognitive States with Graph Theory Network Metrics

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INTRODUCTION

In light of graph theory's recent developments in defining network metrics for complex theoretical models, these metrics can now be applied to real world networks such as the brain[1]. Using functional MRI (fMRI), we are able to treat the brain's functional activity as a network by quantifying correlations of brain activation between distinct regions of interest (ROIs). These correlations are treated as edges, and the ROIs as nodes. These graph theory algorithms allow us to uncover characteristics of the brain as a whole, as well as properties particular to specific nodes.

Previous studies[2,3] have shown how patterns of whole-brain functional connectivity can be used to differentiate cognitive states. Nevertheless, the large dimensionality of the feature space associated with the human brain connectome makes analysis and interpretation a challenging task. Discovering meaningful ways to compress such vast amounts of information, while maintaining the powerful classification capability of previous methods, would not only ease computational hurdles, but help uncover the primary drivers of distinct mental states. This exploratory project attempts to survey graph theory network metrics to determine if they can help dramatically reduce the dimensionality of the data without compromising the information that permits unsupervised detection of cognitive states.

After collecting fMRI data as subjects perform 4 different tasks, we compute the network metrics, dividing the data into multiple window lengths. The metrics are sorted according to how well the metric values for like-task windows match according to a particular window length (60 TRs). Using an increasing number of metrics, the metrics for windows of the same size are subjected to k-means clustering, where like-task windows will hypothetically group together.

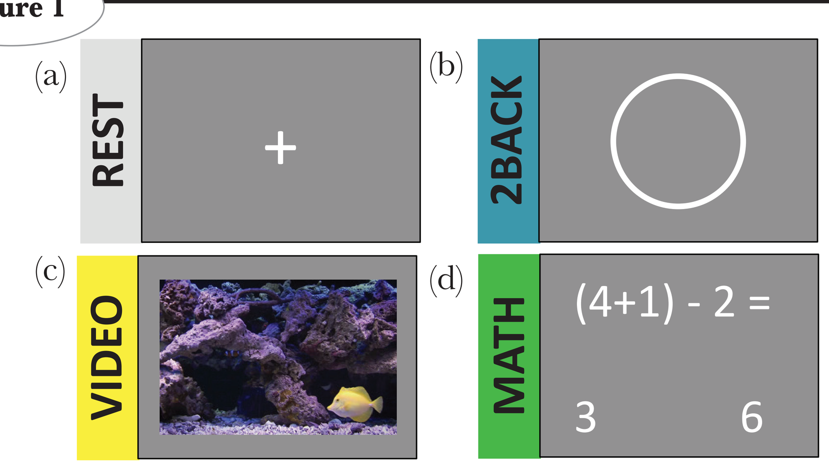
This first attempt at sorting metrics is intended to frame the potential for these metrics to reliably classify cognitive states, as well as identify the most informative metrics for this purpose.

DATA ACQUISITION

DATA COLLECTION PARAMETERS

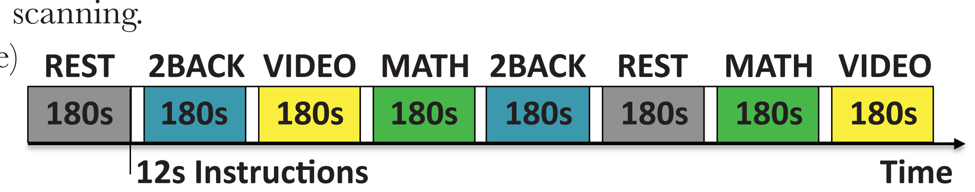
- 10 subjects
- 7T fMRI with 32 channel head coil
- Gradient-recalled, single-shot, echo planar imagine (EPI)
- TR = 1.5s, TE = 25ms, 2 x 2 x 2 mm
- 25 minute and 24 second task paradigm (Figure 1)
- Anatomical: T1-weighted MP-RAGE

Figure 1



TASK PARADIGM

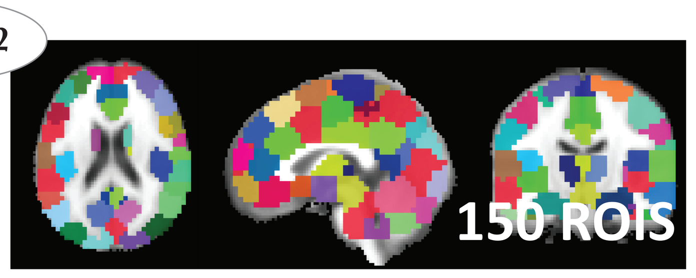
Four distinct tasks are presented to each subject. (a) Rest: Passively stare at the crosshair at the center of the screen and let your mind wander freely. (b) 2Back: Shapes presented in a series. Press a button when the shape on the screen is the same as the one two shapes before. (c) Video: Press a button to indicate each red cross appearance. Left button if cross is over clown fish, right button if over any other type of fish. (d) Math: Press a button to select the correct answer (bottom right/left) to the operation at the top. (e) Subjects were scanned for approximately 25 minutes as they performed the four tasks. Each task was performed for 3 mins on two different runs within the 25 mins of scanning.



Preprocessing

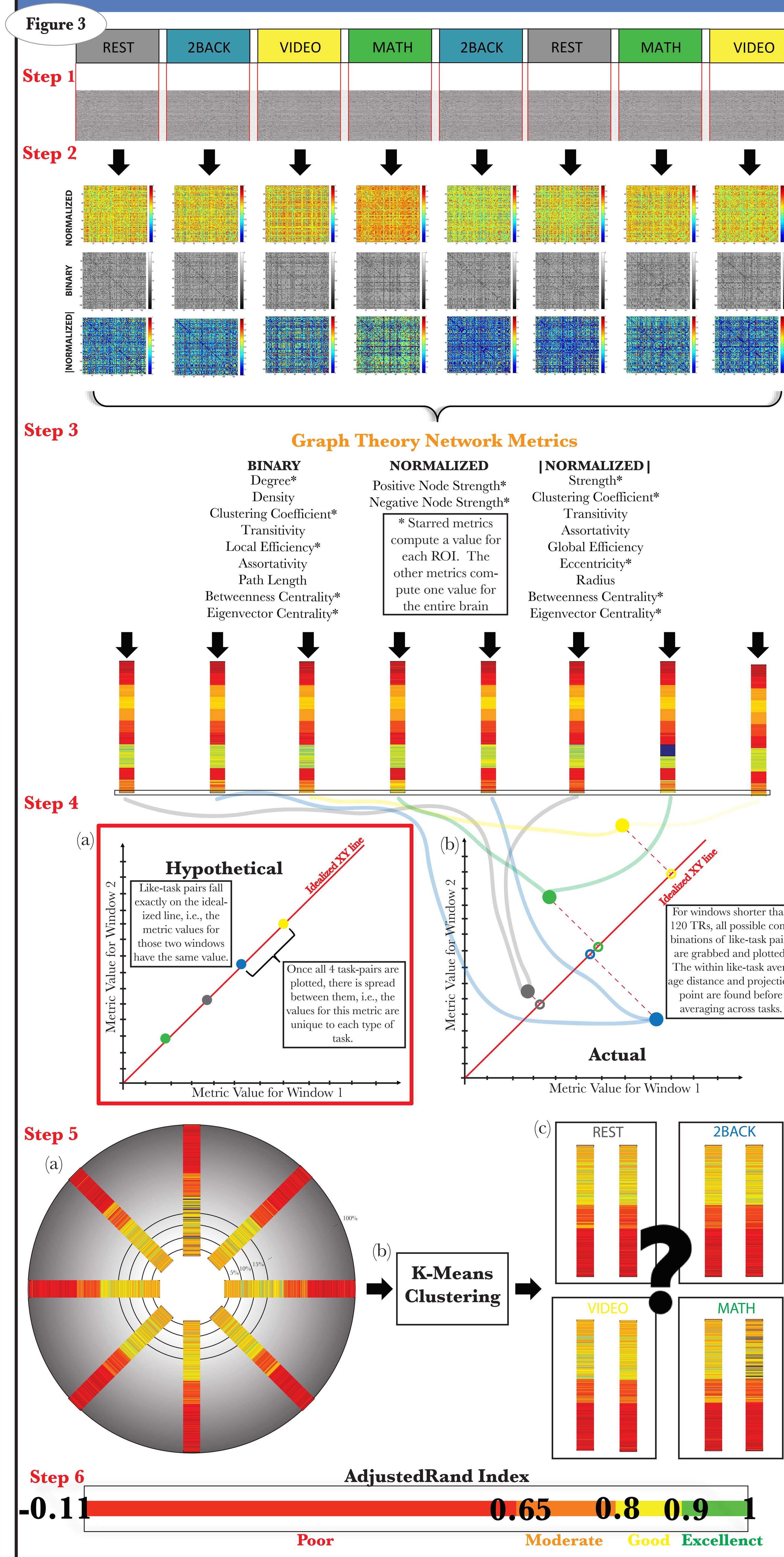
- Despiking
- Physiological noise correction
- Slice-time correction
- Head motion correction
- Removal of local WM signal
- Removal of CSF signal
- Removal of motion and 1st dx/dt
- Intensity normalization
- Bandpass filtering (0.001-0.2 Hz)
- Spatial Smoothing (FWHM=4mm)
- Pacellate brain into 150 ROIs based on Craddock Atlas[4] (Figure 2)

Figure 2



METHODS

Figure 3



Grab the timeseries for each window. In this example, one window was defined as one task block, or 120 TRs. While not shown here, we also devided the task blocks into smaller windows of 60 TRs, 40 TRs, 30 TRs, 20 TRs, and 10 TRs.

For each window, 3 connectivity matrices were computed. These matrices are used to compute the network metrics. The normalized matrix shows all correlations, including negative correlation values, corrected to have 0's along the diagonal. A threshold of 70% was applied to the next two matrices to enforce small-world properties of the brain. The binary matrix denotes ROIs that are or are not correlated. The absolute normalized matrix takes the absolute value of the correlations and expresses the strongest 70% with weights.

Algorithms from the Brain Connectivity Toolbox [1] were used to compute network metrics for each window. The inputs for these algorithms are one of the 3 correlation matrices computed in Step 2. The metrices either produced a value for the entire brain or for each ROI. The resulting values were not normalized; thus, some metrices gave small values (e.g., between 0-1), while others had very large values. For each window, the values for all metrices were stored in a single vector. Here, those vectors are shown with a log colorscale to show that there is differentiation at all number scales.

The Brain Connectivity Toolbox has a large number of available metrics, not all of which were used here. Reasons for absence include: metric intended for directed networks, metric had multi-dimensional options, metric was dependent on community structure (heuristic results), metric did not give a value for the whole brain or per ROI, metric took prohibitive time to compute, or as seen in Step 4, the metric does not have a spread greater than zero.

(a) One metric at a time, we grab the values for the like-task pairs. We plot them relative to the idealized XY symmetric line. If the metric performs "perfectly," we would expect the like-task pair points to land directly on the line and to be distinct between tasks.

(b) In reality, the points may fall away from the line and may overlap. If there was no separation between tasks (the "spread"), we went back to Step 3 and removed that metric from our analysis. We then calculated the average distance from each point to the line for a given metric (the "error"). The metric vectors were reordered, with metrics with small error expected to be the most informative, and those with large error to be less informative.

Example of reordering:

In this analysis, we used the metric sorting determined by the windows with a length of 60 TRs (not shown) to simplify the analysis to one window length for exploratory purposes, while also obtaining multiple windows within each task block.

(a) In increments of 5%, the top performing metrics in Step 4 are grabbed from the metric vectors for each window. In the sphere, the lighter to darker gradient shows the direction in which more metrics are included in the following analysis.

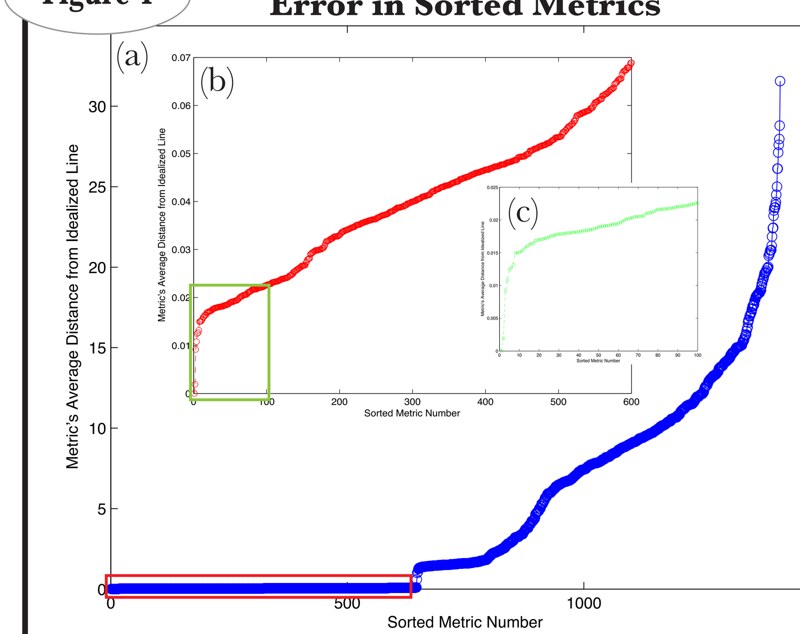
(b) For each set of vectors of increasing 5% length and of the same window size, the vectors are blindly submitted to k-means clustering. Clustering went through 25 iterations to overcome the potential for false centroids.

(c) If the k-means clustering effectively groups together the vectors of like tasks, we would know, first, if our sorting criteria is meaningful, and second, how many of the best performing metrics are needed to group like-tasks together.

The Adjusted Rand Index [5] is used to measure how well the k-means clustering grouped together like-tasks.

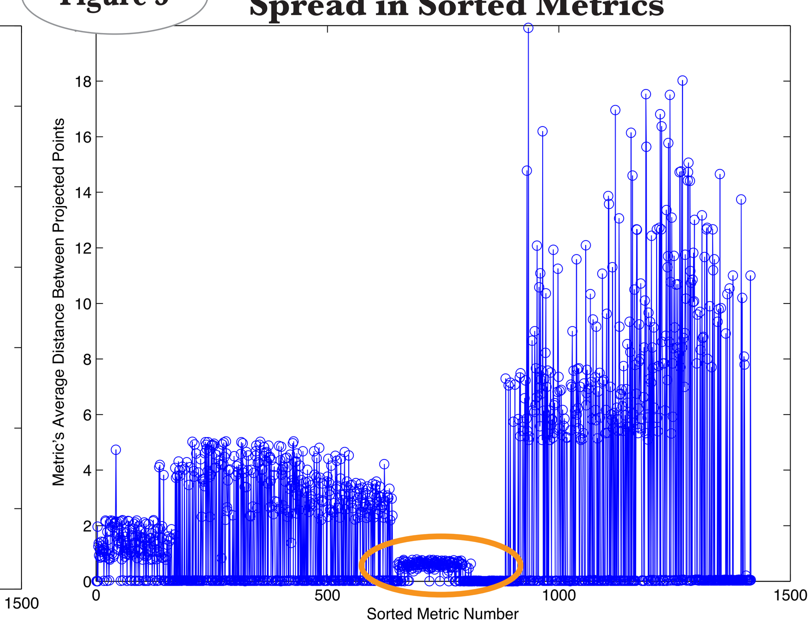
RESULTS

Figure 4 **Error in Sorted Metrics**



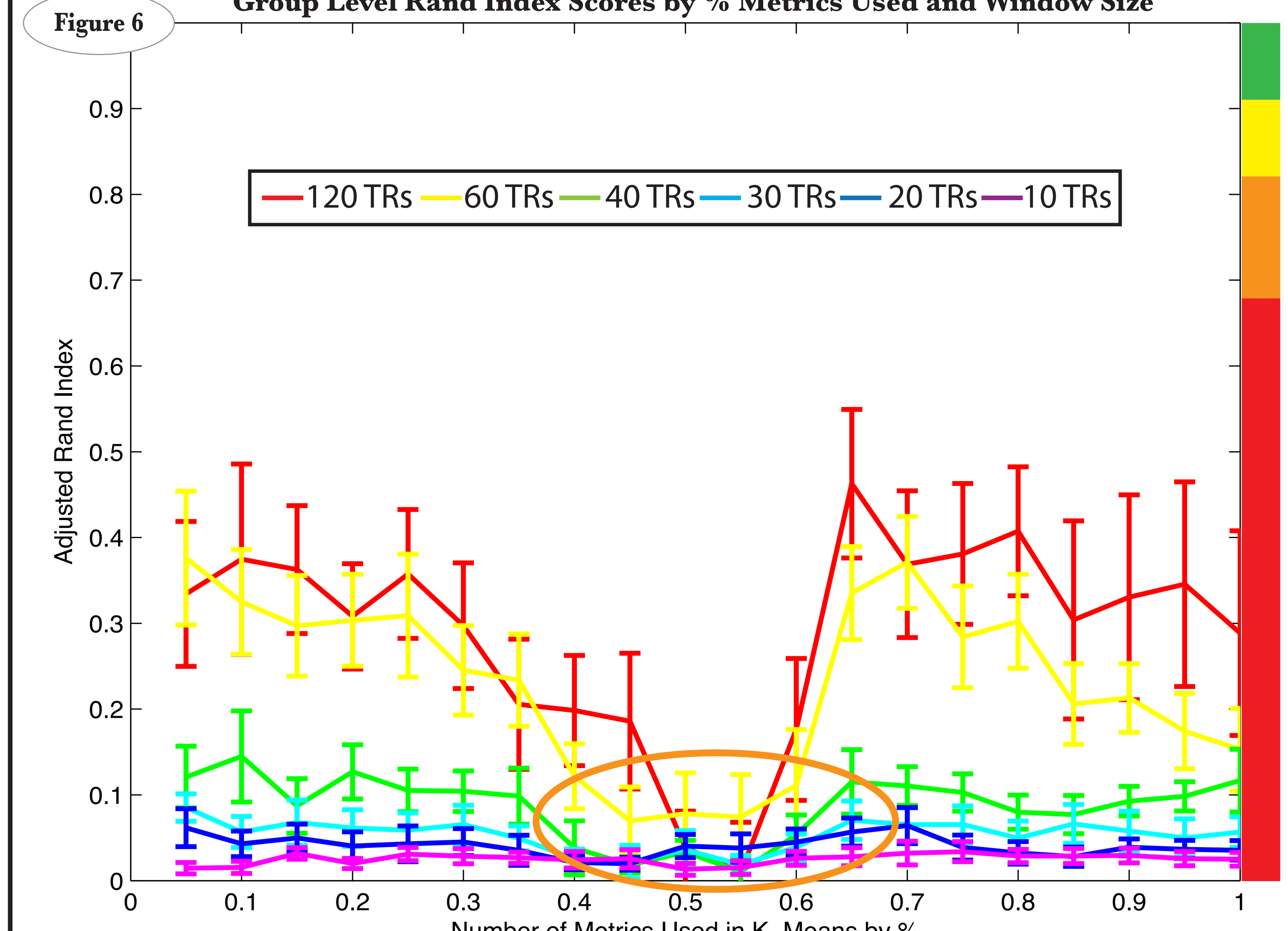
(a) For a representative subject, after the metrics have been sorted, the average distance from the idealized line, or the error, for each metric. (b) Zoomed in on low values in (a) that fall within the red box. (c) Zoomed in once more on the lowest values for the error. Across subjects, low error metrics included density, binary path length, binary local efficiency, and binary transitivity.

Figure 5 **Spread in Sorted Metrics**



For the same representative subject in Figure 4, the spread, or average distance between projected points, for each metric in the order of the sorted metrics. Because we expect metrics with larger spread to be more informative than metrics with smaller spread, we see here that our current sorting paradigm is not ideal, because it does not take advantage of the spread.

Figure 6 **Group Level Rand Index Scores by % Metrics Used and Window Size**



Group-level results (10 subjects), showing the average Adjusted Rand Index Scores for each window size. The standard error is shown in the error bars. Along the left side of the figure, the color grating for the Adjusted Rand Index is shown. No set of metrics for any window size is able to group the like-tasks with a score better than "Poor." The larger window sizes perform better, as expected, according to previous studies using the same task and window construction paradigm. We expect that if the early metrics are unable to group together like-tasks, as more metrics enter analysis, the grouping should improve, because more information is being added. This does not happen. Circled in orange is a realm of a combination of metrics that perform worse than expected. If we look to the metrics added in during that realm, as shown in the orange circle in Figure 5, we see these metrics are possibily uninformative because their spread is so small and they may be adding a detrimental amount of noise to the system.

POTENTIAL FUTURE DIRECTIONS

- Include more metrics from the Brain Connectivity Toolbox
- Investigate whether the metric values for some ROIs are more informative than others
- Incorporate the spread of the metrics into the sorting procedure
- Try a different statistial approach to ranking metrics
- Consider the effect of threshold on the absolute normalized and binary matrices
- Look at effect of ROI size on resulting metric values
- Find way to normalize metrics so values fall within manageable range

CONCLUSIONS

This project is a first attempt at developing a method that will sort graph theory network metrics in a way that illuminates which metrics are most informative in clustering temporal windows of the same task. Using a blind approach, such as k-means clustering, should allow the most informative metrics to group together tasks of the same type while introducing minimal external information.

Here, we have implimented a sort criteria based on the error of the metric, relative to the idealized XY line. This approach is capable of sorting the like-task windows better than chance in some instances, but is not capable of clustering the windows with moderate to excellent success according to the description of the Adjusted Rand Index.

Two metrics, binary radius and binary efficiency, proved to be non-informative in differentiating between the 4 tasks in this study. This was determined during Step 4, where we saw that the spread for these metrics was zero, meaning that they gave the same values regardless of task.

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