The Predictive Value of Functional Connectivity

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Background

Considerable effort has gone into developing descriptive metrics of connectivity patterns in the human brain [1]. However, little is known about the predictive utility of functional connectivity (i.e., how well a given connectivity pattern can explain future activity). Here we tested this by investigating how connections from other brain areas can be used to generate a predictive model of future activity in a target brain region.

Isolating out the network component in a given region's activity can also provide clues as to the nature of the task-related computations being performed. To this end, we also aimed to use the learned functional network to identify what proportion of task related activity can be explained by network driven (i.e., distributed) computations, as opposed to purely local computations within a region of interest (ROIs).

Methods

1 Data Collection

Thirty healthy participants (8 men, ages: 19-29) were scanned on a 3T Siemens Verio at the Scientific Imaging & Brain Research Center at CMU.

Participants were tested on 2 protocols:

- Stop Signal Task (2 runs, 351 volumes, TR = 1500ms, TE = 20, 3.2 x 3.2 x 4.0 mm, 30 slices)
- Resting State fMRI (1 run, 280 volumes, TR = 2000ms, TE = 20, 3.5 x 3.5 x 3.5 mm, 30 slices)

Go Trial

Stop Trial

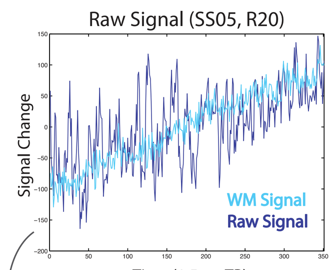
2 Signal Processing

i) All data were motion corrected, slice time corrected, and normalized to MNI-space using SPM8.

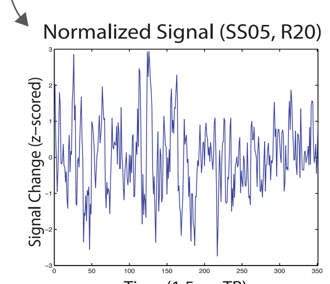
ii) The average white matter signal, taken from the corpus callosum, was regressed out of each voxel's time series (to account for physiological noise).

iii) Each voxel's time series was then converted into a standard normal range using a z-transform.

Raw Signal (SS05, R20)



Normalized Signal (SS05, R20)



3 Region Segmentation

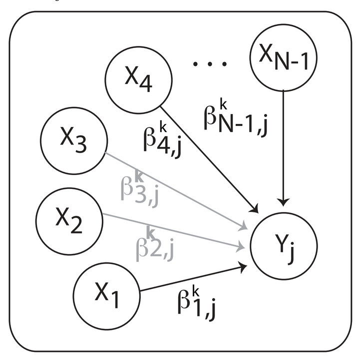
Regions of interest (ROIs) were generated for all cortical areas and mid-brain nuclei using a 600 region parcellation of the AAL atlas.

The time series for each ROI was obtained by averaging the signal from all voxels within the ROI mask.

4 Model Training

Lasso Regression [2,3] was used to learn the weighted connections to each node j, from all n-1 other ROIs.

$$\beta_j^k = \underset{\beta_j^k}{\operatorname{argmin}} \tfrac{1}{2}\left(\sum_{i=1}^{t}(y_i - \beta_j^{kT} x_i)^2 + \lambda\|\beta_j^k\|_1\right)$$



5 Model Testing

The coefficient of determination (r^2) was used to measure how well the weighted inputs to each ROI could be used to predict the time series in a target ROI.

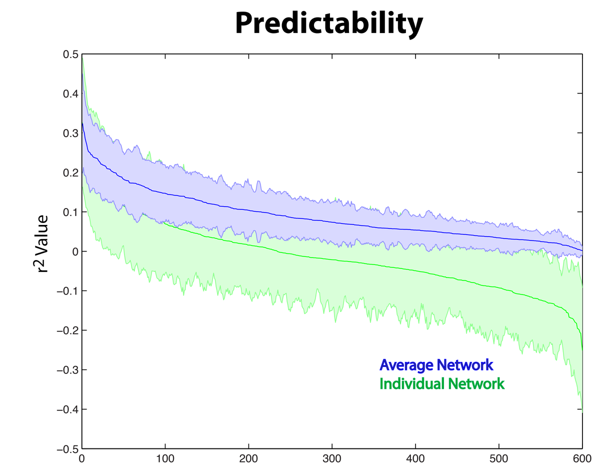
$$R^2 = 1 - \frac{\sum_{i=1}^{t}(\hat{y}_i - y_i)^2}{\sum_{i=1}^{t}(y_i - \bar{y})^2}$$

Result I: Network Performance

In total four networks were evaluated:

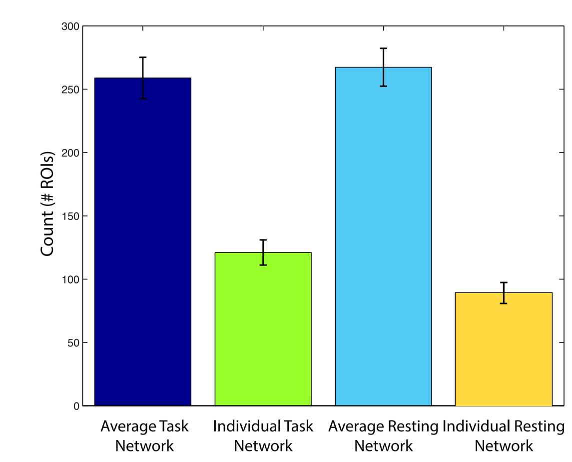
i) Individual subject networks from task data
ii) Average network connectivity across subjects from task data
iii) Individual subject networks from resting-state data
iv) Average network connectivity across subjects from resting-state data

Predictability



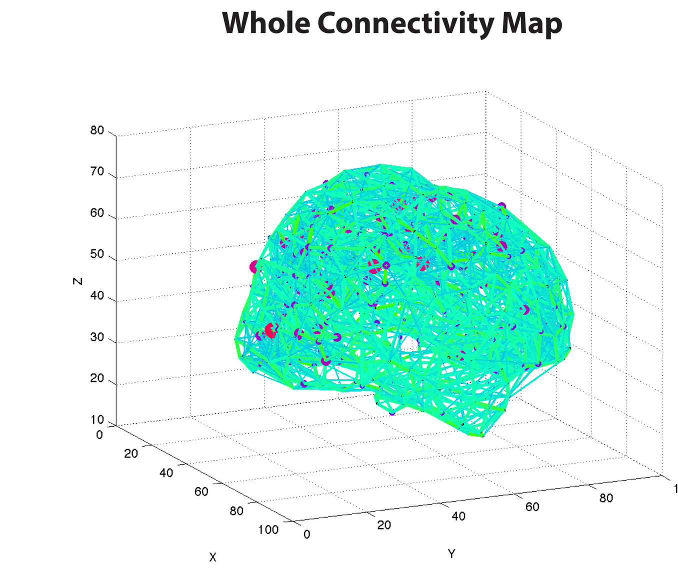
Cross validation of ROIs and 95% confidence interval. Data shown only for networks trained on task data.

Number of ROIs Predicted Above Chance



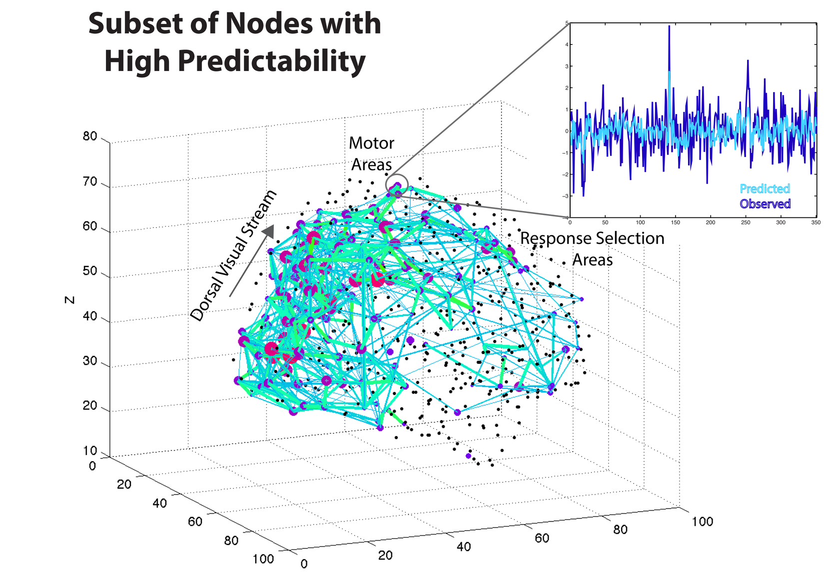
Error bars show a 95% confidence interval.

Whole Connectivity Map



The full average network learned on reactive task data

Subset of Nodes with High Predictability

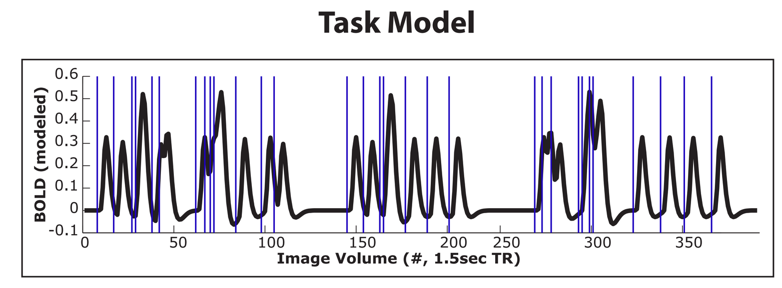


Connections are shown if and only if both end point ROIs are "predictable" (i.e., adjusted 95% confidence interval does not include zero) and the weight of that link is above 0.0075. Inset: predicted and observed values for subject SS05 for ROI 4 (r-square = 0.23)

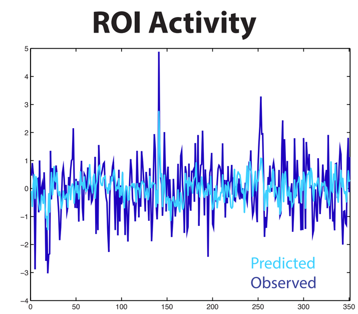
Results indicate that using average networks significantly improved performance. Networks trained on resting state data differed from networks trained on task data. A region was considered "predictable" if its 95% lower confidence bound (Bonferroni-corrected) was above 0.

Result II: Task Variance

Task Model



ROI Activity



Task Fits

Model 1: Raw signal

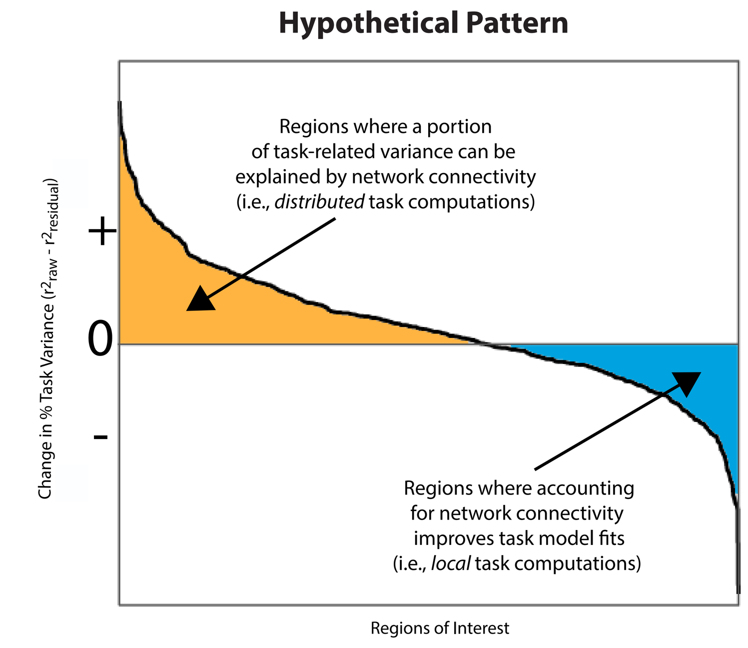
$$\hat{y}_{raw} = \hat{\beta}_{raw} X_{task}$$

Model 2: Network effects removed

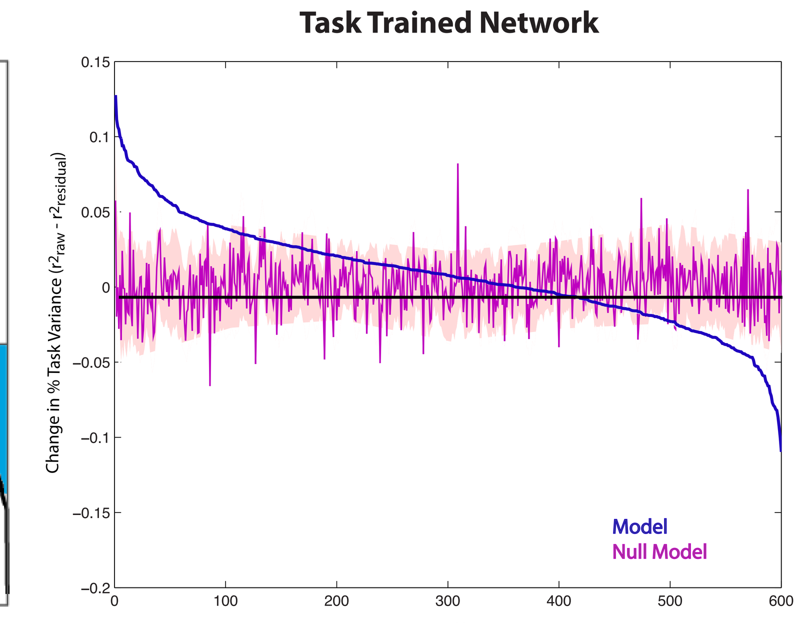
$$\left(\hat{y}_{raw} - \hat{y}_{predicted}\right) = \hat{\beta}_{residual} X_{task}$$

Fits to the task model were evaluated at each ROI both before and after removing network level signals.

Hypothetical Pattern



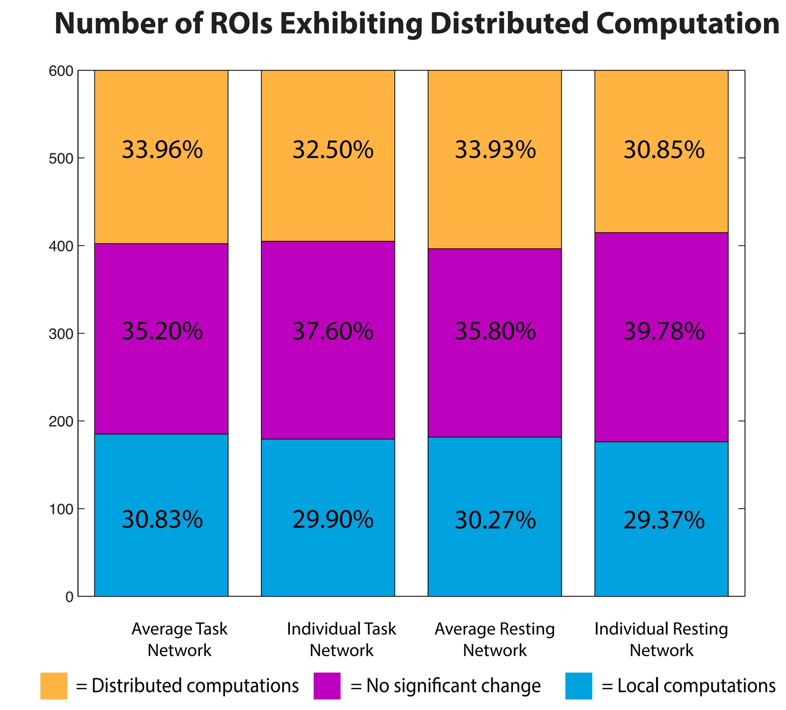
Task Trained Network



Regions that are above the null model represent network driven computation and those below the null model exhibit local computation. Null models were calculated through repeated permutations where the signal from the target ROI was scrambled on each permutation.

We next wanted to determine how much of task-related activity in the fMRI signal can be explained by network-level computations (i.e., shared processing across connected regions), versus local computations within a region. This was done by seeing how well we could predict task-related activity before and after subtracting the network component from the ROI signal. When removing the network compnent impairs task-model fit (i.e., raw minus residual is positive) this indicates that the region's computation is at least partially network driven. When this difference is negative (i.e., removing the network component improves task-model fit) we can conclude that the network is hurting predictability, and the region's computation is more local.

Number of ROIs Exhibiting Distributed Computation



Significance was calculated with a Bonferroni correction

Summary & Conclusions

i) Using cross-validation it is possible to identify neural regions whose time-dependent activity can be predicted by the weighted inputs from other areas.

ii) Individually trained networks likely contain a detrimental amount of noise and average networks provide better predictive capabilities.

iii) The location of predictable nodes is consistent with regions known to be involved in object tracking (i.e., dorsal visual stream), executive control (i.e., prefrontal areas), and motor responses (i.e., motor areas).

iv) Accounting for network-related activity revealed that a rougly equal number of regions rely on distributed computations than local computations when performing a simple sensorimotor task.

References

[1] Sporns, O. (2013). The human connectome: origins and challenges. *NeuroImage*, 80, 53-61.

[2] "Glmnet in MATLAB", Available at http://www.stanford.edu/~hastie/glmnet_matlab/

[3] Tibshirani, R. (1996), "Regression shrinkage and selection via the lasso," *Journal of the Royal Statistical Society. Series B (Methodological)*, pp. 267-288.