Evaluating the predictive power of dynamic fMRI connectivity summary statistics

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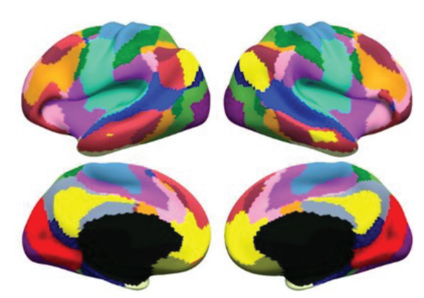
INTRODUCTION

- Brain-behavior models often use resting-state fMRI data in the form of static functional connectivity (FC) matrices as inputs, where each entry corresponds to the Pearson's correlation between time series for a pair of regions of interest (ROIs or nodes)[1].
- This approach has been integral to key neuroimaging findings linking connectivity with behavioral phenotypes[2], yet it provides a potentially limited perspective.
  - By definition, FC describes the 'average' similarity of signals over time, and neglects information about the ebbs and flows of brain activity, i.e., connectivity dynamics.
- To access dynamic connectivity information, we generated a time series for each node pair (or edge), capturing how the two nodes co-fluctuate moment-to-moment, called an **edge time series**[3].
  - This process results in a high-dimensional data structure, describing the instantaneous co-fluctuation between each pair of nodes, for each timepoint.
- Here, we explore multiple summary measures of edge time series -- **time-insensitive** and **time-sensitive** -- and evaluate their predictive ability for cognitive traits. We aim to investigate how much dynamic changes additionally inform brain-behavior predictions over more common static measures.

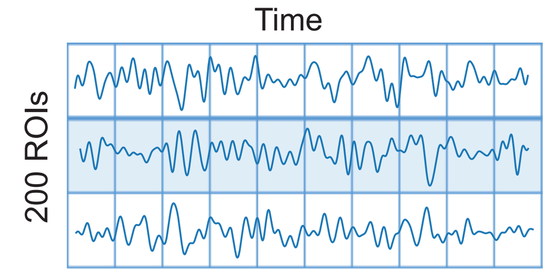
METHODS

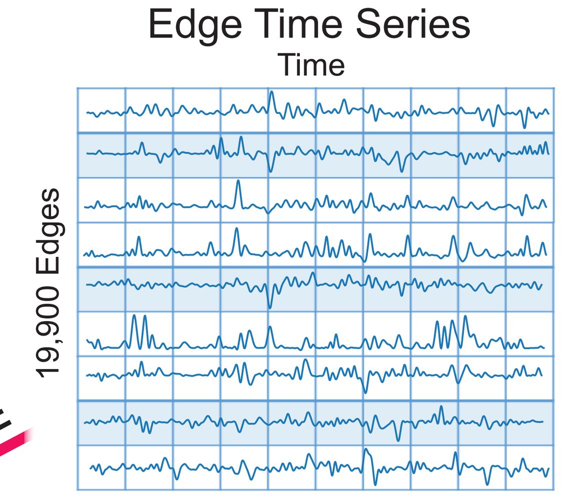
971 Resting-State fMRI Scans[4]
(duration=9.5min; Siemens 3T; TR=650ms)

fMRI Prep Preprocessing[5] + aCompCor Denoising[6]



Alignment to Atlas
Schaefer 200 cortical ROI 17 Network Atlas[7]



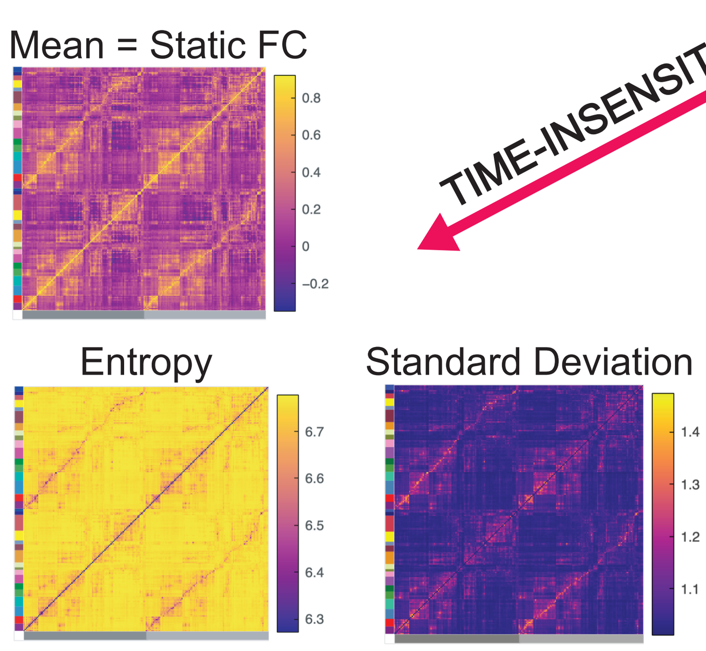


TIME-INSENSITIVE

TIME-SENSITIVE

Calculate multiple summary measures of edge time series for all subjects

- Sample Entropy: conditional property that two windows of size 10 will remain similar, with a shift of 1 TR[8]
- von Neumann Difference: standard deviation of the successive differences of the time series[9]
- Autocorrelation: computed with a lag of 3 TRs (approx. 2s)[8]
- Zero-Crossing: zero-crossing of the autocorrelation function[8]



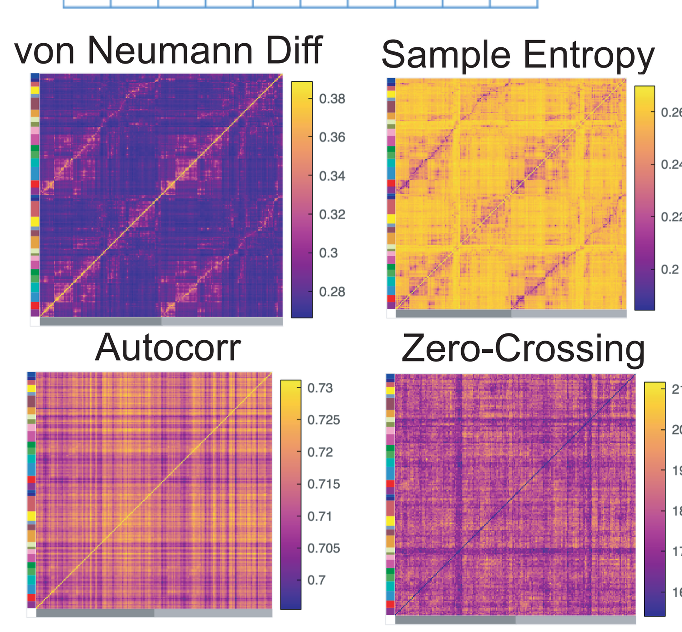


Figure. ROI x ROI matrices each containing a different summary metric of resting-state fMRI edge time series. Each plot shows the average across the dataset. Plots on the left-hand side indicate time-insensitive summary statistics, where as plots on the right-hand side indicate time-sensitive summary statistics.

Feature matrices as input to a brain-behavior modeling framework known as Connectome-Based Predictive Modeling (CPM)[10,11] to predict subject phenotypes

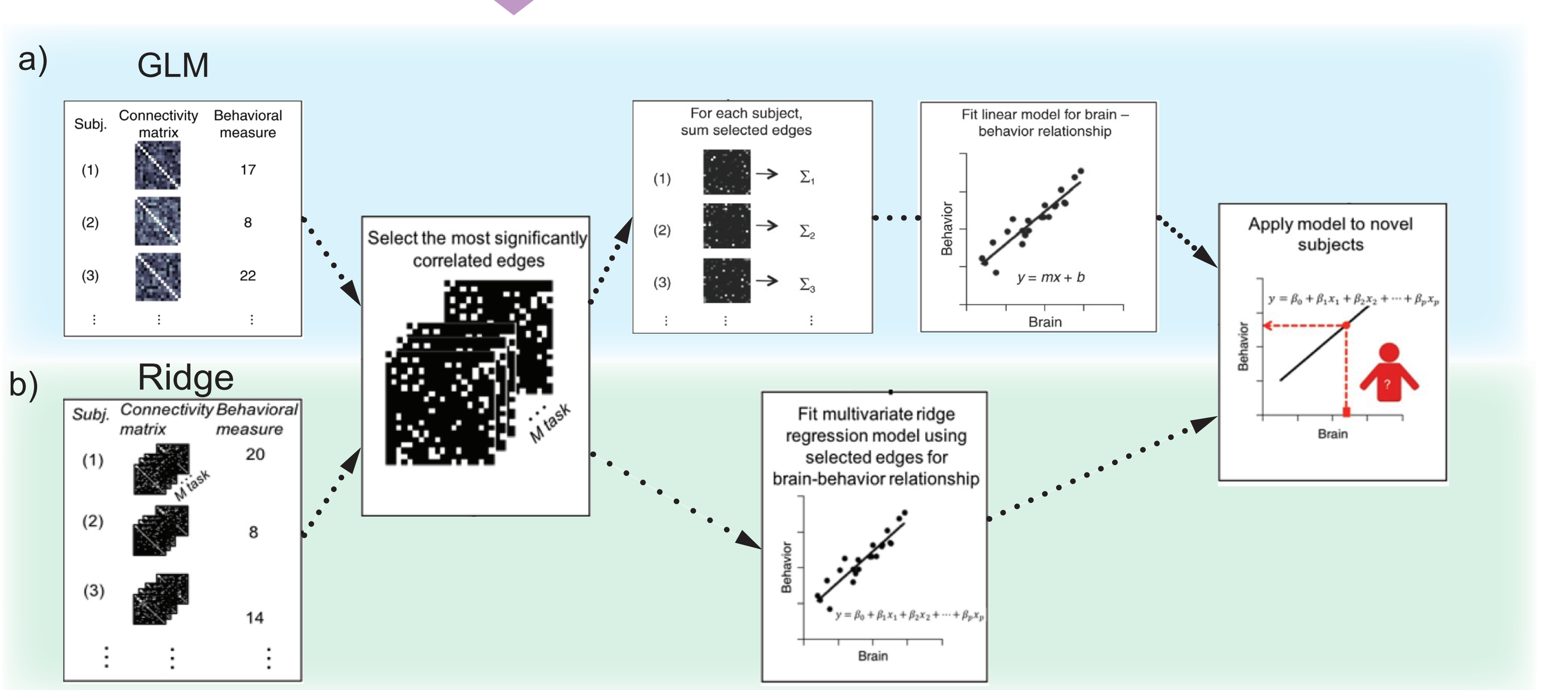
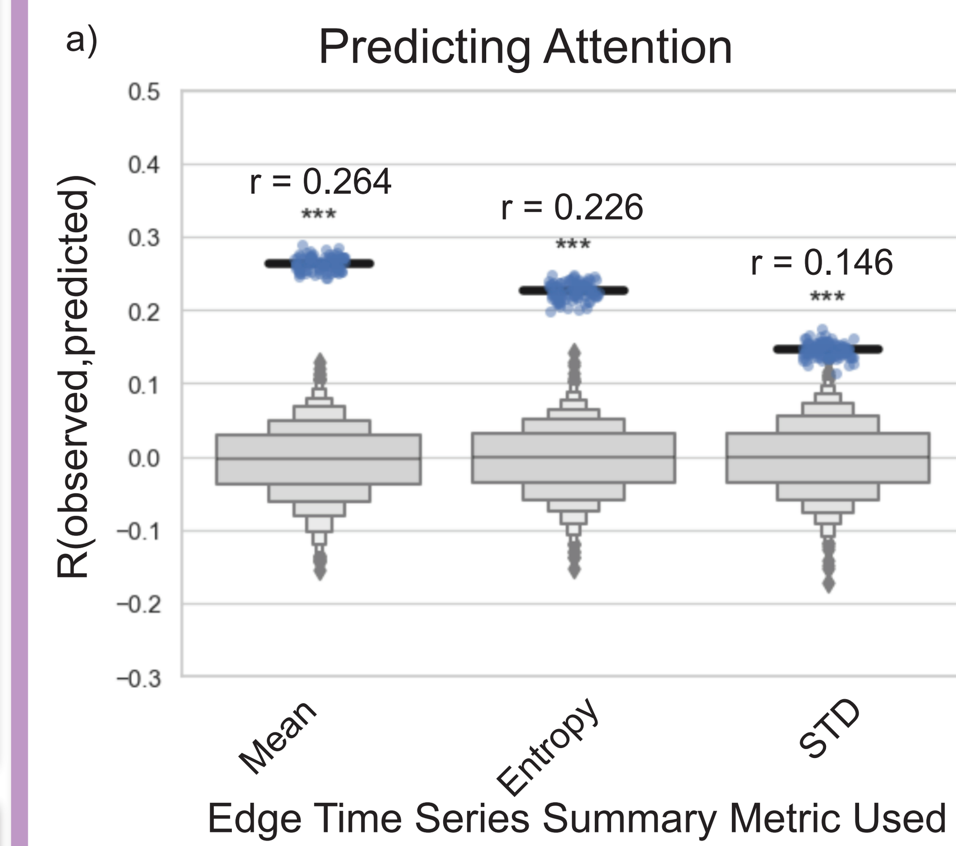


Figure. Description of Connectome-Based Predictive Modeling (CPM) (figure adapted from Shen et al. 2017 & Gao et al. 2019) a) Description of CPM using a general linear model to compute behavioral predictions from one fMRI scan per subject. B) Description of CPM using ridge regression to compute behavioral predictions using multiple representations of fMRI data per subject. Note that shared steps are indicated by being placed in between the blue (panel a) and green (panel b) shaded backgrounds.)

RESULTS



- We used CPM to predict attention and intelligence scores with a 10-fold cross-validation framework using each **time-insensitive** representation of connectivity dynamics and evaluated model accuracy by computing the correlation between the observed and predicted values.
- We were able significantly predict attention and intelligence scores using edge time series mean, entropy, and standard deviation (all permutation-based p-values<0.01)
- **Mean (equal to static FC) consistently performs best.**

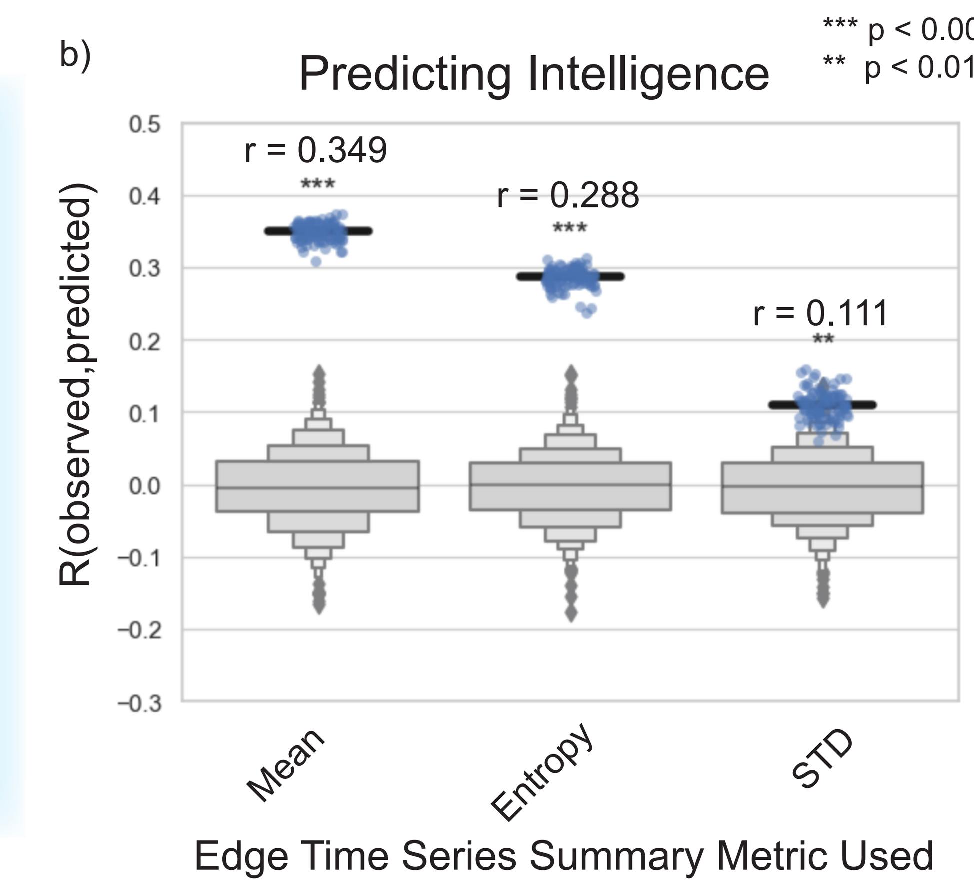


Figure. Connectome-Based Predictive Modeling results for predicting Attention Network Task scores (a) and WASI-II (b) using the edge time series mean, entropy, and standard deviation. Y-axis represents Pearson's R between observed and predicted behavioral values. Blue dots show results of 100 iterations of 10-fold cross-validation using true data, and gray boxen plots show distribution of results from 1,000 iterations using randomized data. Black line represents median accuracy for true models.

- Next, we predicted attention and intelligence using a ridge regression model that included all three **time-insensitive** representations of the data.
- This model performed better than our individual models for attention (r=0.31, p<0.001) and intelligence (r=0.43, p<0.001),
- We found that, across fitting iterations, the model framework repeatedly selected the mean of the edge time series in building these predictions, suggesting that **the mean (or FC) is relatively most predictive.**

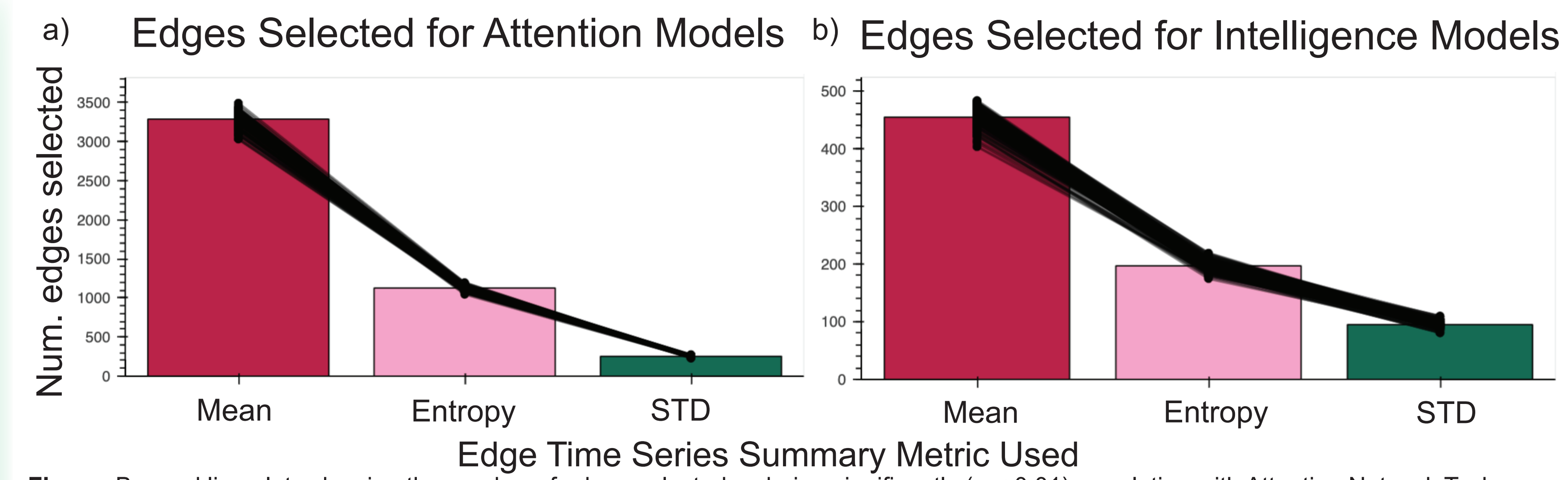
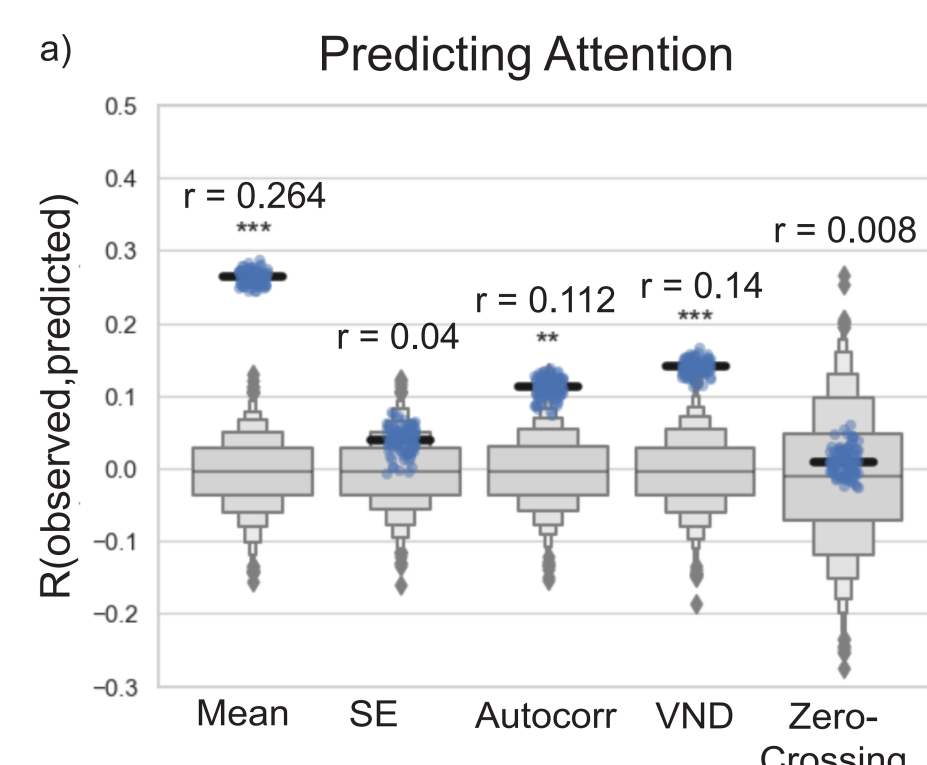


Figure. Bar and line plots showing the number of edges selected as being significantly (p < 0.01) correlation with Attention Network Task scores (a) or WASI-II (b) scores within each metric when all three representations of the data were given to the model at once. Ridge regression was run 100 times. Bars depict the average number of significant edges per summary metric across all iterations, while the lines show the number of edges selected per summary metric in each iteration. Results were consistent across iterations.



- Finally, we computed predictions using several **time-sensitive** summary metrics, including autocorrelation and dynamic entropy.
- **Interestingly, their predictive value proved to be not as significant as that of the mean.**

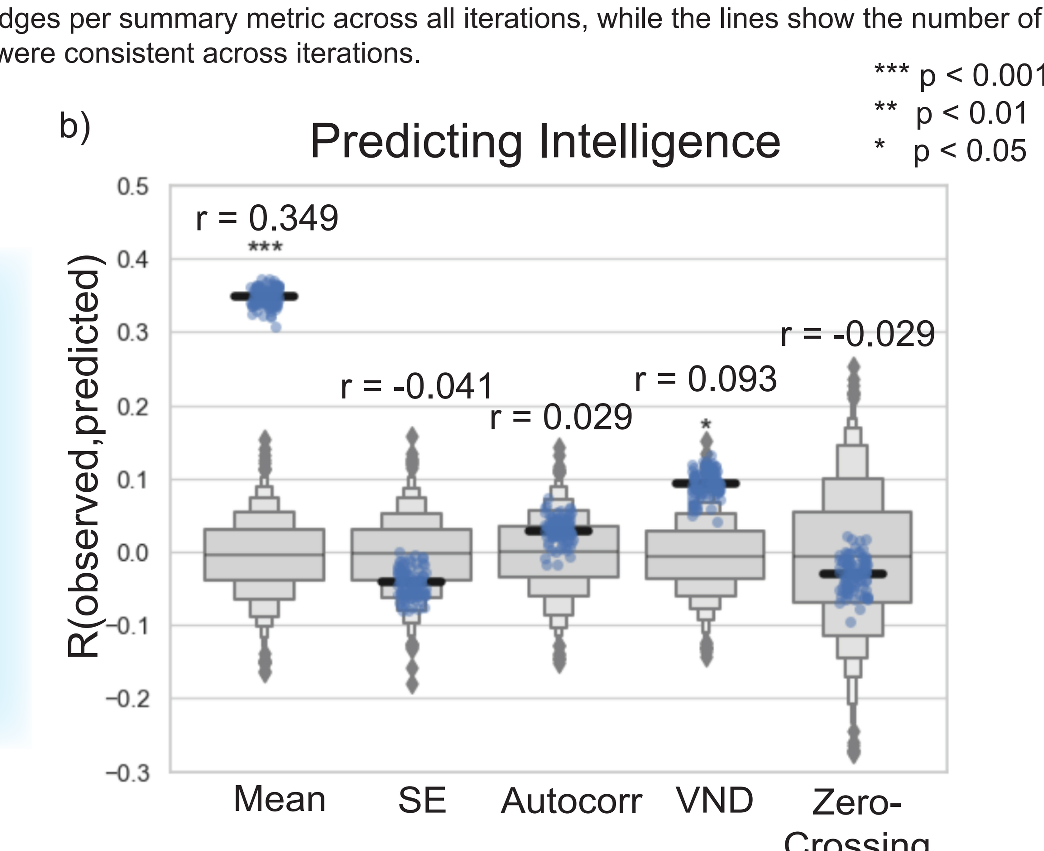


Figure. Connectome-Based Predictive Modeling results for predicting Attention Network Task scores (a) and WASI-II (b) using edge time series mean, sample entropy, autocorrelation, von Neumann difference, and zero-crossing of the autocorrelation function. Y-axis represents Pearson's R between observed and predicted behavioral values. Blue dots show results of 100 iterations of 10-fold cross-validation using true data, and gray boxen plots show distribution of results from 1,000 iterations using randomized data. Black line represents median accuracy for true models.

CONCLUSIONS

- Our results demonstrated that mean co-fluctuation, i.e. functional connectivity, shows predictive power that was unmatched compared to other evaluated statistics.
  - This suggests that **static FC over a 10 minute period may be more predictive of phenotypic traits than the dynamics over this brief period**.
  - These findings are potentially limited by the interaction between preprocessing, such as temporal filtering, and these summary statistics.
- Future work will focus on exploring multivariate combinations of these features, to test whether the performance of static FC can be exceeded.

REFERENCES

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[9] Baracchini 2021
[10] Shen 2017
[11] Gao 2019

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