Hybrid connectome-based predictive modeling reliably predicts individual differences in human intelligence

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Abstract

Individual differences in human intelligence can be modeled and predicted from functional neurobiological connectivity. Many existing predictive methods, however, fail to attend to the higher-order structure and topology of the brain's connectome, and show only moderate performance when generalized to make predictions in new individuals. In this paper, we demonstrate that connectome-based predictive modeling, a common predictive modeling framework for neuroscience data, can be productively modified to incorporate information about brain network topology and individual differences via the inclusion of bagged decision trees and the network based statistic. These modifications produce a hybrid modeling framework capable of leveraging brain network topology and individual differences to generate accurate predictions of intelligence from neuroscience data.

1 Current Approaches for Predicting Individual Differences in General Intelligence

Recent cognitive neuroscience research has begun to turn greater attention to the broad individual differences in functional and neuroanatomical variability that exist between individuals (1). There in an outstanding need for interpretable AI tools that can help address research questions about inter-individual differences in neuroscience data, with important applications to personalizing and optimizing individualized treatments and intervention selections (2). In parallel, there is an emerging need for AI methods capable of generating both scientific explanations and generalizable predictions within a single framework, integrating the tools and perspectives of cognitive neuroscience and computer science together to improve interpretability and replicability of scientific models (3). To establish the efficacy of methods design to address these two parallel needs, we implemented a modified version of connectome-based predictive modeling (CPM) (4; 5), a standard computational approach for predicting behavioral data from neuroscience data.

1.1 Existing Computational Cognitive Neuroscience Approaches for Predicting Intelligence

A central trait underpinning individual differences in human cognitive ability is intelligence (6). While the neurobiological basis of intelligence has long been identified with the function and organization of specific brain networks (7), recent work has begun to establish that that systemwide brain network topology and dynamics are critical sources of the broad individual differences observed in cognitive ability (8).

A diverse set of techniques have been applied to model and predict human intelligence from neuroscience data. Connectome-based predictive modeling (CPM) has previously been deployed to

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predict fluid intelligence scores (4), showing that CPM's predictions could account for 25% of the variance observed across actual fluid intelligence. Other approaches, such as cortical hyperalignment, have accounted for up to 39% of the variance in general intelligence on the basis of single brain region's connectivity, and on average account for 27% of variance in general intelligence when using whole-brain connectivity (9). The efficiency of weakly-connected edges (extracted from windowed functional connectivity) have been used in a correlation framework to account for 37.5% of the variance in IQ (10). Elastic Net models are able to account for 20% of the variance in intelligence, on the basis of distributed network of resting state connections that span the functional connectome (11). Each of these methods has desirable properties—use of strong connections, use of weak connections, native interpretability, predictive accuracy—but none have a specific focus on fitting or personalizing models on the basis of both network topology and individual differences.

Modeling and generating predictions from individual differences in functional connectivity remains an important goal in neuroscience (12), and will require AI techniques that can model individual variability from neuroscience data in an interpretable manner. Here, we investigated the feasibility of modifying CPM to create a hybrid predictive modeling framework that incorporates information about network topology and individual differences. CPM performs well in a variety of contexts and prediction problems (5), and explains training data through a natively interpretable linear model. One previously unremarked feature of CPM is that it ablates brain network topology during feature selection. Further, CPM fits a linear model across the entire training population, and is therefore unable to attend to residual variance and sources of individual differences that exist only within specific subpopulations of data. As neuroscience has established that individual differences in network topology are important for explaining cognitive abilities, we attempted to modify CPM to account for network topology and individual differences.

1.2 Connectome-based Predictive Modeling

We began by deploying standard connectome-based predictive modeling to quantify the baseline variance in general intelligence in our sample accounted for by standard CPM (5). CPM filters brain regions by applying a threshold to the statistical significance of a region's correlation to the behavioral outcome, maximizing the proportion of true positives edges included in the model. These features are then summarized (i.e., added) to create a single value per subject, which train a linear model between aggregate neuroscience data and behavioral outcome. The procedure is performed under cross-validation to generate behavioral predictions for each subject. Our baseline implementation of CPM incorporated edges with both positive and negative relationships to intelligence simultaneously, aggregating edges by sign and then combining those two values to produce a single value per subject.

1.3 Network-Based Statistic

to include information about network topology, we modified CPM's selection step by replacing the mass-univariate feature selection with the network based statistic (NBS) model (13). NBS uses permutation testing to assess the relationship between individual network edges and a behavioral outcome. Unlike the significance-based feature selection deployed by CPM, NBS explicitly considers network topology by selecting edges that meet a significance threshold and form a topologically connected network. Although an isolated functional edge contains information about the BOLD timeseries of two incident regions, the mesoscale and macroscale topology the larger networks cannot be easily inferred or reconstructed from many such aggregated weights. Deploying NBS to perform feature selection allows our hybrid modeling framework to train on features that not only relate significantly to intelligence, but also form a connected network, allowing network topological to influence the feature selection process.

1.4 Bootstrap Aggregation

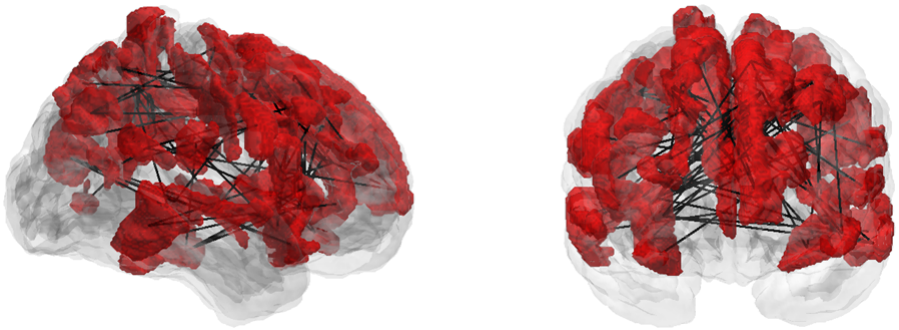
We further modified CPM to attend to individual differences by eliminating the feature summarization step, and instead trained with disaggregated features (topologically connected functional edges) using bagged random forests (14). Bagged random forests have have several desirable properties, including a low number of model parameters and resistance to overfitting in the training population (as individual trees are uncorrelated). Ensemble learning methods can of course have very different aims and predictive performance compared to statistical regression, and our intention is not to directly

compare the two. Here, we selected bagged random forests for two reasons. First, disaggregating edge strengths avoids information about network topology, which may represent a new source of individual difference variability between subjects. Bagged random forests are capable of training on these individual edges while still producing a regression output. Second, each tree is bootstrapped by oversampling from a subpopulation in the data (ie, bootstrap resampling), allowing for an ensemble of models that are trained (and overfit) with variability unique to subpopulation of individuals. The resulting decision trees do not model variability common to the whole sample, but instead will overfit to variance unique to the bootstrap replicate, characterizing sources of individual difference unique to that subpopulation. In turn, aggregating the predictions of many decision trees can lead to good performance when attempting generalize from highly variable data (such as functional connectivity data, see (15)).

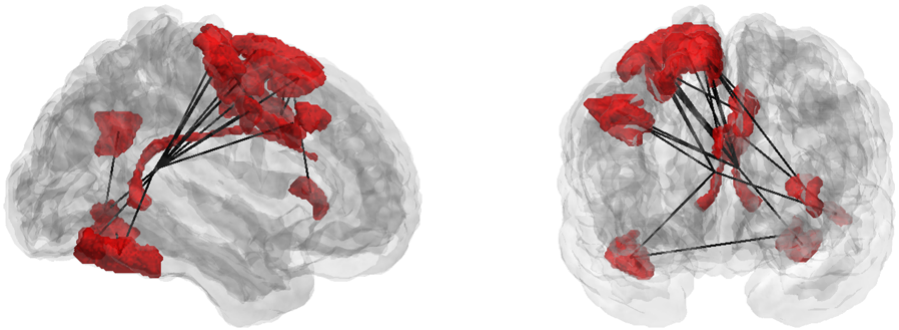
1.5 Data Acquisition

We acquired a large ($N = 297$) dataset of 10-minute resting state EPI scans using 3 Tesla MRI, and processed them using reproducible methods for analysis of neuroimaging data (via ICA-AROMA denoising (16) through FMRIPREP (17) and xcpEngine (18)). Diffusion tensor imaging data was also acquired in $N = 288$ subjects on the half-shell and processed using FSL's FDT and bedpostx for probabalistic diffusion tensor tractography (19). Imaging data were parcellated using a multimodal 360-region atlas of cortical grey matter (20). Additionally, we administered a comprehensive battery of neuropsychological tests and deployed structural equation modeling to assess individual differences in general intelligence. Using these data elements, we investigated the application of our hybrid CPM method to predict and explain individual differences in intelligence.

1.6 Results and Discussion

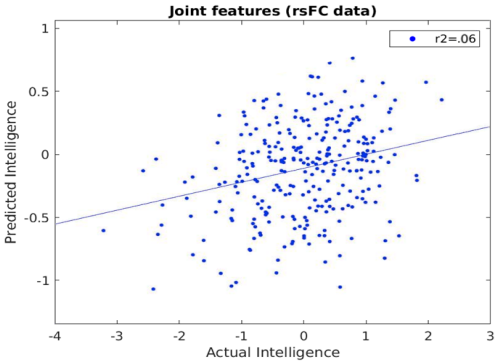


(a) NBS identifies a network of weak connections from resting state connectivity data at $t < -3.5$ and $p < .01$ (finding that functional edge strength was inversely related with intelligence).

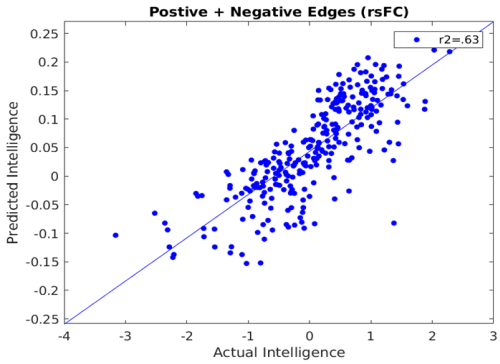


(b) NBS identifies a network of dense structural connections from diffusion tensor tractography that are positively associated with intelligence at $t > 3.5$ and $p < .01$.

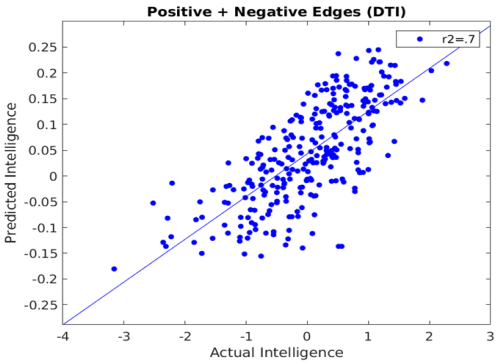
Figure 1: Network-Based Statistic feature selection in functional (a) and structural (b) connectivity data.



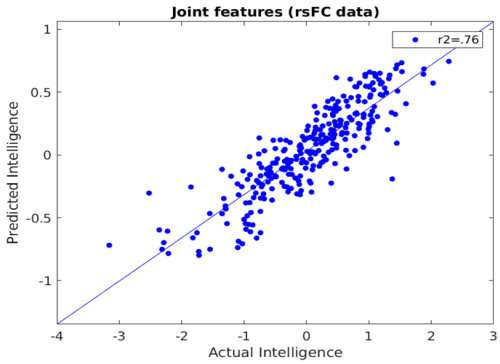
(a) Connectome-based predictive modeling results predict intelligence at $r = 0.26$ and $p = .02$.



(b) Hybrid CPM using resting state connectivity predicts intelligence at $r = 0.79$ and $p < .01$.



(c) Hybrid CPM using structural connectivity predicts intelligence at $r = 0.84$ and $p < .01$.



(d) Hybrid CPM with multimodal selection predicts intelligence at $r = 0.87$ and $p < .01$.

Figure 2: Predictive model performance for CPM (a) and hybrid CPM (b,c,d).

The Network-Based Statistic identified both a functional and structural connectivity network that were reliably associated with general intelligence (fig. 1). Data from both networks produced reliable N-fold predictions of intelligence when combined with bagged random forests, each accounting for 63–70% of the variance between subjects (figs. 2b and 2c . Out of bag prediction error stabilized after about 1,000 training epochs. For both models, predictions were about an order of magnitude smaller than the ground truth data. This may be due in part to the sign consistency of feature-selected edges—all edges had a positive sign, and all shared either a positive (DTI) or inverse (fMRI) relationship with intelligence. T-thresholds were selected to retain a similar number of edges as in standard CPM.

CPM predictive accuracy (fig. 2a) was notably lower for this dataset than in previous reports (4), possibly explained by the smaller sample size, a more robust motion artifact removal (21), and a broader set of cognitive operations entailed by our dependent variable g. Hybrid CPM accounted for notably more variance than standard CPM, though the range of intelligence predicted was narrow.

Standard CPM considered edges both positively and inversely associated with intelligence, unlike the sign-consistent networks identified by hybrid CPM from DTI and fMRI data. To induce this property in hybrid CPM, we feature selected the union of network edges identified from fMRI and DTI data (fig. 2d). This multimodal selection retained weak functional connections inversely associated with intelligence, and added functional edges for which underlying white matter connectivity was positively associated with intelligence. Incorporating both strong and weak functional edges improved prediction accuracy and spread, accounting for 76% of the variance in intelligence. These results demonstrate that hybrid CPM can be trained with multimodal neuroimaging data and generate predictions of intelligence that outperform established methods from the literature. Comparative results from hybrid CPM suggest that both strong and weak functional edges contain predictive signals. Future work using Shapley values to understand individual differences in feature importance is planned, to more precisely interpret these directional relationships. The present findings advance our scientific understanding of the network architecture underlying intelligence and highlight the importance of incorporating network topology into the study of individual differences in cognition.

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