Connectome Fingerprinting Predicts Prefrontal Cortical Activation During Abstract Reasoning

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Abstract:

A key goal of cognitive neuroscience is to understand meaningful differences in brain activity and how this activity maps onto human behavior. Functional Magnetic Resonance Imaging (fMRI) can be used to non-invasively assess human cognition, but it is vulnerable to the blurring of individual differences due to group averaging. Connectome Fingerprinting (CF) is a machine learning technique that uses resting-state brain connectivity profiles to make predictions about individual brain activity patterns. This is useful in brain areas including the prefrontal cortex (PFC), where activity patterns are highly variable across individuals. In this study, we used ridge-regression CF to predict activation in the lateral PFC during an abstract reasoning task. Our results demonstrate that CF is better able to predict individually specific activation patterns compared to the group average. Additionally, the results suggest that model accuracy is influenced by within-participant activation variability. In summary, our study used CF to predict task-evoked activation in the lateral PFC at the individual participant level during an abstract reasoning task. The results showed that CF results in a more accurate prediction of individual brain activity compared to the group average.

Keywords: connectome; ridge-regression; fMRI; machine learning

Introduction

When studying complex cognitive tasks, functional Magnetic Resonance Imaging (fMRI) results in weak and variable individual patterns of brain activity. Group averaging is commonly used to improve the statistical reliability of the signal; however, this technique blurs meaningful individual differences and the fine-scale organization of brain networks (Amunts et al., 2000; Braga & Buckner, 2017). This is particularly problematic in the prefrontal cortex (PFC), a hub for higher-order cognition with known structural (Rajkowska & Goldman-Rakic, 1995) and functional variability (Mueller et al., 2013).

Connectome Fingerprinting (CF) is a machine learning approach that uses the resting-state functional connectivity profile of an individual to predict information about their brain function during a task. CF has been successfully employed during tasks of sustained attention, sensory perception, and working memory (Osher et al., 2019; Tobyne et al., 2018; Tripathi & Somers, 2023). To our knowledge, the use of CF during a higher-order cognitive task such as abstract reasoning has not been evaluated.

Here, we used CF on resting-state functional connectomes to predict individual brain activity patterns in the lateral PFC during abstract reasoning, a goal-oriented process whereby previously learned contextual information is applied in novel situations. We hypothesized that this model would be more accurate than the group average, a key step in a more precise understanding of higher-order cognition at the individual level. Further, we investigated individual-level variability in task activation and its role in model performance.

Methods

Experimental Design & Data Acquisition

We re-analyzed a dataset of 23 healthy participants acquired from Boston University and the greater Boston Area (Morin et al., 2023). All participants were scanned in a 3 Tesla Siemens MAGNETOM Prisma scanner during both resting-state and task-state using a simplified version of the Ravens Progressive Matrices Task (Raven, 1941). Details on task design, data acquisition, and processing metrics can be found in Morin et al., 2023.

Search Space Selection & Model Analysis

Our previous study found lateral PFC activation within the boundaries of the canonical cognitive control network (CCN) (Morin et al., 2023). Here, we created a search space using the Schaefer 400-parcellation of the lateral PFC within the CCN on the cortical surface of the brain (Yeo et al., 2011; Schaefer et al., 2018). The search space consisted of 6,110 & 10,945 vertices in the left and right hemispheres, respectively. For each participant, whole-brain functional connectomes were constructed by taking the Pearson's correlation coefficient between all 400 parcels in the atlas (minus the search space) and each search space vertex.

Consistent with previous research (Osher et al., 2019; Tobyne et al., 2018), we employed a leave-one-out cross-validation ridge regression based on standard multiple linear regression assumptions (Hastie et al., 2009). This process involved two parallel steps: an outer-loop and a nested inner-loop. In each iteration, one participant was left out of the outer loop for testing, while another was left out of the nested inner loop for validation. The model was then trained on the task-evoked activation data of n-2 participants using their concatenated functional connectomes. A grid-search strategy was applied to evaluate 100 hyperparameter values (10^0 to 10^7), whereby the model with the lowest mean squared error was selected. The optimal hyperparameter for each validation participant (n-1) was averaged and applied to the test participant in the outer loop. This was repeated n times. Model accuracies were compared to a leave-one-out group-average computed on the concatenation of the lower-level GLMs via a paired two-tailed t-test.

As individual patterns of brain activity are inherently variable, we tested measures relating to model accuracy in two ways. First, we took the absolute value of all individual task activations subtracted from the group average and correlated them with model accuracies. Next, we split individual scan runs into halves (runs 1-6 & 7-12) for each participant, correlated task activation between halves, and correlated these coefficients with model accuracy (Tripathi & Somers, 2023).

Results

CF Model Accuracy

We used a whole-brain ridge regression model to predict individual brain activity during abstract reasoning. We found moderately accurate CF predictions in both hemispheres (left: R=0.37, right: R=0.45) that were significantly more accurate than the group average (left: R=0.30, right: R=0.38) (left: t(22)=2.11, p=0.04*, right: t(22)=2.56, p=0.017*)[1]. Examples of 3 participant's lower-level task activations, their model prediction activations, and the group averages are shown in Figure 1.

Participant Variability & Model Accuracy

We next assessed how variability within an individual participant might be related to model performance. In both hemispheres we saw an overall trend where larger participant deviations from the group average were related to lower model accuracies (right: R=-0.49, p=0.016*, left=R=-0.33, p=0.1), significantly so in the right hemisphere. We then found that in both hemispheres, as a participant's split-run task reliability increased, the model accuracies increased as well (left: R=0.55, p=0.0062, right: R=0.7, p=0.0002). Combined, these results suggest that participant variability influenced model accuracy. Results of this analysis are shown in Figure 2.

Figures

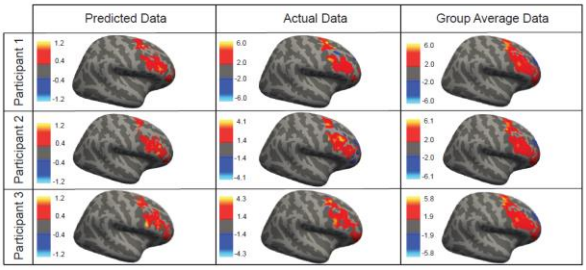

Figure 1. Activation values showing z-statistics within the search space from 3 example participants (left: CF model, middle: lower-level GLM, right: group average).

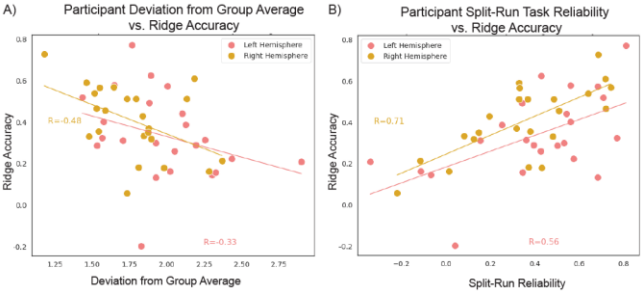

Figure 2. Correlation plots showing the relationship between model accuracy and A) an individual's deviation from the group average, and B) split-run task activation reliability.

Discussion

Our study used CF to predict task-evoked activation in the lateral PFC at the individual participant level during an abstract reasoning task. The results demonstrate that CF results in a more accurate prediction of individual brain activity compared to the group average. Although our accuracy values were moderate in comparison to previous CF work, it is worth noting that these previous studies employed directed attention tasks that elicit strong individual-level activation patterns (Osher et al., 2019; Tobyne et al., 2018). We emphasize that the current study combined CF methods with a higher-order cognitive task and focused on the PFC. Further, we found that our CF model performance was limited by both the reliability of an individual's task activation across runs, and their deviation from the group average. These findings suggest that to improve model predictions, specifically for tasks that elicit more variable activity patterns, training sets based on larger datasets from more heterogeneous samples could be useful.

The results also have relevance for individualized precision medicine. Despite the growing popularity of fMRI in research-based and clinical applications, the acquisition of the data is associated with substantial costs (Mumford & Nichols, 2008) and is not feasible for many patient populations (Specht et al., 2020; Turner et al., 2018). Our results suggest that ridge regression-based CF is better able to predict individual activity patterns than the group average during higher-order cognitive tasks, in our case abstract reasoning. Importantly, this finding emphasizes the ability to look at individual participant activity patterns in smaller sample sizes without excessive amounts of data, facilitating the use of neuroimaging in precision medicine.

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