Predicting individual inhibitory control cognitive function based on multimodal connectomes

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ABSTRACT

This study investigates the potential application of multimodal connectome techniques in predicting individual inhibitory control abilities. Utilizing comprehensive datasets from the UCLA Consortium for Neuropsychiatric Phenomics, which include both structural and functional connectivity data, this research aims to determine whether individual differences in inhibitory control cognitive functions are attributable to variations in these connectomes and whether the spatial distributions of different modalities of connectomes overlap. Inhibitory control abilities were measured using a computerized Stroop task, and whole-brain structural and functional connectomes were constructed by integrating resting-state functional magnetic resonance imaging (rs-fMRI) and diffusion tensor imaging (DTI). By employing Connectome-based Predictive Modeling (CPM) and leave-one-out cross-validation linear regression models, this study seeks to analyze the relationship between brain connectomes and inhibitory control performance.

The results demonstrate that models based on either structural or functional connectomes can effectively predict individual inhibitory control abilities. Functional connectomes showed higher correlations in predicting positive networks, whereas structural connectomes exhibited stronger correlations in predicting negative networks. These findings highlight the critical role of brain structural and functional networks in supporting cognitive control and suggest distinct mechanisms of different networks in cognitive tasks. This study establishes the significant application value of multimodal connectome techniques in precisely predicting individual cognitive functions, providing an innovative research approach for the field of cognitive neuroscience. Although current findings require further validation and expansion, this work lays a solid foundation for utilizing connectome techniques to deeply understand and predict complex cognitive functions, opening new avenues for future clinical and scientific research.

Keywords: inhibitory control, machine learning, connectome, multimodal neuroimaging

1. INTRODUCTION

In modern cognitive neuroscience, a key challenge is comprehending the complex interactions between brain structure and function and applying this knowledge to predict and enhance cognitive functions. Inhibitory control, a fundamental cognitive process, plays a central role in daily decision-making, emotional regulation, and various psychiatric disorders [1]. Research on inhibitory control aids in understanding how the brain manages external information interference and provides a theoretical foundation for treating conditions such as Attention Deficit Hyperactivity Disorder (ADHD) and Obsessive-Compulsive Disorder (OCD) [2]. Therefore, developing models that accurately predict inhibitory control abilities is crucial for mental health and the prevention and intervention of psychiatric disorders.

In recent years, with advancements in neuroimaging technologies and the application of big data, researchers have begun to utilize multimodal connectomes, which include both structural and functional connectivity data, to explore how brain networks support complex cognitive functions. Multimodal connectome analysis integrates data from various imaging techniques, providing a comprehensive method to observe brain network interactions [3]. This approach helps reveal how the brain adjusts its activity patterns across different tasks and states to meet environmental demands [4].

In the study of inhibitory control, the Stroop task is a widely used behavioral test. It assesses inhibitory control by requiring participants to suppress their natural responses to interfering information [5]. This study leverages a rich dataset from the UCLA Consortium for Neuropsychiatric Phenomics, which includes neuroimaging, assessment, and

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clinical information [1]. The computerized Stroop task was employed to measure participants' inhibitory control abilities. Furthermore, connectome analysis was used to predict these abilities [6].

The core hypothesis of this study is to explore whether individual differences in inhibitory control cognitive functions stem from variations in functional or structural connectomes and whether the spatial distribution patterns of different modalities of connectomes overlap. The application of connectome techniques extends beyond depicting the brain's static structure; more importantly, it captures the brain's dynamic functional changes under different cognitive states [7]. By integrating resting-state functional magnetic resonance imaging (rs-fMRI) and diffusion tensor imaging (DTI), this study constructed whole-brain structural and functional connectomes. Using Connectome-based Predictive Modeling (CPM) and leave-one-out cross-validation linear regression models, this study analyzed the relationship between brain connectomes and inhibitory control performance. CPM involves selecting neural connections significantly related to behavioral performance and using linear regression models with leave-one-out cross-validation to aggregate features, train, and predict individual behaviors [8].

In validation analyses, this study employed permutation tests to verify the stability and reproducibility of the predictive models, ensuring the reliability of the findings [9]. Additionally, by comparing the predictive capabilities of functional and structural connectome models, this study revealed differences between the two types of connectomes in predicting inhibitory control abilities. This provides a crucial perspective for further understanding how structural and functional networks support cognitive control [10].

2. METHODS

2.1 Participants

This study relies on datasets provided by the UCLA Consortium for Neuropsychiatric Phenomics, which encompass a broad sample of both healthy individuals and patients with psychiatric disorders. These datasets include neuroimaging, assessment, and clinical information [1]. From the dataset, 130 healthy control subjects were selected. After excluding 28 subjects due to data issues or excessive head movement, a total of 102 participants were included in the modeling analysis. The demographic variables and behavioral data of the participants are summarized in Table 1.

Table 1. Demographic and behavioral descriptive statistics of participants included in CPM analysis.

	ADHD (N=40)	BD (N=49)	HC (N=122)	SZ (N=48)
gender				
Mean（SD）	1.48（0.506）	1.43（0.500）	1.47（0.501）	1.25（0.438）
Median [Min, Max]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]
age				
Mean（SD）	32.1（10.4）	35.3（9.03）	31.6（8.81）	36.2（8.90）
Median [Min, Max]	28.0 [21.0, 50.0]	36.0 [21.0, 50.0]	28.5 [21.0, 50.0]	37.5 [22.0, 49.0]
school_yrs				
Mean（SD）	14.7（1.81）	14.6（1.96）	15.1（1.65）	12.6（1.78）
Median [Min, Max]	14.5 [12.0, 19.0]	14.0 [11.0, 19.0]	16.0 [10.0, 19.0]	12.0 [9.00, 16.0]
scwt_conflicct_rt_effect				
Mean（SD）	142（79.3）	130（54.3）	123（70.7）	130（71.1）
Median [Min, Max]	135 [48.3, 392]	124 [19.2, 292]	114 [3.84, 330]	119 [-25.0, 290]

2.2 Stroop color word task

This study utilized a computerized version of the Stroop task to measure inhibitory control abilities [5]. Participants were required to respond based on the color of the words rather than the text itself. The task comprised two conditions: congruent, where the color and the word matched, and incongruent, where the color and the word did not match. Inhibitory control was assessed by comparing reaction times across these two conditions. The task included 152 trials, with 54 incongruent and 98 congruent trials. The Stroop effect, calculated as the difference in reaction times between incongruent and congruent conditions, was used as an index of individual inhibitory control ability.

2.3 MRI data acquisition and preprocessing

The MRI data used in this study were sourced from the UCLA Consortium for Neuropsychiatric Phenomics dataset and acquired using two 3T Siemens Trio scanners (Erlangen, Germany). The preprocessing of resting-state functional MRI (rs-fMRI) data was conducted using the automated processing pipeline fMRIprep (version 23.1.1). The preprocessing of Diffusion Tensor Imaging (DTI) data, along with fiber tracking and the construction of structural connectivity matrices, was performed using MRtrix3 software (https://www.mrtrix.org/).

2.4 Data analysis

All data analyses were performed using R (version 4.3.0) and MATLAB (version R2020b).

2.4.1 Construction of whole-brain functional and structural connectomes

This study utilized the Shen-268 atlas and the AAL-116 atlas to construct functional and structural connectomes, respectively. The rs-fMRI and DTI data were processed using Pearson correlation, partial correlation, tangent correlation methods, and the tck2connectome function to generate connectivity matrices. To eliminate confounding variables and prevent overfitting, preprocessing controls and the tcksift2 algorithm were employed for optimization [8]. Based on behavioral relevance, the connectomes were ultimately categorized into positive, negative, and overall networks for predictive model construction. The construction process of the whole-brain connectomes is illustrated in Figure 1(A).

2.4.2 Construction of predictive models based on whole-brain functional and structural connectomes

The CPM approach is employed to predict individual behavior by analyzing the relationship between brain connectomes and behavioral performance [6]. This process involves three main steps:

1. Feature Selection: Identify neural connections significantly correlated with behavioral variables using Pearson correlation.

2. Model Training and Prediction: Aggregate these features and train the model using leave-one-out cross-validation linear regression to predict behavior.

3. Performance Evaluation: Assess the predictive performance of the model using Spearman correlation coefficients and root mean square error (RMSE).

The detailed analysis workflow of the CPM process is illustrated in Figure 1(B).

2.4.3 Identification of connectome feature weights

CPM models determine the structural and functional networks associated with executive functions based on optimal thresholds, incorporating connections identified through leave-one-out cross-validation [9]. Using BioImage Suite software, brain nodes are divided into ten networks, and the proportion of connections within each network is analyzed in both structural and functional models, controlling for the total number of connections. The proportion and weight of each network in executive functions are calculated to compare the spatial distribution patterns of structural and functional networks.

2.4.4 Validation analysis

To evaluate the stability and reproducibility of the predictive models, permutation tests were conducted on the best predictive models for the four connectomes across the three subtasks. This involved randomly shuffling the relationship between behavioral variables and connectome features and repeating the CPM modeling 10,000 times to verify the significance of the predictive performance. A permutation test p-value below 0.05 was considered statistically significant.

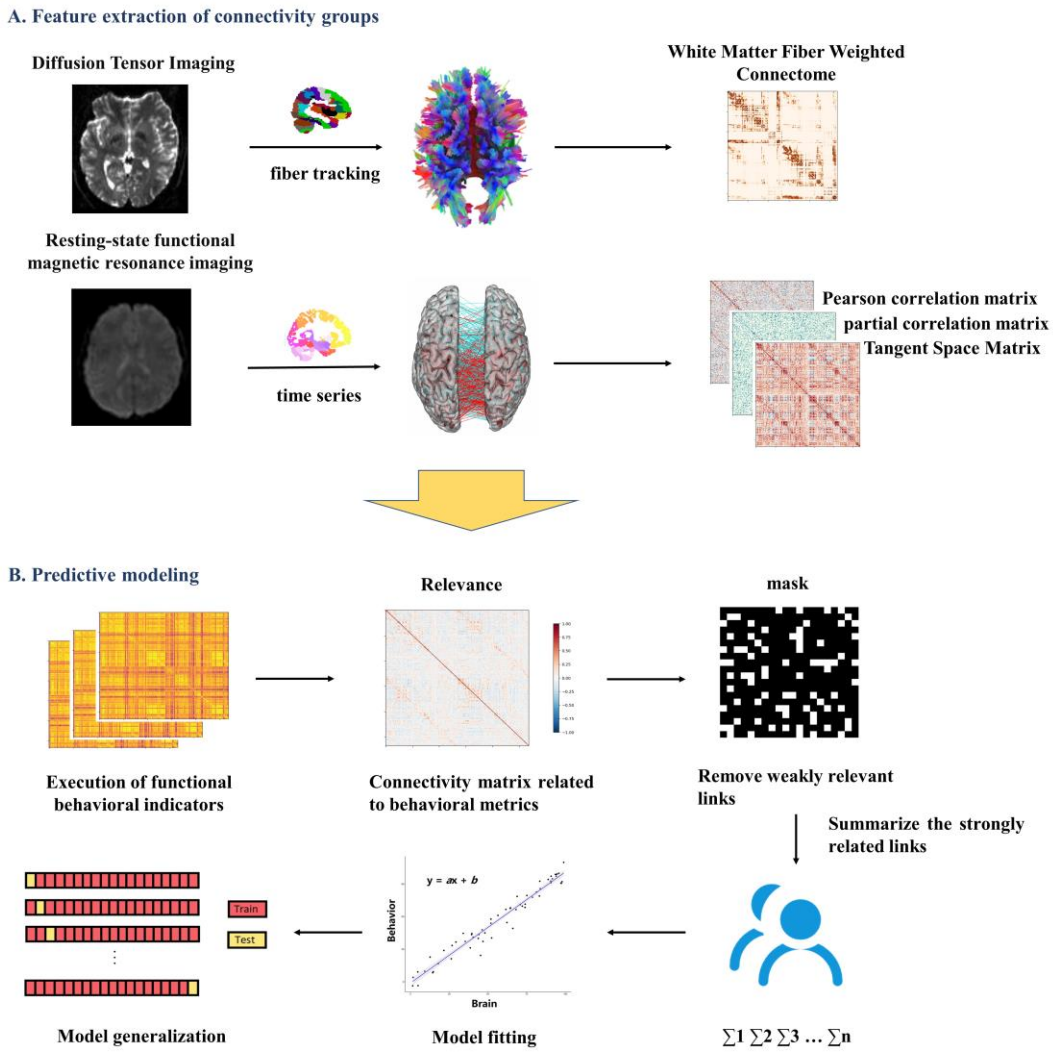

Figure 1. CPM predictive analysis workflow.

3. RESULTS

3.1 Descriptive statistics

A one-way ANOVA was conducted to compare the Stroop effect across different groups. As shown in Figure 2, the main effect of group was not significant, $F(3, 255) = 0.792$, $p = 0.499$, $\eta^2 p = 0.009$. No significant differences in inhibitory control were found between the groups.

3.2 Model performance

The analysis revealed that predictive models constructed using structural and functional connectomes have significant predictive capabilities for individual inhibitory control performance. As shown in Figure 2, the predictive model based on structural connectomes demonstrated a moderate positive correlation within the whole-brain network ($r = 0.30$, $p < 0.001$), a weaker positive correlation within the positive network ($r = 0.19$, $p = 0.004$), and a stronger positive correlation within the negative network ($r = 0.29$, $p < 0.001$). In contrast, the predictive model based on functional connectomes showed a higher correlation within the whole-brain network ($r = 0.33$, $p < 0.001$), a significantly enhanced correlation within the positive network ($r = 0.43$, $p < 0.001$), and a non-significant correlation within the negative network ($r = -0.03$, $p = 0.60$).

Figure 2 illustrates the predictive efficacy of the validated CPM models across various executive function metrics. Notably, the predictive performance of different components ranged from -0.03 (negative network model of the functional connectome) to 0.43 (positive network model of the functional connectome). The functional connectome-based predictive model (FC-CPM) exhibited a significant overall network correlation with observed inhibitory control abilities (r = 0.33, p < 0.001), as shown in Figure 2(a), and demonstrated a stronger correlation within the positive network (r = 0.43, p < 0.001), as shown in Figure 2(c). Similarly, the structural connectome-based CPM (SC-CPM) showed a significant overall network correlation (r = 0.30, p < 0.001), as depicted in Figure 2(b), a weaker positive network correlation (r = 0.19, p = 0.004), as seen in Figure 2(d), and a stronger negative network correlation (r = 0.29, p < 0.001), as illustrated in Figure 2(f). Overall, these findings validate the significant predictive capability of both SC-CPM and FC-CPM models for inhibitory control cognitive performance, confirming the robustness of using connectome-based approaches to establish relationships between brain and behavior.

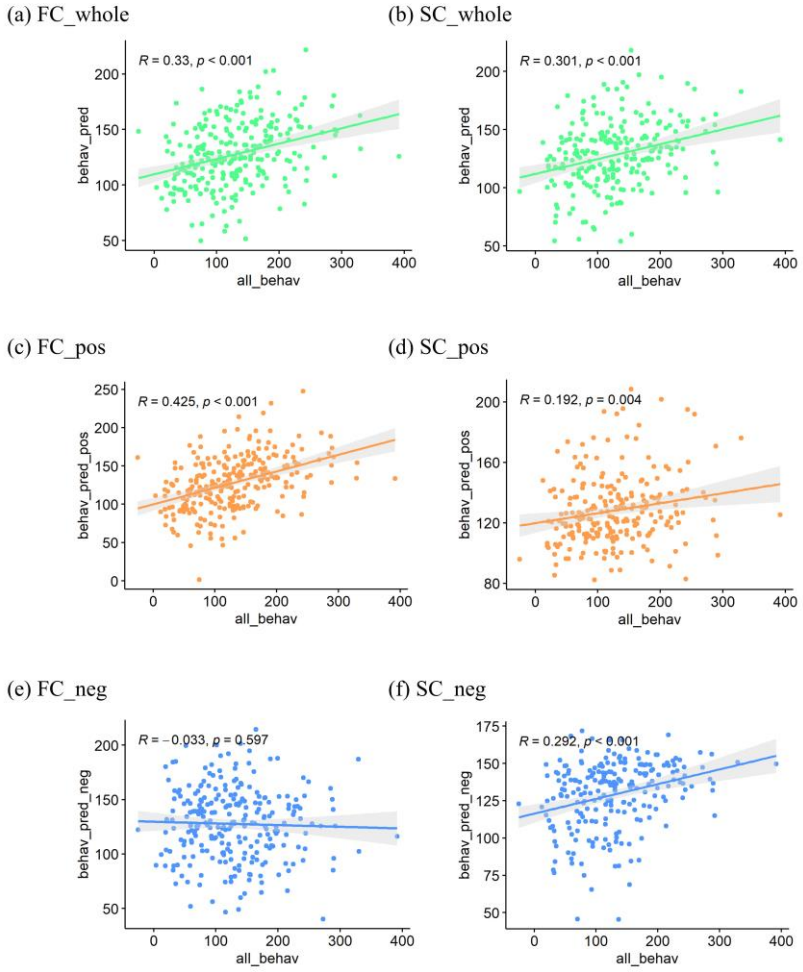

Figure 2. Predictive results of different connectomes for inhibitory control cognitive function.

3.3 Network anatomy

To accurately predict variations in inhibitory control cognitive function and identify the critical brain network characteristics contributing to this prediction, we employed a cross-validation method. In each iteration, the neural connections with the highest contribution to the model were selected and referred to as key connections. As shown in Figures 3(a) and 3(b), in the predictive model constructed using the functional connectome (FC), 30 connections significantly contributed to the positive network for inhibitory control, while 15 connections significantly contributed to the negative network. These connections were consistently retained across all iterations. Similarly, as shown in Figures

3(c) and 3(d), in the predictive model constructed using the structural connectome (SC), 52 connections significantly contributed to the positive network for inhibitory control, while 7 connections significantly contributed to the negative network. These connections were also consistently selected throughout the iterations.

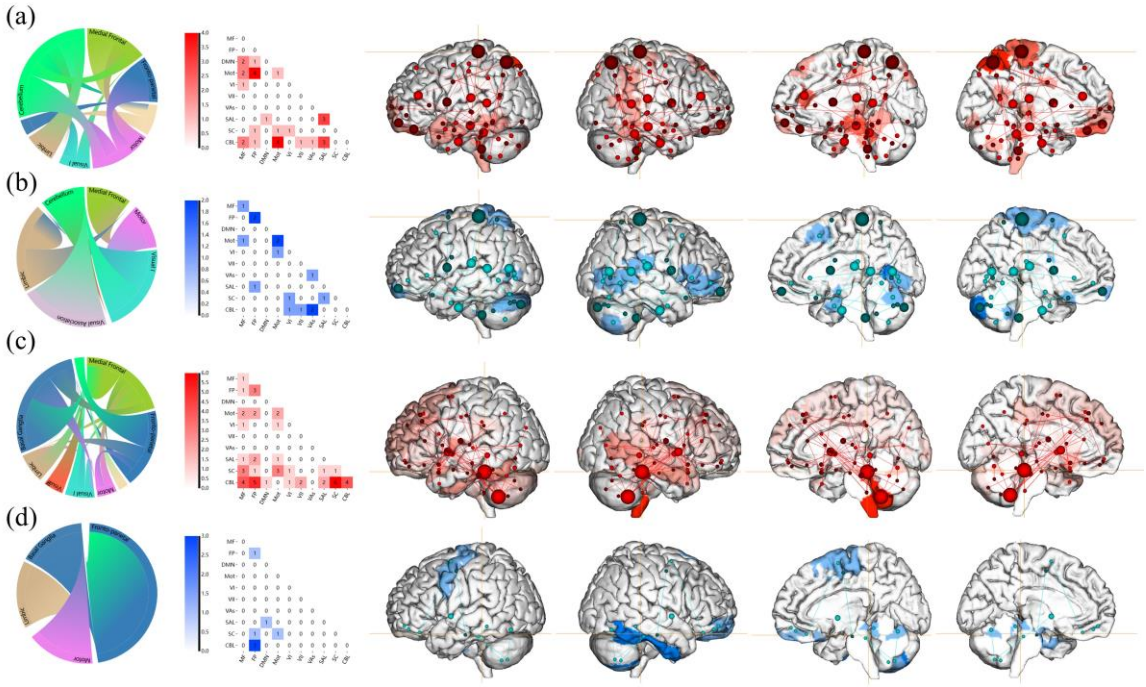

Figure 3. Network anatomy of the predictive model.

4. DISCUSSION

In this study, we explored the feasibility of using multimodal connectome techniques to predict inhibitory control abilities. The results indicate that predictive models constructed from both structural and functional connectomes can effectively predict cognitive performance related to inhibitory control, highlighting the critical role of connectome data in understanding the processes underlying cognitive control.

The findings underscore the key roles of structural and functional network features in inhibitory control, suggesting that these networks can serve as effective biomarkers for predicting individual differences in behavior. Notably, while the negative network in the functional connectome model did not show significant predictive correlation (r = -0.03), the negative network in the structural connectome model exhibited a strong correlation (r = 0.29). This discrepancy reflects the potentially different mechanisms through which structural and functional networks contribute to cognitive control and how they might complement each other in various cognitive tasks.

This study demonstrates the significant potential of applying multimodal connectome techniques to predict individual cognitive functions. By integrating structural and functional information, we can more deeply characterize the brain's complex networks, providing more precise predictive tools for clinical and cognitive neuroscience research. However, the study also reveals areas for model improvement. Future research should consider a broader range of cognitive functions and employ more refined network analyses to enhance the accuracy and explanatory power of predictive models.

5. CONCLUSION

This study investigated the capability of utilizing multimodal connectome techniques to predict performance on inhibitory control tasks. The findings indicate that models constructed from both structural and functional brain connectivity data can effectively predict inhibitory control abilities. Among these, functional connectome models

exhibited higher correlations in predicting positive networks. However, the functional connectome models did not show significant correlations in predicting negative networks, suggesting that the mechanisms through which brain networks contribute to different cognitive tasks may vary.

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