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Multi-Bands Joint Graph Convolution EEG Functional Connectivity Network for Predicting Mental Disorders

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ABSTRACT

As a typical representative of mental disorders, anxiety and depression disorders have occupied a large number of people after the outbreak of the new crown epidemic. However, anxiety and depressive disorders are detected by screening with clinical scales, potentially undermining the efficacy of detecting mental disorders, as it is heavily contingent upon the personal condition of the individual participant and the expertise of diagnosing physician. Therefore, to predict the feasibility of individual-level mental disorders, we developed a multi-bands joint graph convolution network (MBJ-GCN) framework based on electroencephalogram (EEG) brain functional connectivity (FC) networks. The functional connectivity networks are fused with orthogonal power envelopes correlation across five different frequency bands. Furthermore, the five frequency bands of brain FC networks were then integrated using locally weighted clustering coefficients (LWCC), which were then combined into feature vectors to represent the vertexes. After that, we design parallel GCN layers with different inputs via random embeddings, which can recognize intrinsic mental disorder maps from the embeddings in GCNs. Finally, we concatenate the outputs of all GCN layers in the fully connected layer for prediction. The experimental results have shown that our proposed method has low mean absolute error (MAE) and high Pearson correlation coefficient (PCC) performance compared with other prediction methods. It is possible to represent both individual characteristics and clinical information of potential patients using the proposed method. In conclusion, we extend traditional scale interviews to FC-based individual predictions, thereby taking a step towards the development of applicable techniques for quantitative real-world monitoring of mental disorders.

KEYWORDS

functional connectivity (FC); graph convolution network (GCN); electroencephalogram (EEG); mental disorder; individual predictions

A mental disorder is a mental illness[1] characterized by abnormalities in mood, thinking, behavior, or cognition. Diagnosis, prevention, and treatment of generalized anxiety disorder are critical and on the rise due to coronavirus disease 2019 (COVID-19)[2]. It is worth mentioning that the worldwide suffer from depression, accounting for 4.4% of the global population, more than 340 million people. The global prevalence of anxiety disorders is about 3.8%, and about 280 million people suffer from anxiety symptoms to varying degrees. Depression and anxiety are common mental health problems that have a profound impact on an individual’s quality of life and the overall health of society. In the past few decades, the study of depression and anxiety has gradually become an important research field in psychology, psychiatry, and public health. Furthermore, anxiety and depression are associated with abnormal connectivity patterns, particularly impacting different brain regions. This includes alterations within the internal default mode network (DMN) and corticohypothalamic regions[3].

Machine learning techniques have been used to biomarkers using the promise of artificial intelligence in medicine[4]. An electroencephalography biomarker may provide a detection tool for anxiety-depression disorders. Recent developments in machine learning (ML) and deep learning (DL) techniques have made it possible for researchers to analyze multivariate patterns. Support vector machines (SVMs) can achieve high classification accuracy on small datasets based on state-of-the-art machine learning algorithms[5]. It has great potential in high-dimensional data such as neuroimaging, which includes the classification of mental illness. In addition, graph-based deep learning models, i.e., graph convolution networks (GCNs)[6], have shown strong performance in various tasks. In general, a GCN model is a neural network that can specifically exploit the typical graph structure of functional connectivity (FC) network architecture. GCNs also visualize important features to counter typical criticisms of ML as a black box and make it useful in revealing neural signatures of mental disorders[7]. In previous studies, generalized anxiety and depression disorder was examined as potential biomarker, and clinical scales were used as markers of anxiety disorders for association analysis. It is mentioned that few studies have explored the prediction of clinical scale scores using a data-driven approach. Besides, the existing studies have shown that the fusion of different frequency bands is verfied[8]. This means that different band FCs have different structures, containing different individual-specific characteristics.

In this paper, we propose that end-to-end training can be used to learn the weights of edges between large-scale FC networks, which emphasizes the importance of modeling information between FC in connectome-based prediction tasks. Additionally,

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we test the effectiveness of the proposed method on the clinical dataset for anxiety and depressive disorders. To sum up, the proposed multi-band FC network joint GCN has the following advantages:

- According to our knowledge, this is the first study to examine spatiotemporal topological features of fusion of multi-band brain networks.
- We proposed various parallel GCN layers using multiple frequency bands from the large-scale network, which is able to identify the essential mental health information from the GCN graph embedding.
- A significant performance on anxiety and depressive disorder predictive task was found by comparing the proposed framework with the state-of-the-art prediction methods.

1 Method

In this paper, the functional brain network can be effectively fused by using the multi-frequency joint graph convolution network presented. Furthermore, an overview of the proposed method can be found in Fig. 1. A detailed description of the proposed method follows in this section.

1.1 Multi-frequency spatio temporal functional brain network construction

We assume that the electroencephalogram (EEG) data for a subject are $(x_1, x_2, \ldots, x_N)^{\mathrm{T}} \in \mathbb{R}^{N\times M}$, where each vector $x_n \in \mathbb{R}^M$ $(n = 1, 2, \ldots, N)$ contains the trails EEG signals. N represents the number of the trail. A functional connectivity network[9] was constructed utilizing orthogonal power envelope connectivity (Ort-PEC) for obtaining functional network connectivity across multiple EEG frequency bands. Specifically, the analyzed signal for each vertex was orthogonalized to that of all other vertices to remove spurious correlations due to the limited spatial resolution of source estimates to obtain functional network connectivity across multiple EEG bands. Specifically, the orthogonalization component of the analysis signal $Y(T)$ relative to the analysis signal $X(T)$ is defined as

$$Y_{\perp X(t,f)} = \mathrm{imag}\left(Y(t,f)\right) \frac{X(t,f)^*}{|X(t,f)|} \tag{1}$$

where $X(t,f)$ stands for the analytical signal after $X(t)$ is filtered by a filter with a center frequency of f. Then, we use the pearson correlation coefficient to calculate the correlation coefficient between the envelope of $X(t)$ and $Y_{\perp X(t,f)}$ as the relationship between the various source activities. Since the orthogonalization has two directions, i.e., X is relative to Y and Y is also relative to X, we calculate both directions and take the average result as the correlation coefficient between X and Y.

1.2 Local weight clustering coefficient (LWCC) extraction

Extracting discriminative features and multi-frequency bands fusion are key steps in the mental health prediction. In most prior works, the upper half matrix of FC from a subject is usually used as the feature vector. However, this not only leads to destroying the structure of the original network but also brings high dimensional features, which is not beneficial for the mild cognitive impairment (MCI) detection. To solve it, we are going to extract the LWCC $F = \{f_i \mid (i = 1, 2, \ldots, n)\}$ from the brain connectivity matrix $W \in \mathbb{R}^{n\times n}$ to obtain the corresponding feature vectors. For each network (i.e., the i-th node of the network), the edge weights are defined as follows:

$$f_i = \frac{1}{n} \sum_{i\in\psi} \frac{\sum_{i\in\psi}\left(w_{ij}^{\text{ort-PEC}} w_{ih}^{\text{ort-PEC}} w_{jh}^{\text{ort-PEC}}\right)^{\frac{1}{3}}}{\sum_{j\in\psi} w_{ij}^{\text{ort-PEC}} \left(\sum_{j\in\psi} w_{ij}^{\text{ort-PEC}} - 1\right)} \tag{2}$$

where ψ represents the combination of interest in the large network, $w_{ij}^{\text{ort-PEC}}$ denotes the set of vertices directly connected to vertex ij, $\sum_{j\in\psi} w_{ij}^{\text{ort-PEC}}$ is the number of elements in $w_{ij}^{\text{ort-PEC}}$, and $w_{ij}^{\text{ort-PEC}} w_{ih}^{\text{ort-PEC}} w_{jh}^{\text{ort-PEC}}$ is the weight of FC.

1.3 Graph convolution for individual graphs

Mental disorders affect functional connectivity at different frequencies, and a significant improvement has been achieved in the representation of features of model performance. Therefore, we propose a method for predicting mental disorder scale scores using a sharing strategy for fusion of multi-bands information.

The convolutional module extracts the graph $\wp^S(v^S, \varepsilon^S)$, in which v^S contains the nodes (N ROI), and ε^S contains the edges.

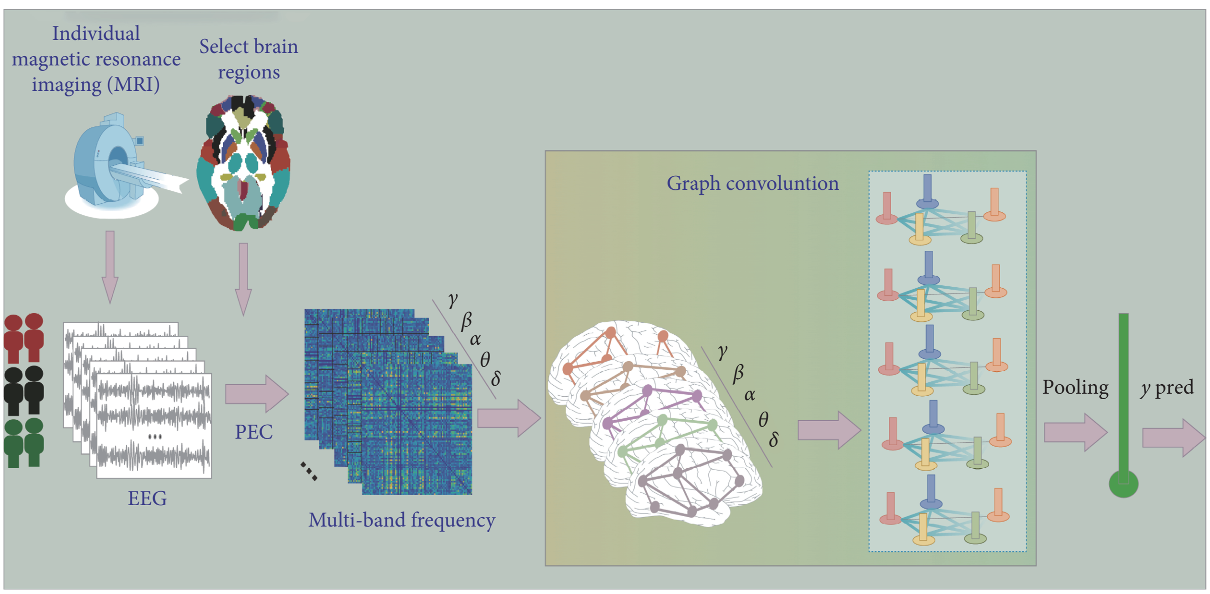


Fig. 1 Proposed multi-frequency joint-GCN method: Functional connectivity extracted from EEG using ort-PEC measures. The inter-network connectivity is represented by edges across different frequency bands, with edge weights configured as learnable parameters. The adjacency matrix of the joint frequency band graph is then analyzed by a share weight graph convolutional network.

Define $A^S \in \mathbb{R}^{N\times N}$ as the matrix representing the weights of edges between pairs of regions of interest (ROIs), M-dimensional node features as attributes assigned to these ROIs, and $\hat{A}^S = D^{-\frac{1}{2}} A^S D^{-\frac{1}{2}}$ as the normalized adjacency matrix, where D is the degree matrix with $D_{ii} = \sum_j A^S_{ij}$. The typical graph convolution f is defined as follows:

$$f(X^S; A^S) = \sigma\left(\hat{A}^S X^S W^S\right) \tag{3}$$

where the activation function $\sigma(\cdot)$ is used to determine the convolutional weights W^S to learn.

In this paper, the corresponding graph convolution is defined with respect to the normalized multi-bands FC adjacency matrix A^{Band}. A^{Band} (band including δ, θ, α, β, and γ) is usually different, reflecting differences between multi-frequency network modes. In order to predict target labels (e.g., the generalized anxiety disorder 7 (GAD-7) and the patient health questionnaire 9 (PHQ-9) scale information) for patients with abnormal mental disorders, we can use the GCN model given a subject's multi-band functional connectivity map.

1.4 Multi-bands joint (MBJ) graph

The previous research consistently showed that anxiety and depressive disorders are caused by different frequency bands. The weights of edges between N networks are set as learnable parameters. We combined the joint normalized adjacency matrix MBJ of different frequency bands to explore abnormalities in psychiatric anxiety disorder fusion, and the graph convolution for fusing multiple frequency bands was defined as $\hat{A} = [\hat{A}^\delta; \hat{A}^\theta; \hat{A}^\alpha; \hat{A}^\beta; \hat{A}^\gamma]$. Besides, $X = [X^\delta; X^\theta; X^\alpha; X^\beta; X^\gamma]$ denote the vertical connections among different frequency functional node features. The graph convolution of the multi-bands joint graph is defined as

$$f(X^{\text{MB}}; A^{\text{MB}}) = \sigma\left(\hat{A}^{\text{MB}} X^{\text{MB}} W^{\text{MB}}\right) = \sigma\left(\begin{bmatrix} \hat{A}^\delta X^\delta \\ \hat{A}^\theta X^\theta \\ \hat{A}^\alpha X^\alpha \\ \hat{A}^\beta X^\beta \\ \hat{A}^\gamma X^\gamma \end{bmatrix} W\right) \tag{4}$$

It is mentioned that we employ LWCC to represent nodes in five frequency band networks. These nodes are then incorporated into a standard GCN using the above adjacency matrix. In order to predict the GAD-7 and PHQ-9, a layer of graph convolution with input dimension of 84 and output dimension of subject is applied, followed by scaled exponential linear unit (SELU) activation, mean pooling, batch normalization, and fulled connected layers. In Fig. 2, we introduce the constructed matrix from 8 major brain networks. The colorbar represents the degree of correlation between different brain areas.

2 Experimental Setting

2.1 Dataset

In order to verify the robustness of our predictive performance in mental disorders, we performed extensive validation on 2 datasets, including the healthy brain network (HBN) dataset[10] and multi-modal open dataset for mental-disorder analysis (MODMA dataset) given in Ref. [11]. Specifically, 62 HBN adolescent anxiety disorder patients were selected and analyzed based on their EEG and MRI images in the HBN dataset. Besides, the 24 patients diagnosed with major depression disorder (MDD) were introduced in the MODMA dataset. The MDD group contains 24 subjects (13 males and 11 females), and the mean and standard deviation of age are 30.18 ± 10.37 and 30.31 ± 10.31, respectively. All participants were assessed using the PHQ-9 and GAD-7. The PHQ-9 was used to assess each MDD participant's level of depression with a score greater than or equal to 5. The GAD-7 score was used to measure the severity of anxiety. In this paper, GAD-7 scores for anxiety disorders and PHQ-9 scores for MDD were 10.77 ± 3.83 and 18.33 ± 3.49, respectively.

2.2 Preprocessing

EEG raw recordings were preprocessed using bandpass filters 0.1–100 Hz, and independent component analysis was performed. The individual head models were constructed based on MRI T1 images using the boundary element method. Then, the EEG time series were mapped to source spatial levels by the eLORETA

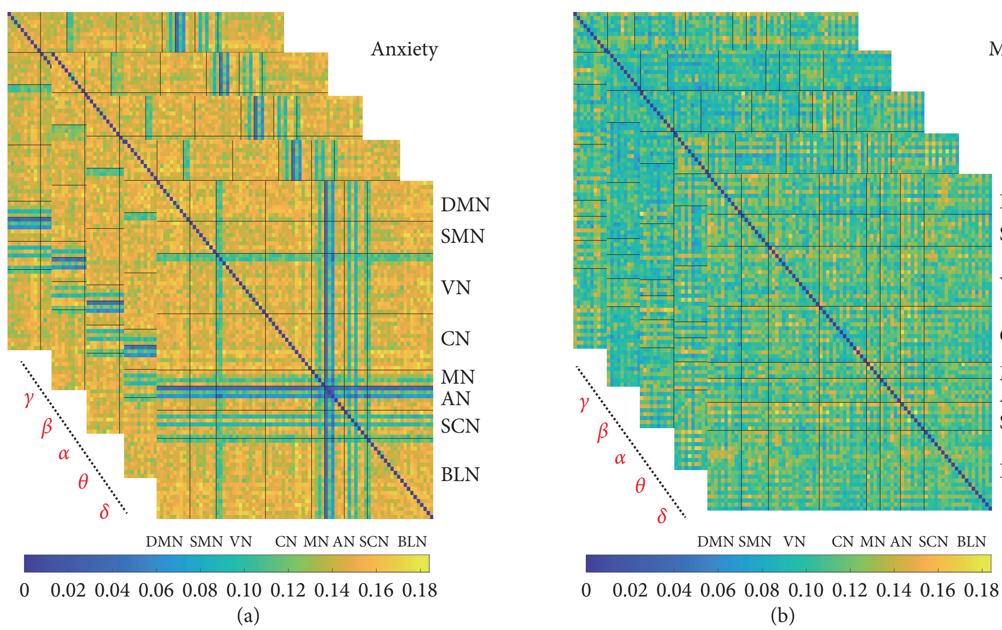


Fig. 2 Constructed matrix constructed based on eight large-scale brain networks, including default model network (DMN), sensorimotor network (SMN), visual network (VN), cognitive network (CN), memory network (MN), auditory network (AN), subscrtical network (SCN), and bilateral limbic network (BLN).

algorithm[12]. 84 ROIs were selected for subsequent analysis according to Ref. [13], and we divided the brain into 8 large-scale networks according to the ROI distribution. Finally, we calculate the functional connectivity between the ROIs of each frequency band, and obtain the brain network under the 5 frequency bands (δ, θ, α, β, and γ).

2.3 Model implementation

MBJ-GCN was implemented in Pytorch 1.10 and trained for 500 epochs with 4 batches using stochastic gradient descent (SGD) optimization. To determine the accuracy of the prediction of GAD-7 and PHQ-9 scores, we use the mean squared error as the training loss, use a learning rate of 0.001, and calculate Pearson correlation coefficient (r) and mean absolute error (MAE) between actual and predicted scores. Finally, the mean squared error is used as the training loss for GAD-7 and PHQ-9 score prediction, and binary cross-entropy is used for clinical score prediction.

2.4 Comparison with baselines

To validate the effectiveness of our proposed method, we compare it with several state-of-the-art brain network prediction methods.

- **Multi layer perceptron (MLP):** As a basic artificial neural network model, MLP is usually used to solve regression problems.
- **SVM:** As a supervised learning algorithm, SVM creates a function that fits the data so that the data points remain as close to the function as possible.
- **Matrix-auto-encider (Matrix-AE)[14]:** The Matrix-AE is used to produce a low-dimensional manifold embedding that can be utilized for prediction.
- **Unified brain network with functional and structural (UBNfs)[15]:** A unified brain network matrix is constructed using a convex optimization method to predict performance for anxiety and depression disorders.
- **Siamese community-preserving graph convolutional network (SCPGCN)[16]:** Graph convolution networks are utilized in Siamese community preserving graph convolution networks to learn different frequency FC joint embeddings for brain networks.

3 Result

3.1 Prediciton by MBJ-GCN

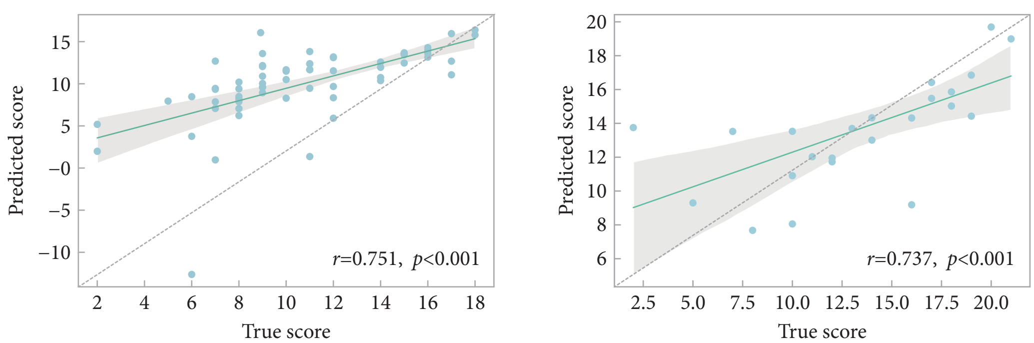
An MBJ-GCN model was constructed to predict anxiety and depression diagnostic scores individually. Furthermore, we performed 10 fold cross-validation analyses to assess and demonstrate the generalizability of our prediction results using FC profiles as a predictor of clinical score changes. The size of the p-value indicates whether the prediction accuracy obtained exceeds that expected by chance, indicating the significance of the prediction model. A correlation analysis of MBJ-GCN between predicted and true scores of mental disorders is presented in Fig. 3. In Fig. 3a, the results show that the correlation between the true label and the predicted label using the anxiety GAD-7 score reaches 0.751 and is significant. Sexual difference, as shown in Fig. 3b, MBJ-GCN is used to predict the correlation between PHQ-9 scores and real labels, reaching 0.737 and having a significant difference. It is worth mentioning that each green point represents an actual score and its corresponding predicted value. Green line is the best fit line or trend line, which is used to express how the predicted score changes with the change of the true score. Most importantly, the correlation coefficient calculated for our predictions exceeded the criterion set by Ref. [17], indicating that the model may be appropriate for analyzing changes in scores associated with mental disorders. Therefore, MBJ-GCN's personalized predictions are highly correlated with correlation analyses between clinical measures for predicting completely unknown subjects.

3.2 Comparison result with state-of-the-art methods

In Table 1, we show the GAD-7 and PHQ-9 score prediction tasks for all compared methods. For the convenience of viewing, we used our method and other methods, using fusion data of different frequency bands as data input. Experimental results show that GCN has advantages in analyzing MCI compared with traditional machine learning methods. We believe that GCNs can effectively use abnormal information of diseases in the task of mental disorder prediction. In addition, the analysis shows that the fusion of LWCC and different frequency bands may be an effective method to extract high-order information of the brain. Overall, the GCN method achieves high efficiency in graph convolutions when extracting informative features from FC networks. Notably, in terms of MAE and Pearson correlation coefficient (PCC) for anxiety and depressive disorders, MBJ-GCN has the best average MAE and the PCC values, which are 2.274 ± 0.999, 2.222 ± 1.051 and 0.759 ± 0.1999, 0.786 ± 0.115, respectively. This phenomenon suggests that multi-band EEG functional connectivity networks contain complementary information about the brain's connectome that can help predict clinical scores for mental disorders. Besides, the predictive performance of GAD-7 scale in anxiety and depressive disorder cross-morbidity is given in Fig. 4.

3.3 Most discriminative regions

After verifying the predictive performance of the anxiety and depression groups under the parallel task, we performed a



(a) Correlation between the predicted and actual scores of anxiety MBJ-GCN

(b) Correlation between MDD MBJ-GCN predicted PHQ-9 scores and the true PHQ-9 scores

Fig. 3 Correlation analysis of the MBJ-GCN between predicted and true scores for mental disorders.

Table 1 Comparison of the prediction performance for anxiety GAD-7 scores and PHQ-9 scores among different methods, in which MAE and PCC were used to perform 10-fold cross-validation.

Method	Anxiety GAD-7 prediction				Depression PHQ-9 prediction			
	MAE		PCC		MAE		PCC	
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation
MLP	2.642	0.964	0.499	0.335	2.548	1.168	0.266	0.227
SVM	3.375	1.013	0.289	0.356	3.271	1.374	0.064	0.143
UBNfs	6.831	1.495	0.123	0.381	5.531	2.874	0.349	0.267
Matrix-AE	2.73	1.139	0.396	0.333	2.559	1.084	0.348	0.348
SCP-GCN	3.434	0.898	0.163	0.199	3.095	1.409	0.502	0.382
Ours	2.274	0.999	0.759	0.199	2.222	1.051	0.786	0.115

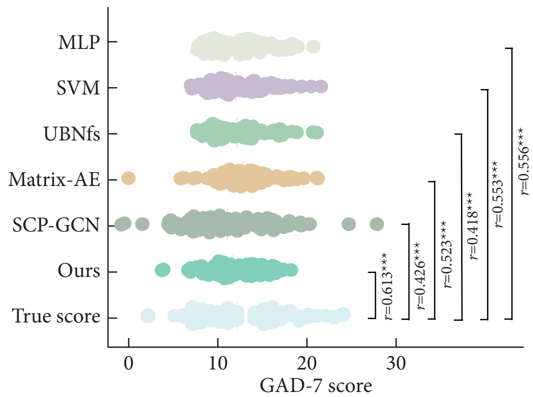


Fig. 4 Predictive performance of GAD-7 scale in anxiety and depressive disorder cross-morbidity, where *r* is the correlation value between the true label and the predicted label, and * represents a significant difference of *p* < 0.001.**

quantitative analysis of both groups using the GAD-7. The large-scale network connection of the frequency band is abnormally connected under $p < 0.001$ in the Fig. 5a. The abnormal *t*-score brain distributions of brain functional connectivity were found mainly in large-scale networks such as the DMN, BLN, and VN, which are associated with the anterior cingulate cortex, hippocampus, fasciculate, and cingulate gyrus. In Fig. 5b, the correlation between the clinical scale scores predicted by our proposed MBJ-GCN and the real scores reaches 0.613, which has a significant correlation and can lay the foundation for the next step of precision medicine.

4 Conclusion and Future Work

To predict objective scales of mental disorders, we propose a new framework named MBJ-GCN that analyzes multi-band brain connectomes with EEG spatiotemporal covariation. We highlight the importance of modeling fusing information between different functional connectivity bands for connectome-based prediction tasks. In this paper, MBJ-GNN is demonstrated to perform well in predicting clinical scores such as GAD-7 and PHQ-9 using data provided by HBN and MODDA. To explore the model's ability to analyze network topology, we only consider network metrics (LWCC) as node features. Nevertheless, our data-driven model provides a useful way to model the complex layered nervous system with broad relevance on neuropsychological disorders. In the future work, we will consider the predictive performance of mental disorders more on multi-task (such as video and visual

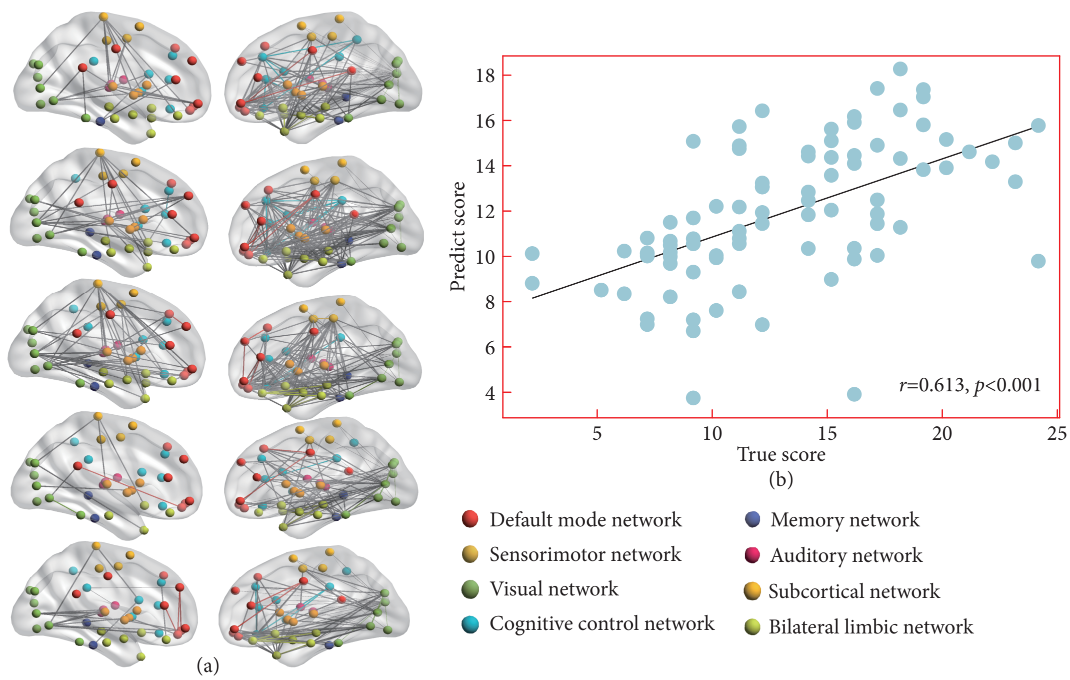


Fig. 5 Statistical *t*-values for the FC matrix in 8 large-scale networks (the anxiety vs. MDD group, *p* < 0.001 value).

learning tasks, etc.) spatiotemporal covariation and spectral characteristics and solve the heterogeneous subtypes of different subtypes of mental disorders to evaluate the predictive performance and introduce treatment efficacy assessment.

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