Atlas-Free Functional Brain Connectome Analysis via Task-Driven Parcellation

Keqi Han[1]   Yao Su[2]   Songlin Zhao[3]   Charles Gillespie[1]   Boadie Dunlop[1]
Daniel Barron[4]   Randy Hirschtick[5]   Liang Zhan[6]   Lifang He[3]   Xiang Li[5]   Carl Yang[1]

[1]Emory University   [2]Worcester Polytechnic Institute   [3]Lehigh University
[4]Brigham and Women's Hospital   [5]Massachusetts General Hospital   [6]Univ. of Pittsburgh

✉ Contact: rgollub@mgb.org   j.carlyang@emory.edu

CODE

SUMMARY

Selecting a suitable brain atlas for node definition is a critical yet challenging step in functional connectome analysis. A mismatched atlas can obscure subtle topographies and undermine the subsequent analysis. In this work, we propose an Atlas-Free functional brain CONnectome analysis (AFCON) that bypasses atlas selection by jointly optimizing an adaptive parcellation module and a graph-based connectome analysis module. Unlike classical methods reliant on fixed, predefined atlases, AFCON adaptively generates task-specific, individualized parcellations from fMRI data, which better align with the prediction task and offer enhanced interpretability. In addition, we introduce two neurobiologically-informed regularizers to ensure plausible parcellations: a balanced distribution regularizer to mitigate extreme parcel size imbalances and a spatial compactness regularizer to promote anatomical coherence. Experiments on ADHD and ADNI datasets demonstrate that AFCON consistently matches or outperforms atlas-based baselines in terms of predictive accuracy while identifying disease-relevant brain regions, enhancing both interpretability and clinical relevance. Notably, this work focuses on the cerebral cortex, serving as an initial step towards potential whole-brain connectivity analysis in the future for more robust clinical utility.
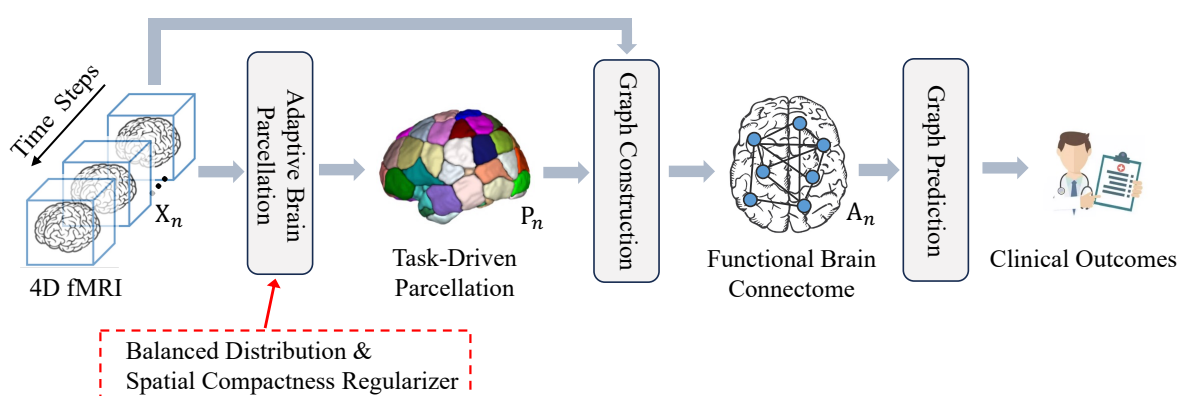
FRAMEWORK

Figure: The Overall Framework of AFCON.

Adaptive Brain Parcellation. We apply a 3D U-Net to generate voxel-wise soft assignments of cortical voxels into K ROIs. During training, Gumbel-Softmax enables differentiable one-hot assignments; during inference, Argmax is used for deterministic parcellation.

To enhance biological plausibility, we introduce two regularizers:

Balanced Distribution Regularizer: Prevents extreme imbalances of ROI sizes by penalizing deviations from a uniform volume distribution:

$$\mathcal{L}_{\text{balance}} = \sum_n \text{KL}(\mathbf{p}_n \parallel \mathbf{u}), \quad \mathbf{u} = \left[\frac{1}{K}, \ldots, \frac{1}{K}\right]$$

where $p_{n,k}$ is the proportion of cortical voxels assigned to ROI k for subject n.

Spatial Compactness Regularizer: Promotes geometric coherence of voxels within each ROI by minimizing spatial variance around soft centroids:

$$\mathbf{c}_{n,k} = \frac{\sum_v \mathbf{coord}_v \cdot s_{n,k}(v)}{\sum_v s_{n,k}(v)}, \quad \mathcal{L}_{\text{compact}} = \sum_{n,k} \frac{\sum_v s_{n,k}(v)\|\mathbf{coord}_v - \mathbf{c}_{n,k}\|^2}{\sum_v s_{n,k}(v)}$$

Graph-based Connectome Analysis. From the parcellation, ROI-wise time series are obtained by averaging voxel time courses. We compute functional connectivity matrices $\mathbf{C}_n$ using Pearson correlation and retain the top 10% positive connections to form sparse brain networks $\mathbf{A}_n \in \mathbb{R}^{K \times K}$. We adopt a Graph Convolutional Network (GCN) to predict target labels:

$$\hat{y}_n = \text{GCN}(\mathbf{A}_n, \mathbf{H}_n)$$

where $\mathbf{H}_n$ is the connection profile node feature matrix (i.e., rows of $\mathbf{C}_n$).

EXPERIMENTS

Datasets. Two rs-fMRI datasets: *ADHD-200* (569 subjects; 43.2% ADHD; 64 timepoints) and *ADNI* (200 subjects balanced between AD and HC; 197 timepoints), both preprocessed using fMRIPrep.

Table: Overall Prediction Performance (mean±std, %).

Model	ADHD			ADNI		
	ACC↑	AUC↑	F1↑	ACC↑	AUC↑	F1↑
GCN	59.7±6.2	63.2±6.9	48.3±12.7	60.5±9.1	65.7±9.2	63.4±8.3
GAT	57.7±2.9	60.3±3.7	53.6±10.0	56.0±2.5	59.4±9.1	55.4±5.7
BrainGNN	53.2±3.8	55.2±3.7	50.3±7.0	51.0±5.4	52.3±6.3	53.2±5.5
BrainNetCNN	56.0±3.3	58.7±6.4	52.1±6.7	58.5±4.6	65.9±7.8	53.6±19.1
BrainGB	56.7±2.7	58.3±4.4	46.0±6.1	56.5±5.8	59.7±4.9	58.2±7.2
BrainNetTF	59.8±5.4	63.8±7.7	45.0±22.8	59.5±5.3	62.3±3.8	59.7±8.6
NeuroGraph	56.5±5.4	59.4±4.3	57.6±4.7	56.5±8.5	57.6±8.2	58.9±11.1
AFCON (K=48)	63.2±2.7	65.6±2.1	56.8±3.5	62.5±6.5	66.1±7.3	62.6±5.7
AFCON (K=90)	60.0±4.9	63.5±3.1	50.7±12.0	61.5±4.1	65.6±5.6	61.5±5.9
AFCON (K=200)	61.8±0.9	62.9±2.0	47.9±6.8	62.0±5.1	66.7±4.2	59.8±7.5
AFCON (K=360)	61.1±3.9	63.4±5.7	49.8±11.6	59.5±3.3	65.1±2.7	55.1±6.8

• AFCON consistently matches or outperforms baselines with lower variances, indicating improved accuracy and robustness.
• Parcellation resolution (i.e., ROI count) affects performance; careful selection is essential based on disease characteristics and research goals.
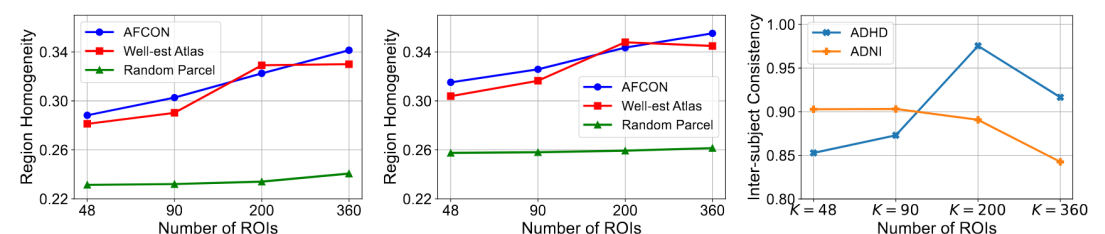
(a) Region Homogeneity on ADHD

(b) Region Homogeneity on ADNI

(c) Inter-subject Consistency

(d) ADHD 48 ROIs

(e) ADHD HC

(f) ADHD Patient

(g) ADNI 48 ROIs
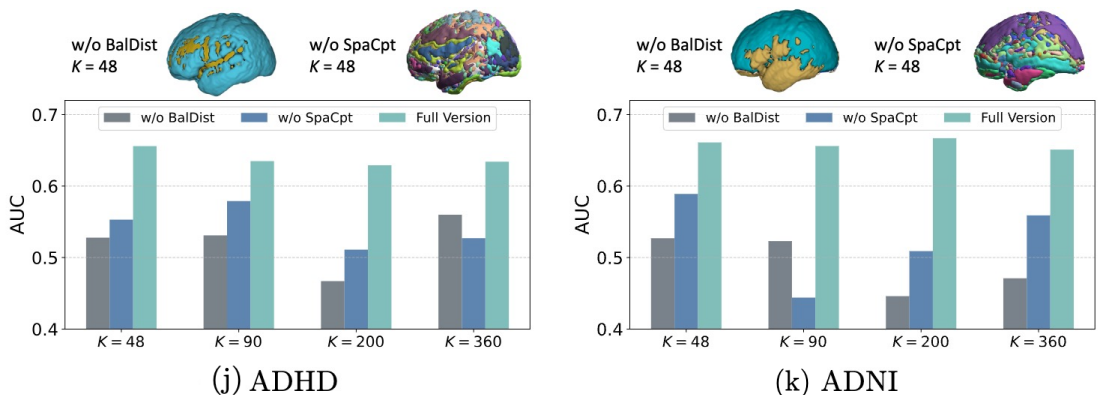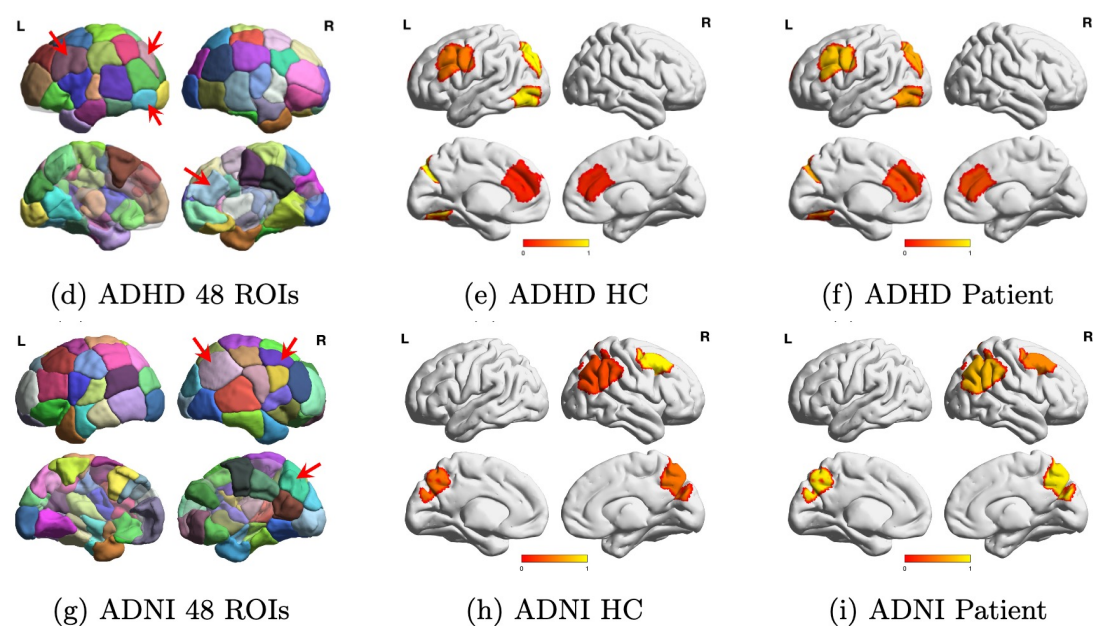
(h) ADNI HC

(i) ADNI Patient

(j) ADHD

(k) ADNI

Figure: (a)-(c) Quantitative analysis of the learned parcellation. (d)-(i) highlight salient ROIs for ADHD and AD. (j)-(k) Ablation Study of the proposed regularizers.

• Fig (a)-(c) show that AFCON produces functionally coherent and consistent parcellations, and identifies clinically relevant regions aligned with known ADHD and AD pathology.
• Regularizers improve performance across cohorts.
Balanced-Distribution contributes more to prediction gains in ADHD, while Spatial-Compactness has a notable impact in ADNI, suggesting that balanced ROI sizes help capture ADHD's diffuse dysconnectivity, whereas compact parcels better reflect the focal atrophy patterns in AD.