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

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Introduction:

Selecting a suitable brain atlas for node definition is a critical yet challenging step in functional connectome analysis (Stanley, 2013). A mismatched atlas can obscure subtle topographies and undermine the subsequent analysis. In this work, we propose AFCON, an atlas-free method that bypasses atlas selection by jointly optimizing an adaptive parcellation module and a graph-based connectome analysis module. AFCON adaptively generates task-specific, individualized parcellations from fMRI data, which better aligns with the prediction task and offers enhanced interpretability. We also introduce two neurobiologically-informed regularizers to ensure plausible parcellations. Experiments on ADHD (ADHD-200 consortium, 2012) and ADNI (Mueller, 2005) show that AFCON outperforms standard atlas-based baselines in prediction, and reveals regional biomarkers that are consistent with their established roles in neural pathology. 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.

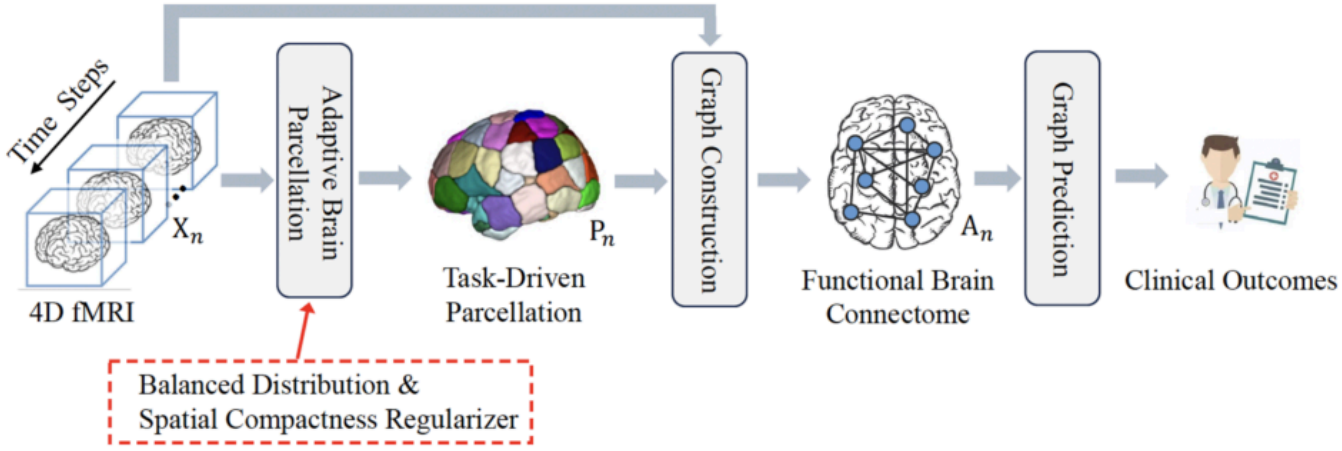


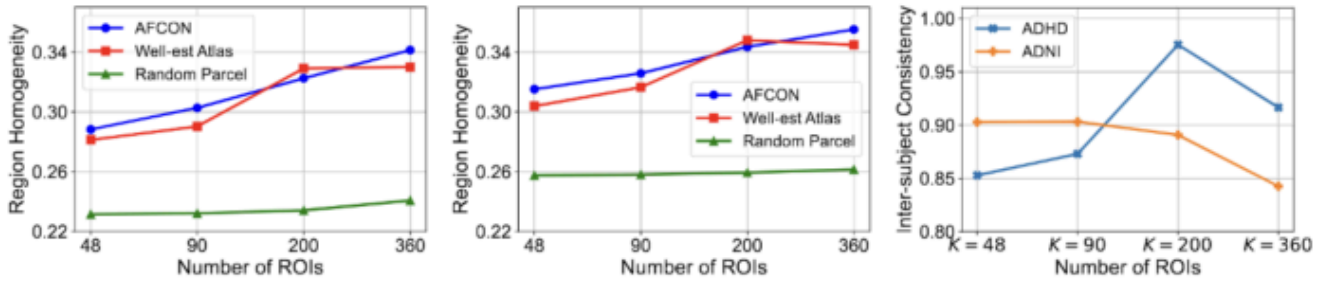
Fig. 1: Overall framework of AFCON, consisting of an Adaptive Brain Parcellation Module followed by Graph-based connectome analysis modules.

Methods:

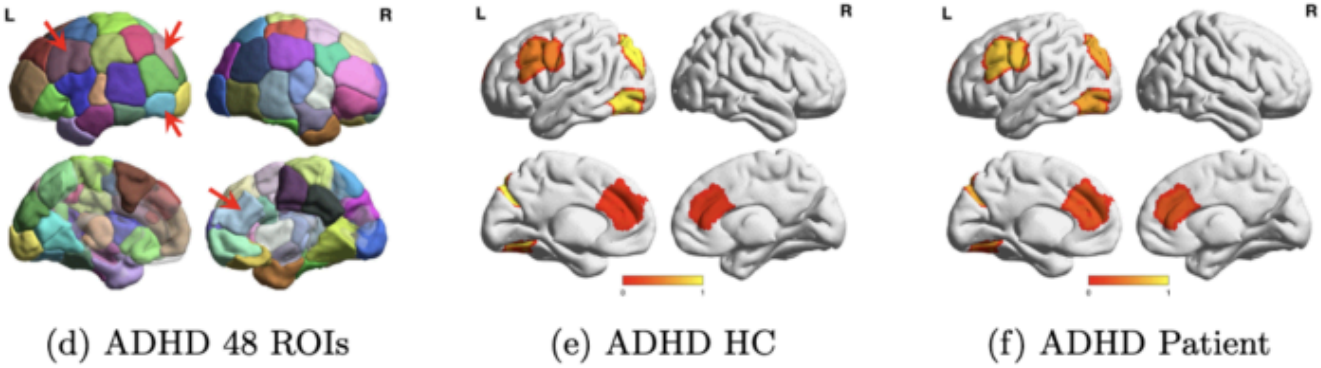
AFCON integrates a 3D U-Net (Ronneberger, 2015) for adaptive brain parcellation with a graph neural network for clinical prediction. The 3D U-Net segments cortical voxels into K non-overlapping ROIs, refined by two regularizers. The balanced distribution regularizer computes the KL-divergence between the ROI assignment distribution and a uniform distribution to ensure comparable parcel sizes, while the spatial compactness regularizer minimizes the variance of voxel coordinates within each ROI to encourage contiguous, anatomically consistent regions. ROI-level signals are averaged to construct a functional connectome that is fed into the GCN (Kipf, 2016) for clinical outcome prediction. We evaluate AFCON on two rs-fMRI datasets: ADHD-200 (569 subjects in total, with 246 ADHD patients) and ADNI (200 subjects in total, with 100 AD patients), both datasets are processed with standard fMRIPrep pipeline (Esteban, 2019), including skull stripping, spatial normalization, segmentation, slice-time correction, susceptibility distortion correction, and motion artifact removal. We compare AFCON against atlas-based brain connectome analysis baselines with four well-established atlases: Harvard-Oxford48 (Makris, 2006), AAL90 (Tzourio-Mazoyer, 2002), Schaefer200 (Schaefer, 2018) and HCP360 (Glasser, 2016).

Results:

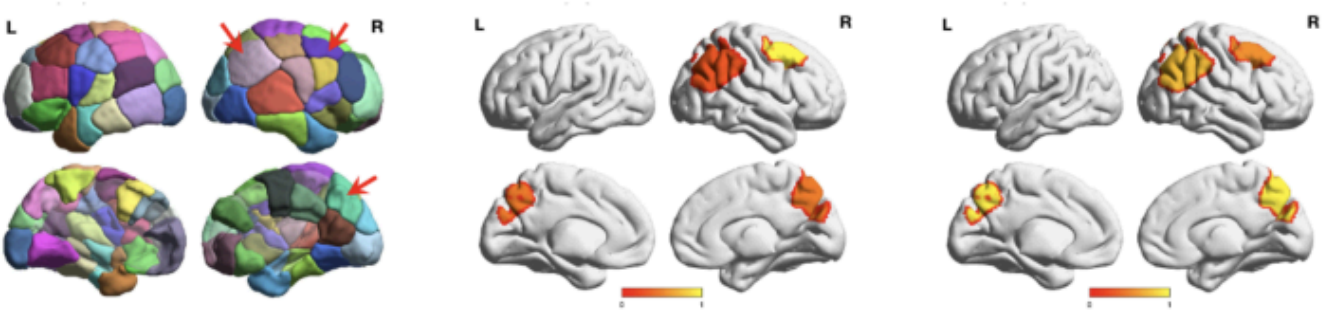
For the disease prediction task, AFCON outperforms atlas-based baselines across multiple parcellation granularities (#ROIs=48, 90, 200, 360) on both the ADHD and ADNI datasets. Quantitative evaluation of the learned parcellations shows that AFCON achieves higher region homogeneity than both well-established atlases and random parcellations, indicating more functionally cohesive ROIs. Additionally, AFCON's parcellations achieve strong inter-subject consistency, preserving shared brain structures across subjects while accommodating individual variability, ensuring robustness for group-level analysis. Qualitative analysis validates AFCON's effectiveness in biomarker identification, revealing that functionally significant ROIs ($p<0.05$), such as the Precentral, Occipital, Fusiform, and Cingulum for ADHD, and the Precuneus, Inferior Parietal, and Middle Frontal regions for AD, which are consistent with existing neuroscientific findings. An ablation study validates the regularizers' role, showing that their removal degrades performance and disrupts plausibility of parcellations.



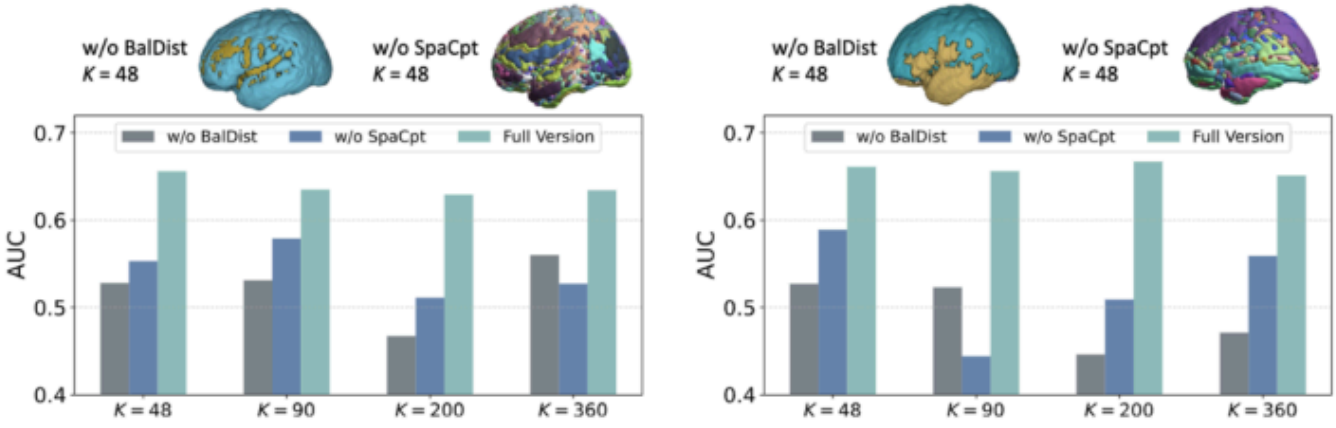
(a) Region Homogeneity on ADHD (b) Region Homogeneity on ADNI (c) Inter-subject Consistency



(d) ADHD 48 ROIs (e) ADHD HC (f) ADHD Patient



(g) ADNI 48 ROIs (h) ADNI HC (i) ADNI Patient



(j) ADHD (k) ADNI

Fig. 2: Experiments results of AFCON framework. (a)-(c) Quantitative analysis of the learned parcellation. (d)-(i) highlight salient ROIs for ADHD and AD respectively. (j)-(k) Ablation Study showing the importance of the proposed regularizers.

Conclusions:

In this study, we introduce AFCON, an atlas-free framework for functional brain connectome analysis that integrates adaptive parcellation with downstream prediction. By jointly optimizing parcellation and prediction, AFCON outperforms classical atlas-based methods and reveals disease-relevant biomarkers in ADHD and AD cohorts. The proposed framework demonstrates the potential to advance clinical diagnosis and treatment by identifying task-specific brain signatures without predefined atlases.

Modeling and Analysis Methods:

Classification and Predictive Modeling
Connectivity (eg. functional, effective, structural)
fMRI Connectivity and Network Modeling [1]
Methods Development
Segmentation and Parcellation [2]

Keywords:

Computational Neuroscience
Design and Analysis
FUNCTIONAL MRI

[1|2]Indicates the priority used for review

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Not applicable

Please indicate which methods were used in your research:

Functional MRI
Computational modeling

Provide references using APA citation style.

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