

Supplementary Materials

for

Topological Alterations of Brain Functional Networks Predict Methylphenidate Response in ADHD

1 Correlation Between Topological and Graph Theory Features

To further examine the relationship between persistent homology-derived topological descriptors and conventional graph theory measures, we computed Pearson correlations between four representative topological features and ten graph theory metrics. The complete correlation heatmap is shown in Figure S1.

Overall, AUC-based topological features showed stronger correlations with conventional graph measures than peak-threshold features. In particular, Betti 0 AUC and Betti 1 AUC were positively correlated with global efficiency, but negatively correlated with local efficiency and clustering coefficient. These findings suggest that persistent homology captures network properties that are partly related to established measures of integration and segregation, while still providing complementary topological information beyond conventional graph analysis.

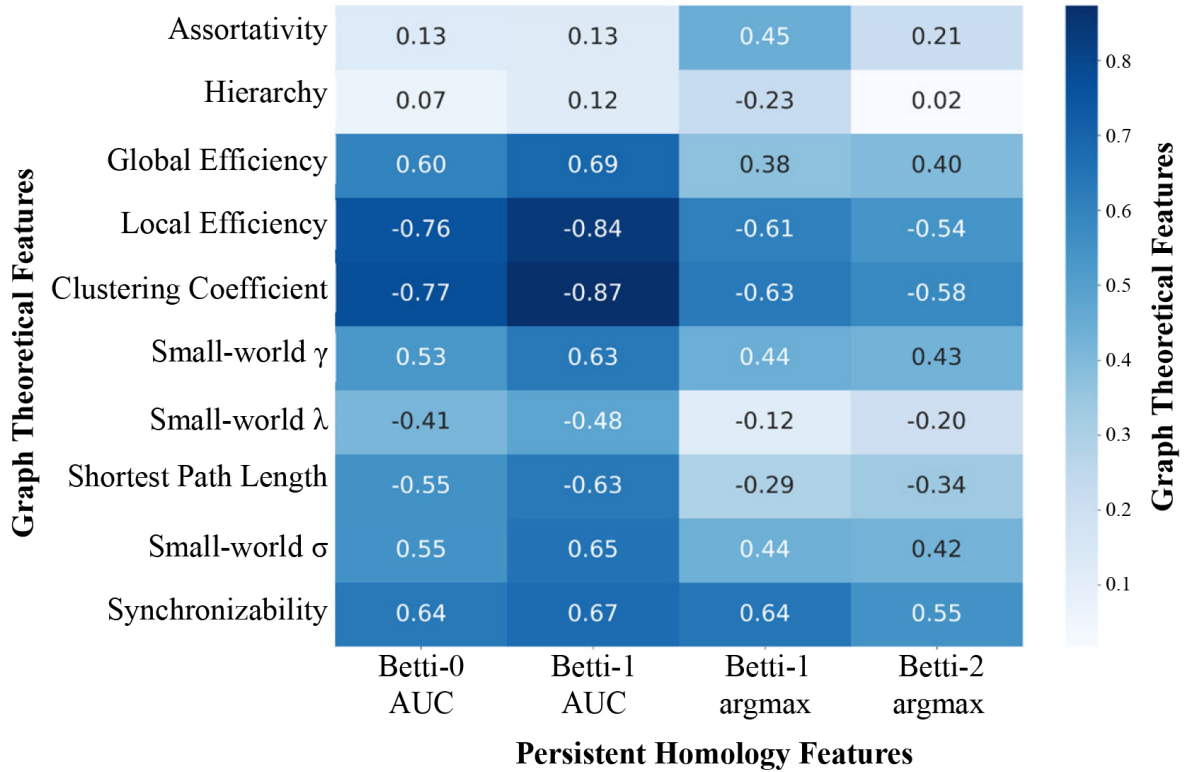


Figure S1: Heatmap of Pearson correlation coefficients between four topological features (Betti 0 AUC, Betti 1 AUC, Betti 1 peak threshold, and Betti 2 peak threshold) and ten graph theory metrics.

2 Complete Correlation Results Between Topological Features and Clinical Improvement

To evaluate the clinical relevance of the topological features, Pearson correlation analyses were performed between persistent homology-derived topological features and the ADHD-RS percentage decline rate across all 83 participants. The complete results are summarized in Table S1.

Betti 0 AUC showed the strongest positive correlation with symptom improvement, followed by Betti 1 AUC and Betti 1 peak threshold. In addition, several Betti 1 values at selected thresholds and Betti 2-derived features were also significantly associated with clinical improvement, further supporting the relevance of baseline topological organization to subsequent methylphenidate response.

Table S1: Pearson correlation between topological features and ADHD-RS percentage decline rate ($n = 83$).

Feature category	Feature	Correlation (r)	p -value
Betti 0 curve	AUC	0.311	0.005
Betti 1 curve	AUC	0.285	0.009
	Peak value	0.130	0.243
	Peak threshold	0.281	0.011
	Value at threshold 0.2	-0.330	0.002
	Value at threshold 0.4	0.334	0.002
	Value at threshold 0.6	0.326	0.002
Betti 2 curve	Peak value	0.257	0.020
	Peak threshold	0.259	0.019

3 Additional Results of Unsupervised Clustering Analysis

We further explored whether the observed group-level topological separation could support label-free classification using a Wasserstein distance-based clustering model. The distribution of accuracies across repeated runs is shown in Figure S2.

The topology-based clustering model achieved a mean accuracy of 0.61, which was slightly higher than the 0.60 obtained by the Euclidean-distance baseline. Although the absolute improvement was modest, the topology-based approach showed relatively lower variance across runs, indicating slightly improved robustness. Because the overall clustering performance remained limited, these results are presented here as supplementary findings.

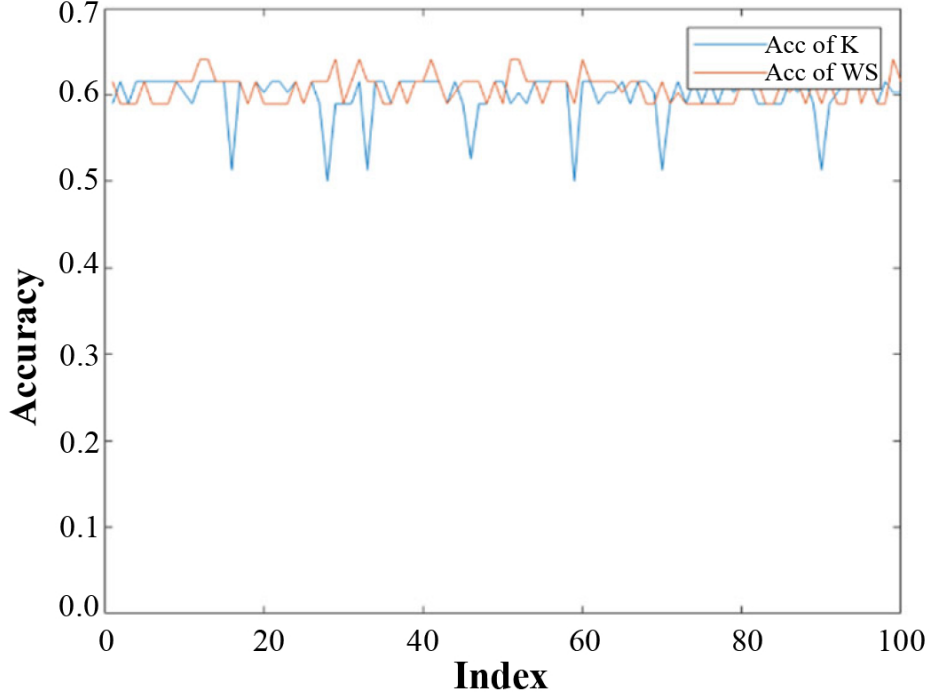


Figure S2: Comparison of clustering accuracy across repeated runs for the unsupervised models. The red line indicates the topology-based clustering model using Wasserstein distance, and the blue line indicates the baseline clustering model using Euclidean distance derived from functional connectivity.