Topological Signatures of Altered Brain Network Centrality in ADHD: A TDA Mapper Study

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Introduction

- ADHD is a common neurodevelopmental disorder characterized by persistent inattention, hyperactivity, and impulsivity.
- A prevailing neurobiological model posits that ADHD arises from atypical wiring and communication within large-scale brain networks.
- However, the functional connectivity literature is marked by conflicting reports, with studies describing both hyperconnectivity and hypoconnectivity.
- A significant limitation of traditional analyses is the practice of averaging data across time , which obscures moment-to-moment fluctuations and may mask the dynamical properties that differentiate clinical populations.
- Topological Data Analysis (TDA) is a mathematical framework for characterizing the shape of complex, high-dimensional data. The Mapper algorithm distills this data into a simplified graphical representation at the single-participant level without collapsing the data's original temporal and spatial scales.
- **Hypothesis:** We predicted that the brain state networks of individuals with ADHD would exhibit a more rigid organization , manifesting as (1) higher network centrality and (2) a positive correlation between centrality and symptom severity

Materials and Methods

Dataset and Participants

- This study utilized publicly available data from the ADHD-200 Global Competition.
- We selected three sites with sufficient sample sizes: New York University (NYU), NeuroIMAGE (NI), and Oregon Health & Science University (OHSU).
- Participants were diagnosed with ADHD or as Typically Developing Controls (TDC). Phenotypic data included age, sex, and ADHD Rating Scale IV scores

TDA: The Mapper Pipeline

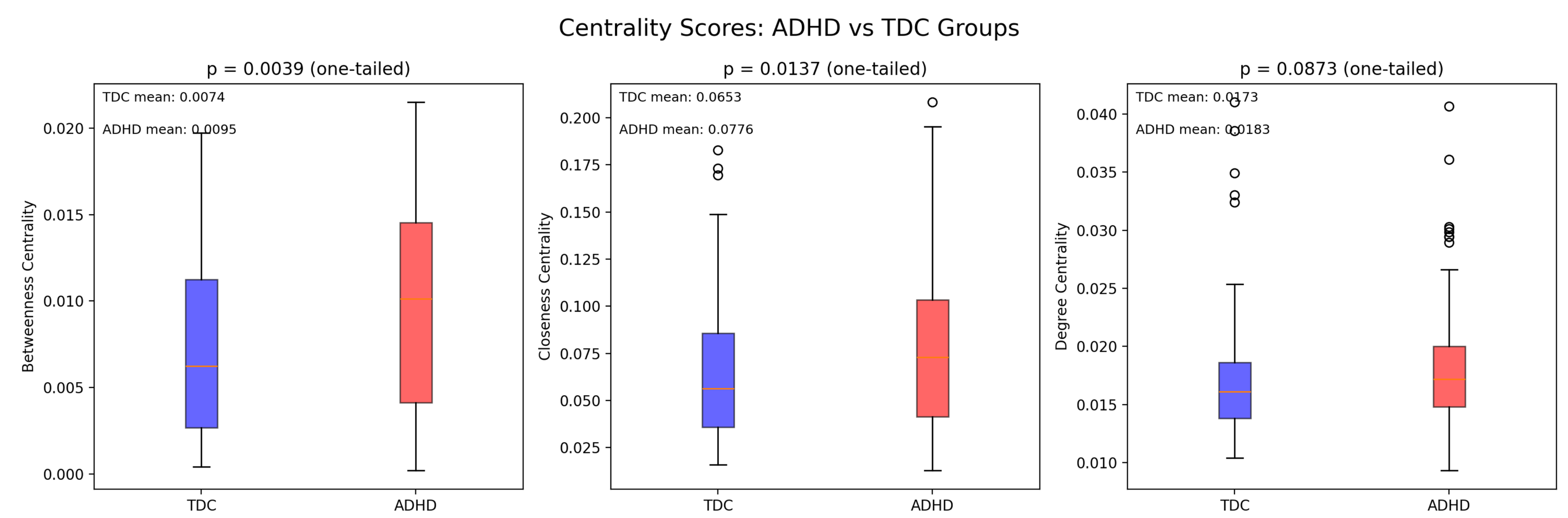
1. **Input Data**: Preprocessed 4D rs-fMRI data was reshaped into a 2D matrix (time points × voxels).
2. **Distance Metric**: A pairwise Euclidean distance matrix was computed between all time points.
3. **Filter Function**: Principle Component Analysis (PCA) projected the high-dimensional data into a 2D space.
4. **Covering & Binning**: The 2D embedding was covered by a set of overlapping square bins.
5. **Partial Clustering**: Within each bin, time points were clustered in their original high-dimensional space.
6. **Graph Construction**: A graph was built where each cluster becomes a node. An edge connects two nodes if their underlying clusters share at least one time point. Nodes represent recurring brain states, and edges represent transitions between them.

Graph-Theoretic Analysis

- **Degree Centrality:** The number of edges connected to a node; a "hub" state.
- **Betweenness Centrality:** The fraction of all shortest paths passing through a node; a "bridge" state.
- **Closeness Centrality:** How quickly all other nodes can be reached; an "efficient" state.

Results

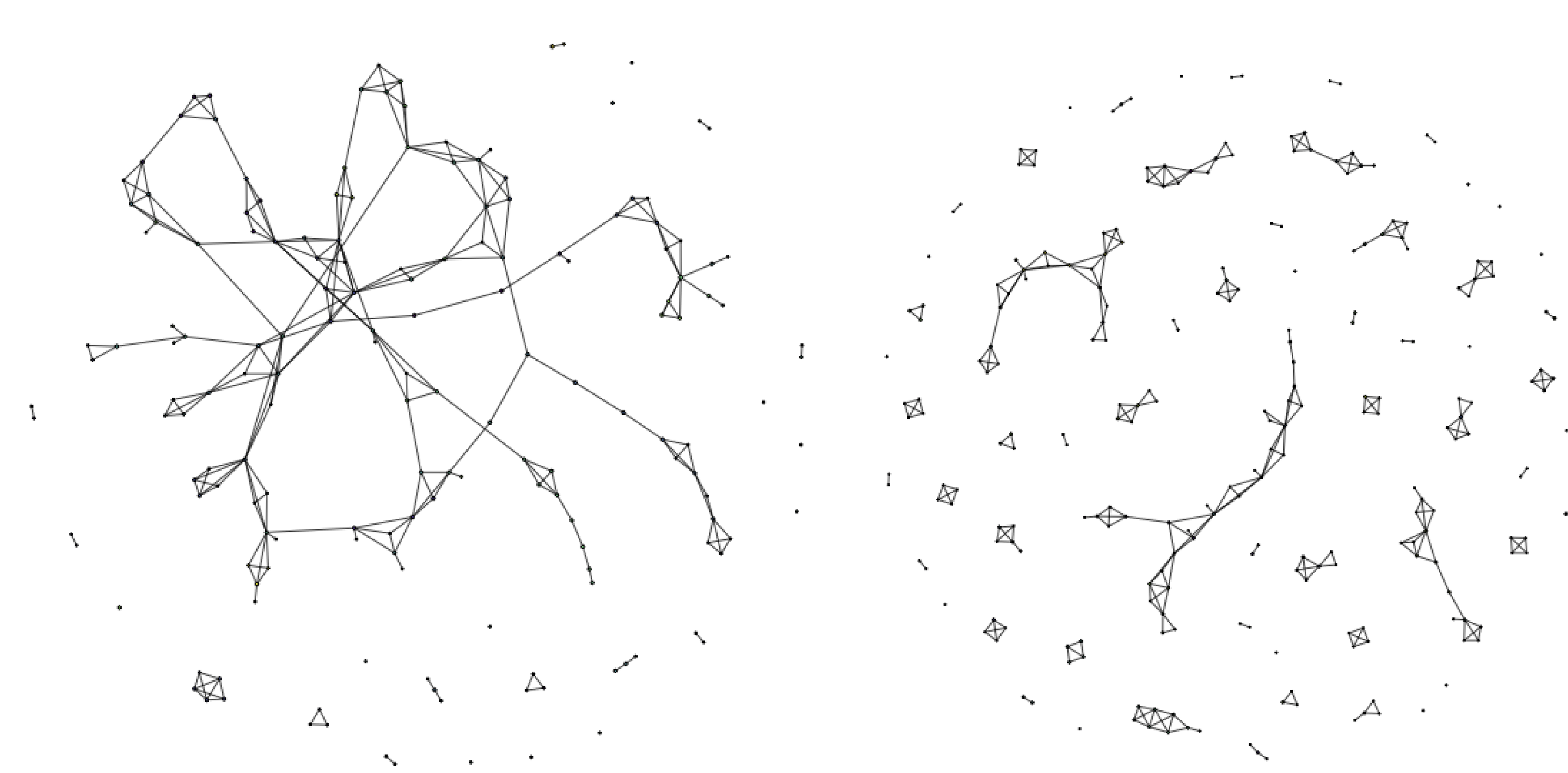
Increased Network Centrality in ADHD at Select Sites



Group Differences in Centrality Scores for the NYU Dataset. Box plots compare betweenness, closeness, and degree centrality between Typically Developing Controls (TDC) and individuals with ADHD. The ADHD group shows significantly higher betweenness and closeness centrality.

	Betweenness		Closeness		Degree	
Site	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
NYU	**0.0039**	0.371	**0.0137**	0.306	0.0873	0.188
NeuroIMAGE	**0.0508**	0.483	**0.0351**	0.536	**0.0039**	0.805
OHSU	**0.0577**	0.376	0.1003	0.305	0.1758	0.221

Summary of Group Differences in Centrality Measures Across Three Sites. One-tailed p-values and Cohen's d are reported for the comparison between ADHD and TDC groups.



Example Mapper Graphs Illustrating Topological Differences. The graphs visualize the brain state networks for two representative participants from the NYU cohort. The left panel shows the shape graph from a participant with a high ADHD Index and high mean betweenness centrality, illustrating a highly interconnected core structure suggestive of a rigid dynamical system. Panel (b) shows the shape graph from a TDC participant with low mean betweenness centrality, displaying a more fragmented and peripheral structure, which may reflect a more flexible and exploratory traversal of brain states.

Centrality Correlates with Symptom Severity in the NYU Cohort

	ADHD Index		Inattentive		Hyper/Impulsive	
Centrality Measure	**r**	**p-value**	**r**	**p-value**	**r**	**p-value**
Betweenness	0.154	**0.0126**	0.122	**0.0378**	0.177	**0.0049**
Closeness	0.112	0.0525	0.078	0.1292	0.111	0.0542
Degree	0.047	0.2483	0.018	0.3987	0.047	0.2460

Summary of Pearson's Correlations between Centrality and ADHD Symptoms (NYU Dataset). One-tailed p-values are reported.

Discussion

- Our primary finding is that individuals with ADHD (in the NYU and NeuroIMAGE cohorts) exhibit significantly higher centrality in their brain state networks.
- High centrality suggests a dynamical system characterized by a densely interconnected core of states. In the resting state, this is atypical and suggests brains in the ADHD group may be "rigidly locked" into constrained, repetitive patterns of activity , rather than flexibly exploring a diverse repertoire of states.
- This "topological rigidity" could be the neural substrate for the cognitive inflexibility and attentional lapses common in ADHD. The positive correlation between centrality and symptom severity in the NYU cohort supports this model.
- The failure to replicate these findings across all three sites is a critical result , underscoring the challenge of inter-site heterogeneity in the ADHD-200 dataset. Our mixed results likely reflect a combination of true biological heterogeneity within the ADHD diagnosis and methodological variance across imaging sites.

Conclusion

TDA-Mapper is a powerful method for examining the dynamical organization of brain activity in ADHD. Our findings suggest ADHD is associated with increased centrality of brain state networks at rest, a signature that may reflect an inefficient and rigid functional organization. This work simultaneously highlights the critical need for data harmonization to translate advanced computational tools into reliable clinical applications.

References

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