Spatial and Temporal Shapes in ADHD Brains

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1 Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a mental disorder associated with structurally underdeveloped cortical and subcortical areas as well as functionally disrupted network or circuit. This project studies 10 ADHD vs healthy resting-state fMRI dataset [1] and investigates spatial and temporal shapes based on graph embeddings and dimensionality reduction methods. Prior to the analysis, dataset was preprocessed using Python Nilearn package with Harvard Oxford atlas, standardization and detrending applied. The project code can be found here: `https://colab.research.google.com/drive/18Q0MJg4MesgYXxn97k8GC2_mCF58NMQu?usp=sharing`.

2 Methods and Results

2.1 Spatial Behaviour

For each subject, fMRI data was mapped to atlas to produce data of shape (number of ROIs × resting-state time) where number of ROIs was 48 and 21 for cortical and subcortical atlas mappings respectively. Pairwise Pearson correlation matrix (functional connectivity) between ROIs was then calculated to form of a graph where ROIs are nodes and edges are present if correlation between ROIs is above certain threshold. Mean absolute functional connectivity and multiple graph measures as described below were then deduced to study the spatial property of the graph. Note that the implementation and explanation are based on Python package Networkx.

- clustering coefficient:
$$\frac{2\,(\#\text{triangles through a node})}{(\text{degree})\,(\text{degree}-1)} \quad (\text{averaged over nodes})$$
- degree coefficient: average number of edges per node
- global efficiency: inverse of shortest distance between nodes, averaged across pairs of nodes

Although the following results are not statistically significant under t-test due to limited sample size and subject variability, median of mean absolute correlation and all graph measures were lower for subjects with ADHD compared to healthy subjects, in both cortical and subcortical graphs across all 5 edge threshold from 0.3 to 0.7 with an increment of 0.1. This suggests that ADHD (sub)cortical areas may show less correlated, clustered, connected network with an inefficient functional behaviour for across-ROIs communication.

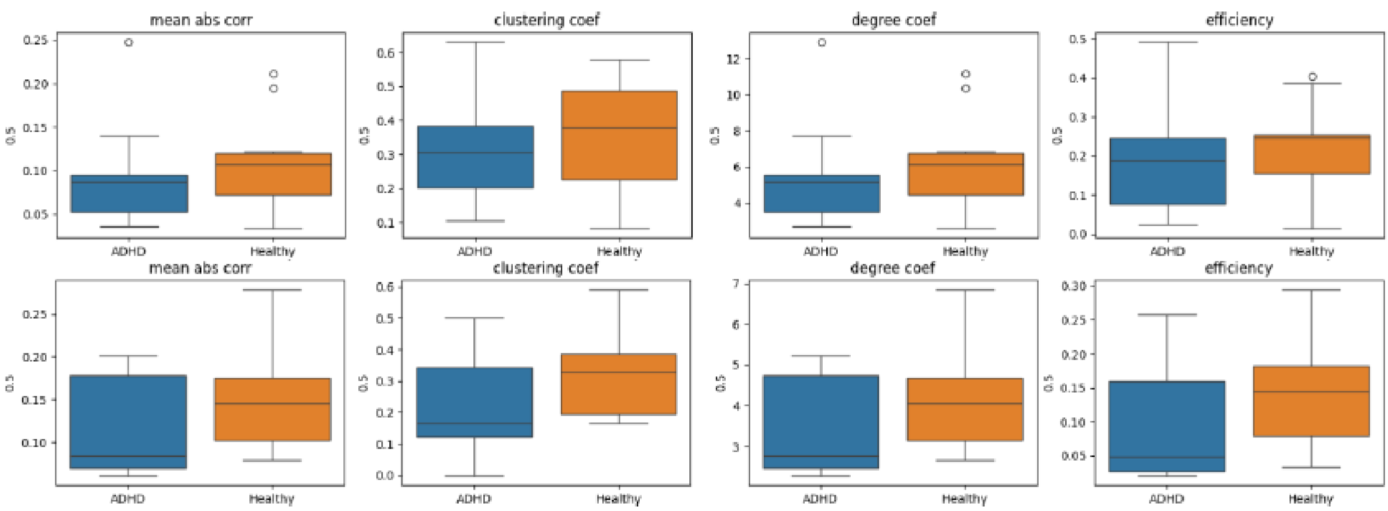

Figure 1: Graph Measures when edge threshold = 0.5 (Top) Cortical (Bottom) Subcortical

2.2 Temporal Behaviour

2.2.1 Dynamics

For each subject, correlation between the ith fmri image and the i+1th fmri image was averaged to study the temporal consistency/fluctuation during resting-state. Note that [2] implemented an advanced version of such correlation to study Bold signal change and emphasized its difference from simple mean signal change. Although not statistically significant, both areas, subcortical areas in particular, showed less mean correlation for subjects with ADHD, suggesting less consistent and more fluctuating BOLD signal across time.

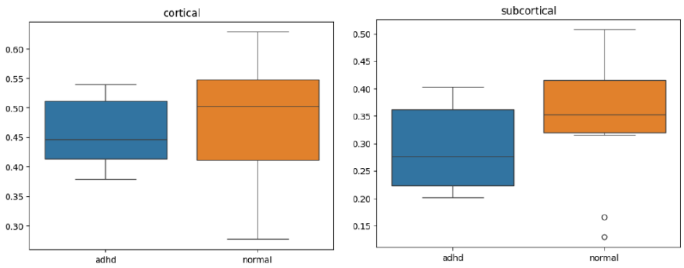

Figure 2: Mean correlation between consecutive fmri images (left) Cortical (right) Subcortical

2.2.2 Shape

The follow-up question is the degree to which such inconsistent and fluctuating temporality occur in subcortical areas. As a starting point, each subject's fMRI data of the shape (number of ROIs × resting-state time) was dimensionality-reduced to a vector with shape (2× resting-state time) where PCA, T-SNE and LLE were implemented; each 2D timepoint was then scatter-plotted to analyze how dynamics differ across time. Note that the across-time dimensionality reduction and plotting were directly inspired by [3], which suggested a topology-based framework for studying task fMRI dynamics. Results are as follows, where multiple subjects with ADHD showed mixing timepoints on the plot yet healthy subjects were not different, inspiring further quantitative investigation.

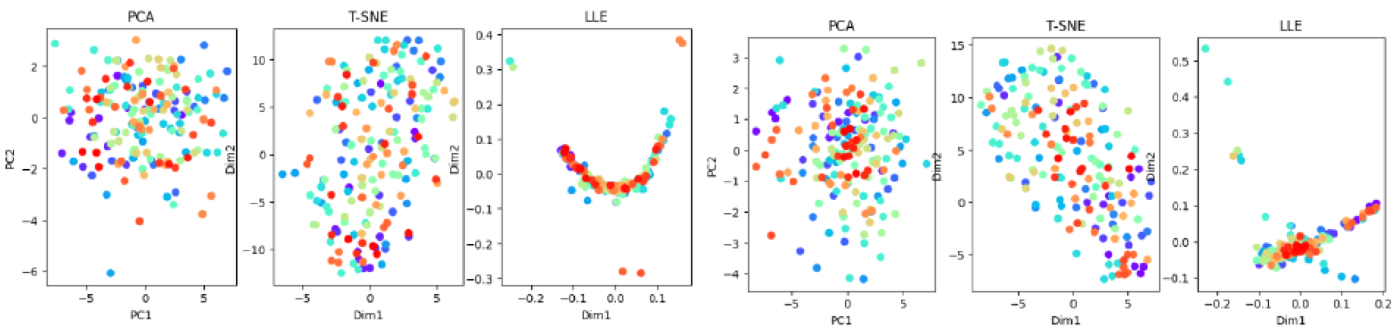

Figure 3: Dimensionality-reduced timepoints scatterplot in the subcortical area (left) ADHD (right) Healthy

As an indirect quantitative analysis, Support Vector Classifier with linear kernel was implemented to predict roughly how much time has passed since the start of taking fMRI in bins of 5, given dimensionality-reduced timepoints. The accuracy of each prediction was then calculated to study how well the timepoints represent the actual time bins. The accuracy deduced showed a lower distribution (though not lower median) for ADHD subjects using all 3 dimensionality reduction methods, suggesting their timepoint features may be less representative of actual time and more fluctuating than healthy subjects. Note that the explained variance ratio of PC1 is also lower in ADHD subjects suggesting their non-linear, high-variance timepoints dynamics. The classification pipeline directly followed [4].

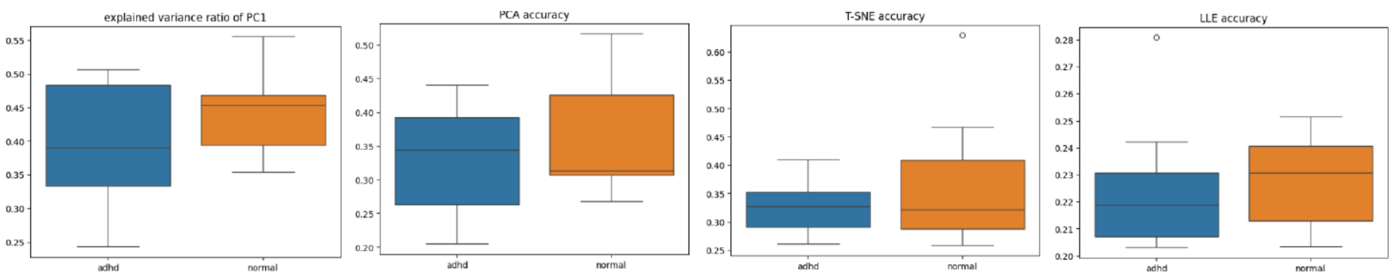

Figure 4: (left) PC1 explained variance ratio (right) Prediction (classification) Accuracy both in the subcortical areas

3 Discussion

This study compares ADHD vs healthy subjects based on spatial graph embeddings and temporal dimensionality-reduced dynamics, and the observed patterns may indicate the spatially less correlated/clustered/connected/efficient (sub)cortical areas and temporally fluctuating subcortical areas in ADHD brains. Note that the results in this project are not statistically significant and there are rooms for further investigation on temporal shape with increased sample size and complex topological data analysis techniques (e.g. mapper algorithm/persistent homology diagram).

References

[1] P. Bellec, C. Chu, F. Chouinard-Decorte, Y. Benhajali, D. S. Margulies, R. C. Craddock, The Neuro Bureau ADHD-200 Preprocessed repository. *NeuroImage*, 2017.

[2] L. Möhring, J. Gläscher, Prediction errors drive dynamic changes in neural patterns that guide behavior. *Cell Reports*, 2023.

[3] M. Saggar, O. Sporns, J. Gonzalez-Castillo, et al., Towards a new approach to reveal dynamical organization of the brain using topological data analysis. *Nature Communications*, 2018.

[4] W1D4-2 Dimensionality reduction:
`https://colab.research.google.com/drive/1XlLMnmbt9eOkWnqc-UkUJUpY96m20iQw?usp=sharing#scrollTo=1_NCBkQQ1_zm`

- ChatGPT-4o (Pro) for code writing and debugging (e.g. Nilearn and Networkx)
- Networkx Reference for graph measure implementation and explanation: `https://networkx.org/documentation/stable/reference/index.html`