

# Final Project: Graphical Models for ASD Connectivity

Zhenkun Fang - zf2352

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## Goal and Motivation

The human brain acts as a complex system of interacting regions. Modeling these interactions as a graph—where nodes represent regions of interest (ROIs) and edges represent functional connectivity, which allows researchers to understand the organizational principles of neural communication. A key application of these models is distinguishing between neurotypical brain function and identifying alterations associated with conditions such as Autism Spectrum Disorder (ASD).

In this project, I estimated functional brain networks using resting-state fMRI time-series data. My analysis has one primary objective:

**Group Comparison:** Quantitatively compare the connectivity patterns of ASD subjects versus NT controls to determine if the inter-group differences exceed the natural intra-group variability.

## Data

I analyzed resting-state fMRI data from the ABIDE (Autism Brain Imaging Data Exchange) repository. The dataset consists of blood-oxygen-level-dependent (BOLD) signals extracted from 160 Regions of Interest (ROIs) based on the Dosenbach atlas.

### Data Preprocessing:

I analyzed fMRI time-series data extracted from 160 Regions of Interest (ROIs). The raw data files were processed to ensure correct dimensions (180 timepoints  $\times$  160 ROIs). I calculated the Pearson Correlation Matrix for each subject to represent their functional connectivity.

# Methods

## Functional Connectivity

For each subject, I calculated the  $160 \times 160$  Pearson correlation matrix ( $S$ ), where each entry  $S_{ij}$  represents the marginal linear association between the time-series of ROI  $i$  and ROI  $j$ .

## Group Comparison Strategy

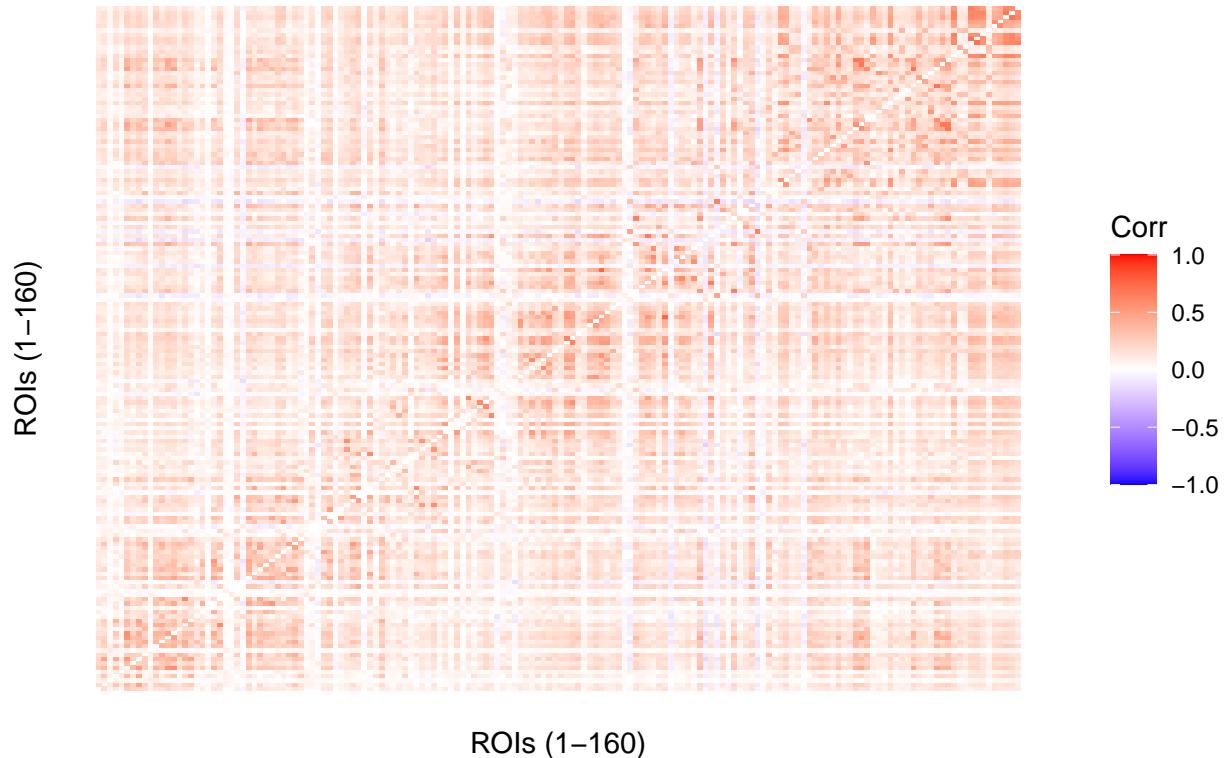
To assess whether ASD and NT subjects exhibit distinct network “signatures,” I performed a distance-based analysis:

1. Metric: I calculated the Euclidean distance between the vectorized correlation matrices of every pair of subjects.
2. Comparison: I divided these pairwise distances into two categories:
  - Within-Group: Distance between two ASD subjects OR between two NT subjects.
  - Between-Group: Distance between one ASD subject and one NT subject.
3. Hypothesis Testing: I performed a two-sample t-test to determine if the Between-Group distances were significantly larger than the Within-Group distances.

# Results

## Average Functional Connectivity

Figure 1. Comparison of Euclidean Distances in Functional Connectivity



**Figure 1** shows the average functional connectivity matrix across all subjects, where each cell represents the mean Pearson correlation between the time series of two ROIs out of 160 total ROIs. Warmer colors (red) indicate stronger positive correlations, cooler colors (blue) indicate negative correlations, and white indicates near-zero correlation.

Overall, the matrix is dominated by light red and near-white values, suggesting that most ROI pairs exhibit weak to moderate positive functional connectivity on average across subjects. Strong negative correlations are rare, indicating that anti-correlated activity between regions is not prominent at the group level.

## Group Differences (ASD vs. NT)

To quantify the distinctiveness of the groups, I performed a two-sample t-test comparing the distribution of inter-subject distances.

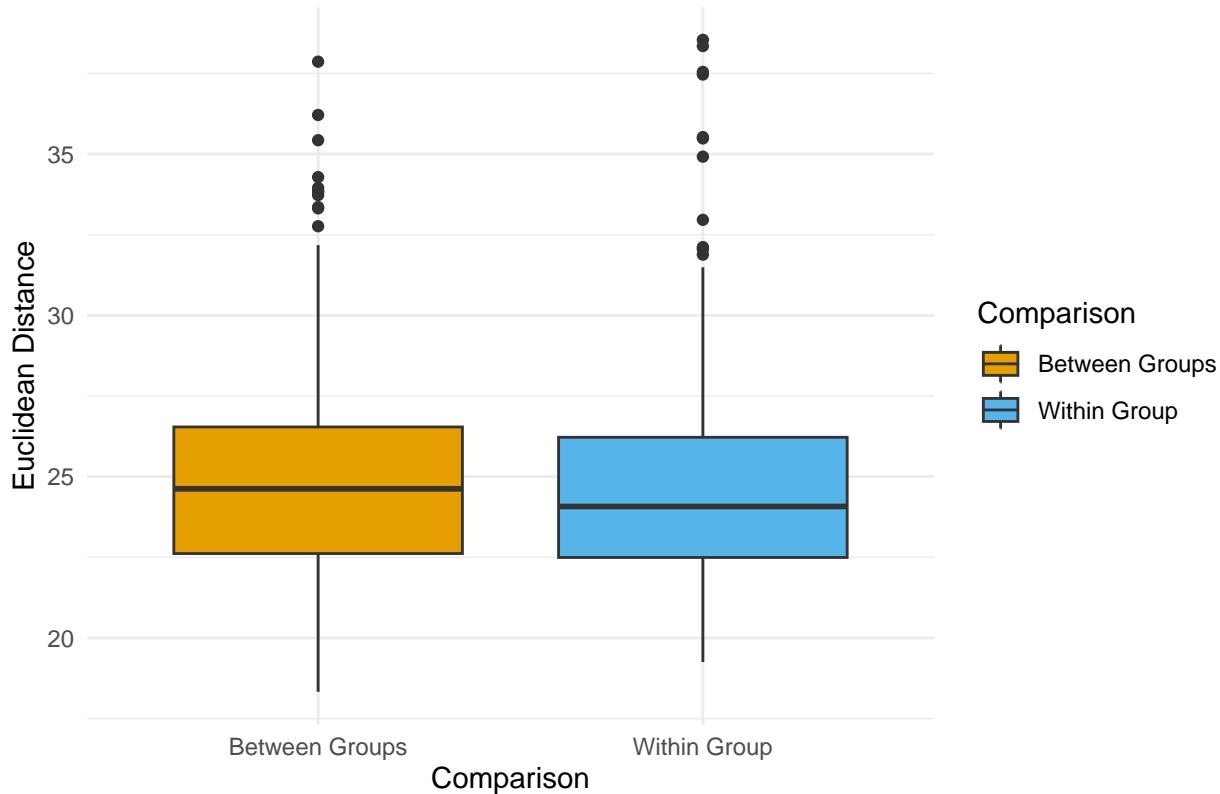
The analysis compared the mean Euclidean distance between subjects of different groups (ASD vs. NT) against the mean distance between subjects within the same group.

Between-Group Mean Distance: 25.00

Within-Group Mean Distance: 24.92

The t-test yielded a p-value of 0.414. This result is not statistically significant, indicating that the group-level differences are not large enough to overcome the high inter-subject heterogeneity found in this sample.

**Figure 2. Heterogeneity Analysis**



**Figure 2** display a substantial overlap between the “Within-Group” and “Between-Group” distributions. Visually, the median distance for mixed pairs is similar to the median distance for pairs within the same group. This indicates that the functional connectivity difference between an ASD subject and a control is not noticeably larger than the natural variability found between two neurotypical individuals.

## Conclusion

### Interpretation of Findings

In this project, I investigated whether functional brain networks could distinguish individuals with Autism Spectrum Disorder (ASD) from Neurotypical (NT) controls. My primary finding—that the topological distance between groups is not significantly larger than the distance within groups—highlights a critical challenge in computational psychiatry known as **heterogeneity**.

These results align with the “idiosyncratic connectivity” hypothesis described in the course readings (e.g., *Dajani et al., 2019*). While ASD is diagnosed behaviorally, the underlying neural mechanisms are likely diverse. Unlike a focal lesion which produces a consistent network disruption, ASD appears to involve subject-specific alterations.

## Limitations

Several limitations should be noted. First, the sample size ( $N = 27$ ) is relatively small for high-dimensional fMRI data ( $p = 160$  ROIs), limiting the statistical power to detect subtle group effects. Second, resting-state fMRI is sensitive to head motion, which can introduce spurious correlations; while the data was preprocessed, strict motion censoring might further refine the results.

This analysis demonstrates that Autism Spectrum Disorder does not manifest as a single, uniform disruption of the functional brain network. Instead, the high degree of biological heterogeneity suggests that future research should move beyond case-control averages and toward characterizing the unique connectivity fingerprint of each individual.