Network Analysis and Classification of ASD using fMRIs

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1 Introduction

Autism spectrum disorder (ASD) is characterized by qualitative impairment in social reciprocity, and by repetitive, restricted, and stereotyped behaviors/interests. Previously considered rare, ASD is now recognized to occur in more than 1% of children [1]. Despite continuing research advances, there is still an urgent need for methods to diagnose ASD at earlier ages and more reliably.

In this paper we examine the potential of diagnosing ASD by extracting, analysing, and classifying networks from functional magnetic resonance images (fMRIs). We extract functional networks using independent component analysis and time series analysis. We perform graph analysis using global and nodal measures on the networks to look for quantitative differences between the networks of ASD and TD subjects. We use a support vector machine to classify the networks and perform a grid search using stratified 5-fold cross validation to determine its accuracy.

2 Data

We will be working with functional magnetic resonance imaging (fMRI) data aggregated by the Autism Brain Imaging Data Exchange (ABIDE) initiative, collected from 16 international imaging sites [2]. The data consists of fMRI scans along with an extensive array of phenotypic information of 1,112 subjects, including 539 from individuals with ASD and 573 from typical controls, all between the ages 7 and 64, with a median age of 15. The control and experimental group don't have statistically significant differences in their sex, age, mean and maximum head motion, or their full-scale, verbal, and performance IQ [1].

Data from ABIDE was preprocessed by five different teams using their preferred tools. Functional preprocessing was performed using: the Connectome Computation System (CCS), the Configurable Pipeline for the Analysis of Connectomes (CPAC), the Data Processing Assistant for Resting-State fMRI (DPARSF) and the NeuroImaging Analysis Kit. Due to the controversies surrounding bandpass filtering and global signal regression, four different preprocessing strategies were performed with each pipeline: all combinations of with and without filtering and with and without global signal correction. To limit the variance between outputs to just preprocessing, statistical derivatives for each pipeline and strategy were calculated by the CPAC software [1].

Due to space and processing limitations, we examined the functional networks of 58 subjects with ASD and 62 under typical development (TD), for a total of 120 subjects. Additionally, to reduce the number of confounding factors, we selected subjects who were exclusively right-handed, and between the ages of 13 and 18, inclusive.

3 Methods and Results

In this section we detail our work on extracting functional networks from the fMRI data, present our analysis of these networks, and show the methods to classify ASD.

3.1 Network Extraction

The Nillearn library is very helpful for extracting networks from fMRIs. It has inbuilt functions for accessing the preprocessed ABIDE data, performing independent component analysis (ICA), extracting regions of interest (ROI), performing time series analysis (TSA), and getting connectivity measures [3]. We use all these functions to create our networks.

We begin by fetching the 120 subjects discussed in the Data section and their corresponding fMRIs and category (ASD/TD). ICA is a useful approach for finding independent sources from fMRI images. ICA and similar techniques can be therefore used to define regions or networks that share similar blood-oxygen-level-dependent (BOLD) signals across time. The CanICA is an inbuilt Nilearn function that incorporates information both within-subjects and across subjects to arrive at consensus components. Using CanICA, we fit an ICA object with ten components to all the fMRIs in our dataset. The individual components can be retrieved in the brain space. The plot for the 10 ICA components we attained is illustrated in the figure below.

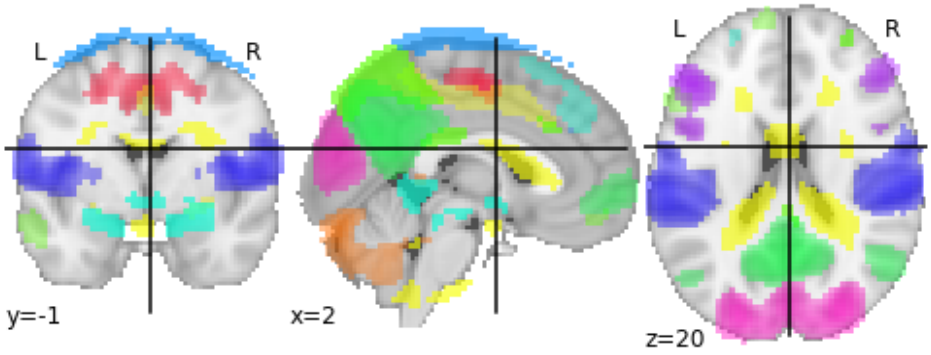

Figure 1: 10 ICA Components

The ten components retrieved from ICA are functional components, meaning they represent regions of the brain that have distinct BOLD signals. We want to convert these to regional components so we can have nodes with physical coordinates in the brain space. These are called regions of interest. Regions of interest must be continuous to represent physical regions of the brain. To get regions of interest, we use the Nilearn inbuilt regions extractor that takes in the functional components we got from ICA and converts them into regional components. The extractor splits the functional components into physical components. For example, the functional component hightled in blue as seen in the y- and z-axis view of figure 1 above, will be split into two regions of interest since it is not continuous. All functional components are split into either 2, 3, or four regions of interest, culminating to 35 regions of interest as seen in figure 2 below.

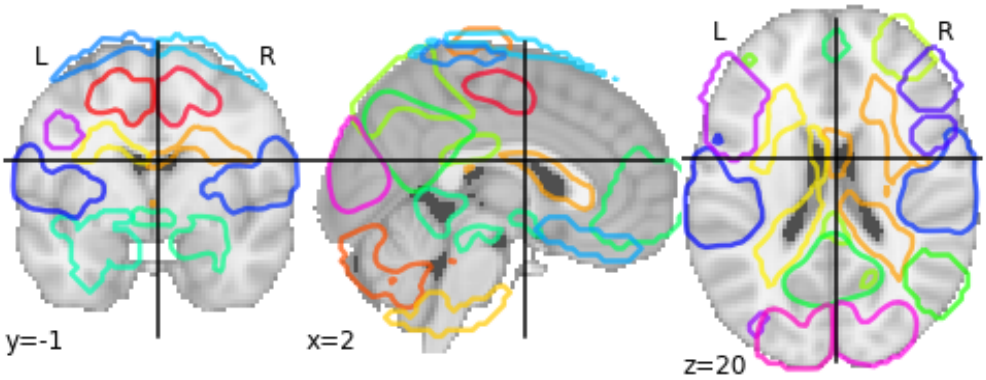

Figure 2: 35 Regions of Interests

We can find the centroid of each region and let those represent the coordinates of the nodes of our network. The nodes are displayed in figure 3 below.

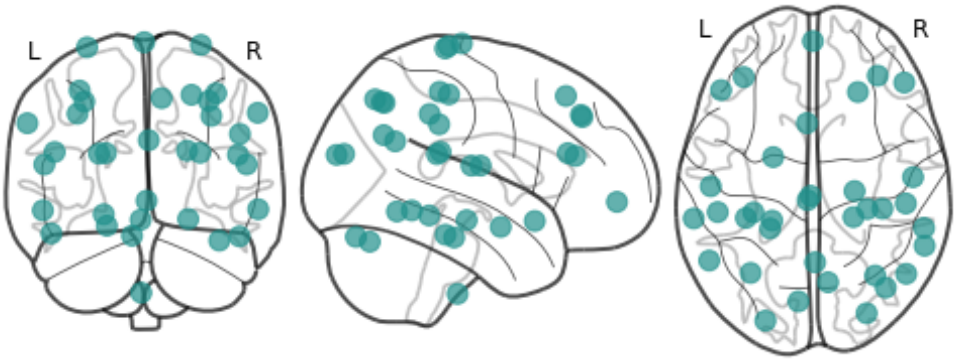

Figure 3: 35 Nodes

Now that we have our nodes, we want to find how they interact with each other. To do this, we find the time series data for a brain and calculate the correlation matrix for all of the ROIs. Each correlation matrix is a square matrix of 35 rows and columns where the i-j value represents the mean correlation between the ith and jth region of interest. The correlations between the regions become the weights of edges between nodes in the graph. Once the correlation matrix is calculated for each brain, the mean correlation matrix for ASD and TD can be computed. The mean correlation matrices for ASD and TD subjects are shown in figure 4 below. These mean correlation matrices can be used to create average ASD and TD graphs. The 120 individual graphs will be used for classification, while the average graphs will be used for network analysis. The average graphs can be seen in figure 5 below.

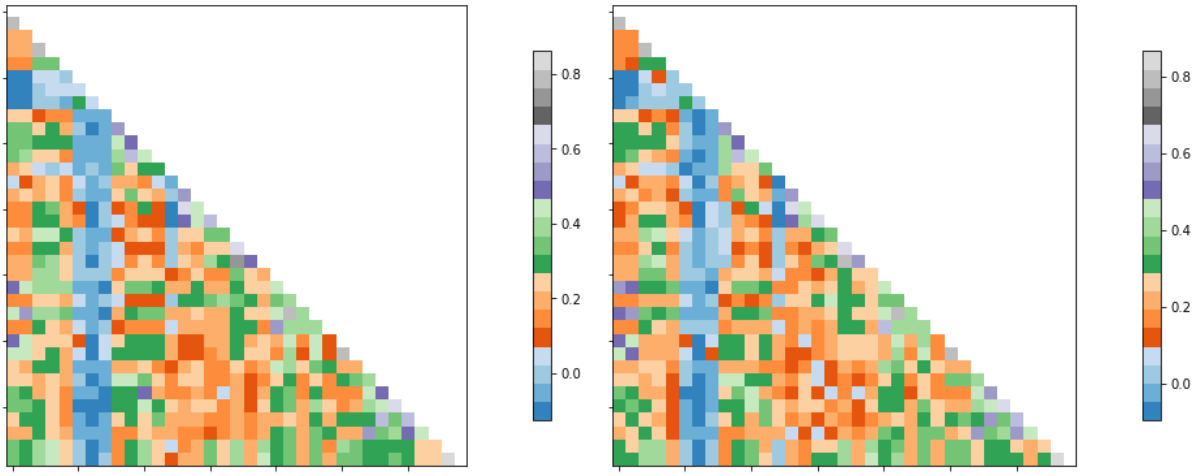

Figure 4: Mean Correlation between 35 ROIs for ASD (left) and TD (right)

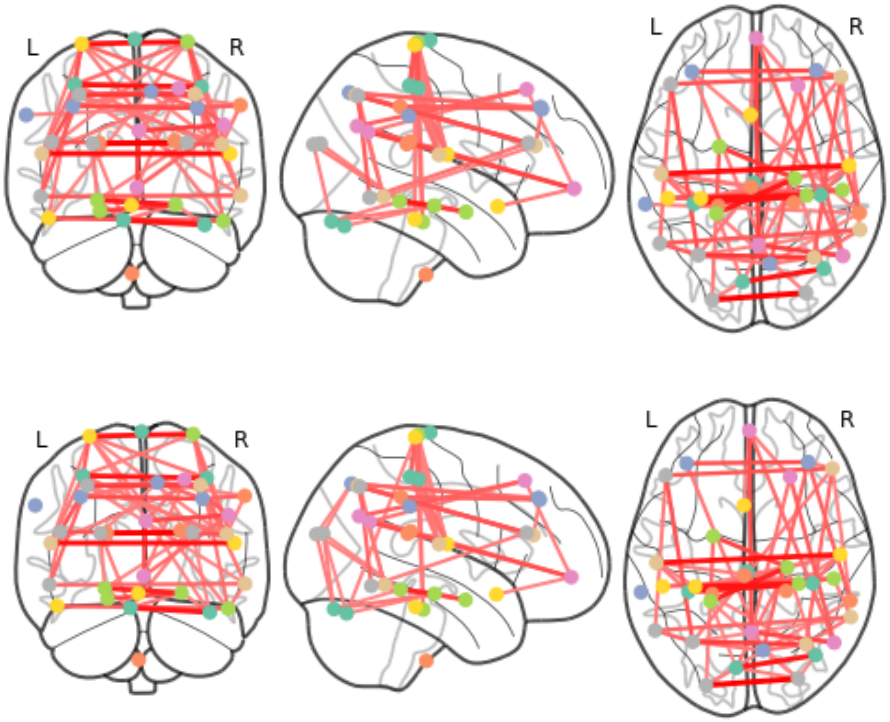

Figure 5: Correlation between ROIs for ASD (top) and TD (bottom) with 80% Threshold

We correspond each region of interest to a biological region of the brain by using the Harvard-Oxford Atlas that has 96 labeled regions [4]. We accomplish this by finding the closest atlas coordinate to each of our 35 node coordinates. For instance, the teal color node at the top of the leftmost diagram in figure 5 above corresponds to the Left Inferior Frontal Gyrus which has a number of functions including the processing of speech and language. We will use the associative biological labels for each ROI for our analysis.

3.2 Network Analysis

We now analyze the networks that we previously extracted using the Networkx library [5]. For analysis, we use the ASD network that was created by averaging all of the individual ASD networks. The same is true for the TD network. There are very few graph analysis algorithms that can be used on full-connected weighted and signed graphs, so we converted our networks to sparse binary graphs. This was done by only including the top 20 percentile of edges in our ASD and TD networks. We will use various tools and measures to analyze the graphs. Some of these measures are on an entire graph, while others capture information on a per-vertex basis.

In Table 1, we compare the overall density, transitivity, and clustering between the ASD and TD networks. First, note that the density of the two networks are equal, which is necessary to compare further metrics. Then, it is apparent that both the transitivity and the clustering measures are higher in the ASD network than in the TD network. This clearly shows that the ASD networks on average have more dense clusters of nodes. Biologically, this suggests that ASD brains have more regions of dense neural connection than typical, but fewer connections spanning these dense regions.

Measure	ASD Network	TD Network
Density	0.2067	0.2067
Transitivity	0.5259	0.4685
Clustering	0.5685	0.5185

Table 1: Global Measures Comparing ASD and TD

We can compare the ASD and TD networks using centrality measures. Table 2 shows the region of interest that corresponds to the node with the maximum value and its measure for degree, closeness, and betweenness centrality. ASD - TD and TD - ASD represents the difference between the centrality measure for each node.

Network	Degree	Closeness	Betweenness
ASD	LSPL: 0.5294	LSPL: 0.6013	LSPL: 0.1357
TD	LSPL: 0.5294	LSPL: 0 .5888	LSPL: 0.1319
ASD - TD	LPC: 0.1176	LPC: 0.0943	LPC: 0.0497
TD - ASD	RSFG: 0.0876	RMFG: 0.0616	RSFG: 0.0410

Table 2: Nodal Measures Comparing ASD and TD.

Abbreviation	Brain Region
LSPL	Left Superior Parietal Lobule
RPG	Right Postcentral Gyrus
LPC	Left Precuneus Cortex
RSFG	Right Superior Frontal Gyrus
RMFG	Right Middle Frontal Gyrus

Table 3: Region Labels Key

LSPL is the part of the brain involved with spatial orientation, and receives a great deal of visual input as well as sensory input from one's hand. LSPL has the largest measures for each of the three types of centrality for both the ASD and TD network, which makes sense since it interacts with many parts of the brain [6]. LPC is primarily responsible for receiving and processing sensory input such as touch, pressure, heat, cold, and pain. LPC has a higher centrality in the ASD network than TD. RSFG and RMFG are involved with high-level cognitive function, including attention, working memory, and social emotional evaluation of stimuli. RSFG and RMFG have a lower centrality in the ASD network than the TD. Our analysis of these networks is supported by scientific studies on ASD.

3.3 Classification

We trained a classifier to label our extracted functional networks as either ASD or TD in order to estimate how well the networks capture differences between ASD and TD brains. For this analysis, we started with the 120 adjacency matrices created during network extraction. The 35 nodes represent areas of concentrated activity in the brain, and the weighted edges represent the correlation of activity between two regions. Each 35x35 adjacency matrix was processed by removing the upper triangular section of the matrix including the main diagonal. This eliminated redundant and meaningless entries from the matrix which provided no value for classification. The matrices were then flattened, giving us 120 feature vectors of dimension 1,156.

We chose our classifier to be a default Scikit-learn support vector classifier (SVC) because our task involved supervised learning for binary classification, which SVCs excel at, and we chose accuracy to be our performance metric because our dataset was split roughly equally between ASD and TD subjects. We then performed a grid search to determine the best hyperparameters for our model. We ran stratified 5-fold cross validation for varying values of C, the regularization term of the SVC, and for a value we will call the threshold percentile. The threshold percentile is a percentile of edge weights for each feature vector below which all weights are set to zero. For instance, if the threshold percentile is 70%, the smallest 70% of edge weights for each feature vector will be set to zero. We decided to employ threshold percentiles because we determined

during network analysis that on average, the edges of functional networks of ASD and TD subjects are mostly the same, leading us to believe that most connections would hold insignificant predictive power. Thus, removing the majority of the connections was meant to lower the chance our classifier would learn spurious correlations.

Through grid search, we obtained our best accuracy of 0.6167 with C being 10, and the threshold percentile being 88%. We saw significant performance increases for certain high threshold percentiles for C = 1 and C = 10, confirming our hypothesis that most edge weights held insignificant predictive power. High threshold values also made performance more volatile, which is expected as the total number of features are reduced. Averaging over all the threshold percentiles, our classifier clearly performed best with a C value of 10. This indicated that our classifier did not benefit from regularization. This means our classifier was not in danger of overfitting, and thus would likely perform significantly better with a larger training set. The results of our grid search are in figure 6 below.

The accuracy of 0.6167 indicates that there are non-trivial differences between our extracted functional networks of ASD and TD subjects. We believe that with a larger training set accuracy could significantly increase, and thus that diagnosing ASD by extracting and classifying functional networks is a promising approach.

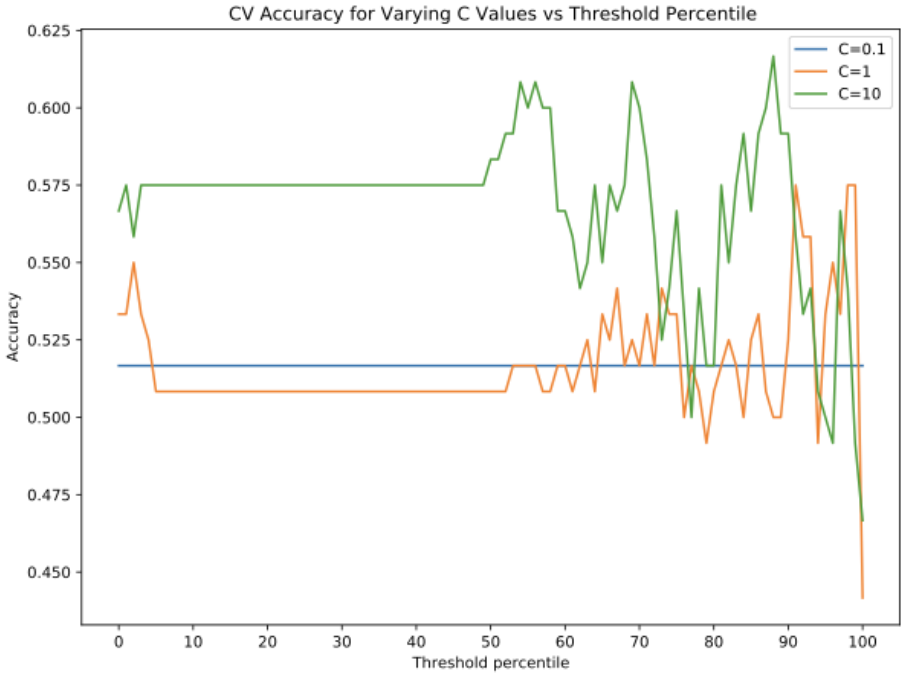

Fig. 6: The results of our graph search. Accuracy was overall highest for C = 10, meaning that our model did not need regularization. This indicates that overfitting was not an issue, and our classifier would likely be able to perform better with a larger training set. The maximum accuracy is 0.6167 with C = 10 and threshold percentile = 88%.

4 Conclusion

In this paper, we extracted functional networks from fMRI data from ASD and TD subjects, analyzed the characteristics of their average networks, and trained a classifier to discriminate between ASD and TD networks. We found that the transitivity and clustering measures for the average ASD graph were higher than that of the average TD graph, indicating that ASD brains tend to have stronger neural circuits with fewer connections between them. We also found that the Frontal Gyrus region which is involved with high-level cognitive function is more connected in the TD network than ASD, and the Postcentral Gyrus which processes sensory input is more connected in ASD subjects than TD. Finally, using classification we determined that there are non-trivial differences in the extracted functional networks for ASD and TD subjects. Due to our classifier not benefiting from regularization, we infer that there is potential for classifiers to achieve accuracy significantly above our value of 0.62 if a larger training set is used. We believe this shows that network extraction for classification has potential as a diagnostic tool for ASD.

Collaborators

Rajas Gupta: Network extraction, network analysis
Vijay Sharma: Network classification, additional research
Code: https://github.com/rajasg/asd_project

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