

Exploring the Impact of Autism Spectrum Disorder on the Structural Connectome

John Popeck

Computer Science

College of Computing and Informatics at Drexel University

Philadelphia, United States

jp3798@drexel.edu

Abstract—Recent studies have begun to examine whether patients with neurological disorders show distinctive network properties in their connectomes. If so, the findings have the potential to lead to increased understanding of the underlying nature of the disorders, as well as more accurate diagnoses. In this paper I explore the structural connectomes of individuals with autism spectrum disorder (ASD), and compare them to a control set of individuals without the disorder. I attempt to determine whether there is a group difference for any network measures between the ASD set and the control set, and whether a classifier can be trained to identify whether a connectome is from an individual with ASD. I also investigate whether any network measure shows a correlation with the level of severity of ASD.

I. INTRODUCTION

Network neuroscience involves the study of connectomes, which are matrix representations of brain networks encompassing the pairwise connections between the various regions of the brain. Overall the field attempts to understand how connectomes relate to the brain's capacity and function. In recent years a specific area of focus has been how diseases and disorders impact the connectome. Since the connectome represents the network of communication patterns between different brain elements, it provides a powerful tool to study the nature of neurological disorders which impact the way the brain operates.[2]

Autism spectrum disorder (ASD) is one such neurological disorder which has received this attention. ASD is a common disorder that affects close to one percent of the population, making it an obvious and important candidate for study.[3] Studies analyzing graph theory measures of the connectomes from subjects with ASD have shown that ASD connectomes exhibit some distinctive network properties. A 2015 study of structural connectomes found that subjects with ASD had decreased global efficiency, increased characteristic path length, and decreased strength of connections.[3] A 2021 study of functional connectomes found a higher mean modular variability in ASD subjects, suggesting more overall instability in global brain dynamics.[4]

In addition to network analysis, researchers have also used connectomes to investigate finding classifiers and biomarkers for ASD. A classifier or biomarker for ASD would be an objective empirical measure which can be shown to clearly predict whether an individual has the condition or not. Research on ASD classifiers does not always involve

connectomes. For example, Tunc et al.[1] used evaluation scores like MESL (Mullen Scales of Early Learning) and VABS (Vineland Adaptive Behavior Scales) as input data to a machine learning technique called a Support Vector Machine (SVM) to establish an ASD classifier. The classifier achieved high performance, with an accuracy of 84%.[1] Several studies searching for classifiers using functional connectomes have also been performed, with good results. One in particular showed that a functional connectome collected from a subject at the age of six months could be used to predict autism status at the age of 24 months.[5]

In this paper I will attempt to add to the previous work done on both network analysis and on finding a classifier for ASD. I will use a dataset with structural connectomes from both ASD subjects and healthy controls, compute graph theory measures on the connectomes, and attempt to determine if there is a significant statistical difference between any measure for the ASD set and the control set. I will then input the data into a Support Vector Machine and use it to generate a classification boundary which can be used to predict whether an individual has ASD or not. Finally, I will also analyze whether any of the computed measures correlate to the severity of ASD diagnosed in each subject.

II. MATERIALS AND METHODS

A. Materials

My analysis will be performed on the CHARM dataset, provided by Penn Medicine. The CHARM dataset contains structural connectomes from around 400 subjects. The data was collected from eleven different sites, and the subjects are a mix of patients with ASD and patients without ASD (healthy controls).

Each subject has only one brain image, but connectomes were generated using two different atlases, with the end result that there are two connectomes for each subject. The two atlases used are the Desikan atlas and the Schaefer atlas. The Desikan atlas has 86 regions, and thus connectomes created using this atlas have 86 nodes in their network. The adjacency matrix from these connectomes is size 86 x 86 and has non-zero values in every position where there is a connection between regions. The edges are weighted, with greater values indicating a stronger connection between the two regions. The Schaefer atlas has 220 regions, and connectomes created using

this atlas have 220 nodes. Edges are also weighted in these connectomes, and so adjacency matrices are similar as to what was described for the Desikan atlas connectomes, except they have size 220 x 220.

Each subject also has their sex, age, diagnosis (ASD or non-ASD), Autism Diagnostic Observation Schedule Calibrated Severity Score (ADOS_CSS), Social Communication Questionnaire (SCQ) score, and IQ recorded. I will use the diagnosis to distinguish between subjects with ASD and subjects without ASD. I will use the ADOS_CSS and SCQ score to interpret ASD severity. The ADOS_CSS score ranges from 1 to 10 with a higher score representing a more severe level of ASD.[1] The SCQ score can range from 0 to 39 with a higher score representing more social impairment.

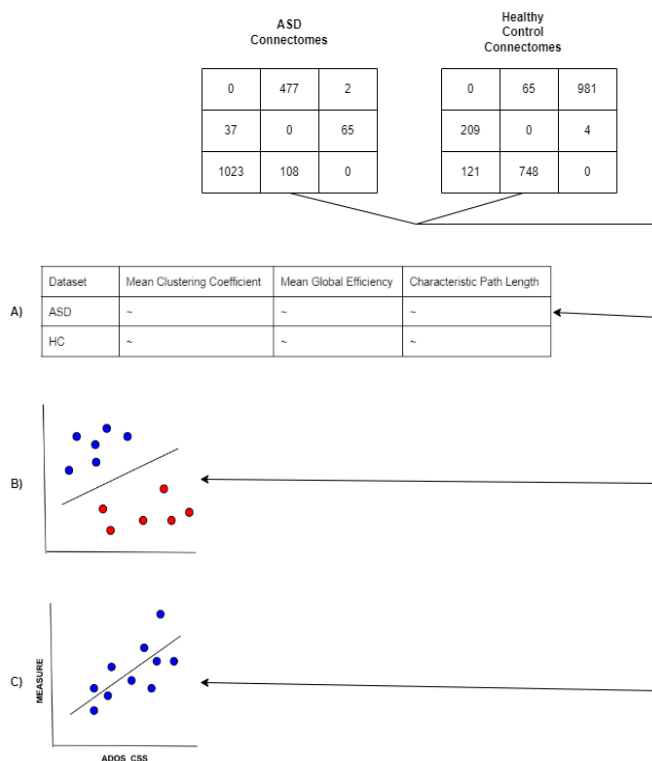


Fig. 1. Structural connectomes from both ASD subjects and Healthy Control subjects will be used A) to calculate and analyze graph theory measures B) as input into a Support Vector Machine, to determine a classifier for ASD C) to check for a correlation between graph theory measures and autism severity scores like ADOS_CSS

B. Methods

To calculate graph theory measures, I will rely on code from the Brain Connectivity Toolbox.[6] I plan to compute the key node level and network level measures we discussed in class, such as degree distribution and measures related to functional segregation and integration. To determine significant differences between the ASD and control sets I will compare mean, standard deviation, and possibly use a two-sample t test.

I will use the Support Vector Machine machine learning technique to attempt to determine a classifier for ASD from the connectomes. Afterwards, I will use machine learning

metrics like accuracy and precision to review the success of the resulting classifiers. I will use two different SVMs; one for the Desikan atlas connectomes and one for the Schaefer atlas connectomes.

To test for links between specific graph theory measures and autism severity, I will use statistical correlation tests between the computed measures and the ADOS_CSS and SCQ scores. I will explore the best correlation tests to use, with Pearson correlation being a possible candidate.

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