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Diagnostic Classification of ASD Improves with Structural Connectivity of DTI and Logistic Regression

Ravi RATNAIK[a,1], Chetan RAKSHE[a], Manoj KUMAR[b] and Jac Fredo AGASTINOSE RONICKOM[a]
[a] *School of Bio-Medical Engineering, Indian Institute of Technology (BHU), Varanasi, Uttar Pradesh, India*
[b] *Neuroimaging and Interventional Radiology (NIIR), National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru, India*
ORCiD ID: Ravi Ratnaik https://orcid.org/0000-0001-9785-8414

Abstract. In this study, we examined the structural connectivity (SC) of autism spectrum disorder (ASD) and typical development using the distance correlation and machine learning algorithm. We preprocessed diffusion tensor images using a standard pipeline and parcellated the brain into 48 regions using atlas. We derived diffusion measures in white matter tracts, such as fractional anisotropy, radial diffusivity, axial diffusivity, mean diffusivity, and mode of anisotropy. Additionally, SC is determined by the Euclidean distance between these features. The SC were ranked using XGBoost and significant features were fed as the input to the logistic regression classifier. We obtained an average 10-fold cross-validation classification accuracy of 81% for the top 20 features. The SC computed from the anterior limb of internal capsule L to superior corona radiata R regions significantly contributed to the classification models. Our study shows the potential utility of adopting SC changes as the biomarker for the diagnosis of ASD.

Keywords. Autism spectrum disorder, diffusion tensor imaging, structural connectivity,logistic regression

1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impaired communication, reciprocal social interaction, restricted and stereotyped pattern of behavior. The presence of these impairments is variable in range and severity and most often changes with the acquisition of other developmental diseases. ASD is diagnosed based on subjective clinical scores, which can be time-consuming and challenging, with limited accuracy. Studies have demonstrated that structral connectivity (SC) modeled by tracking the neural fibers between the brain regions could be valuable tool for diagnosing

[1] Corresponding Author: Ravi Ratnaik, email: ravi.jrf.bme23@itbhu.ac.in

ASD [1]. A promising non-invasive magnetic resonance imaging technique for identifying microstructural alterations or variations associated with neuropathological conditions and response to treatment is diffusion tensor imaging (DTI). The amount, degree of anisotropy, and orientation of directed diffusion can be characterized from DTI by us- ing the measures such as mean diffusivity (MD), fractional anisotropy (FA), radial dif- fusivity (RD), axial diffusivity (AD), and mode of anisotropy (MO) [2]. The complex brain networks based on inter regional SC exhibited excellent properties and good test-retest reliability. The anisotropic and diffusivity measures of the structural network re- flect individual differences and provide discriminative power to diagnose various brain disorders. The SC matrix yields many features, and the feature reduction method helps clinicians to understand pathological abnormalities. Machine learning algorithms help to make an informed decision about the brain of ASD compared to typically developing (TD) subjects based on the identified features [3]. In this study, we computed the SC of DTI measurements using Euclidean distance. XGBoost was used to identify the significant features and logistic regression (LR) classification model for accurate identificationand characterization of brain microstructural connectivity in ASD and TD.

2. Methods

The proposed pipeline for the diagnostic classification of ASD is shown in Figure 1.

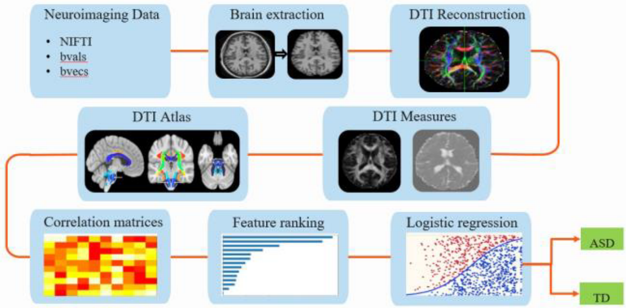


Figure 1. Process pipeline of the proposed framework

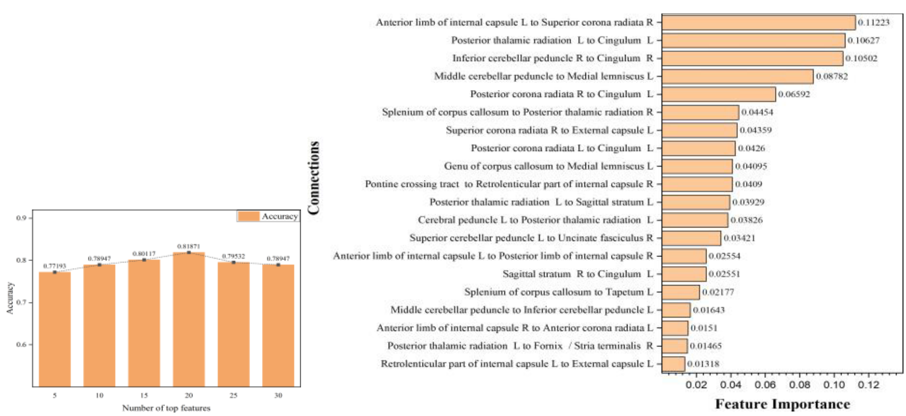
This study includes DTI data from ASD and TD subjects publicly available in the Autism Brain Imaging Data Exchange (ABIDE-II) database. We considered the imagesof 33 ASD and 24 TD participants contributed by the site San Diego State University (SDSU) [4]. The demographic information of participants considered in this study is shown in Table 1. We preprocessed the DTI images using the standard pipeline, whichincludes skull-stripping, eddy current correction, and fitting of diffusion tensors. The FSL package of version 6.0.5 was used to calculate diffusion tensors along with eigen- values, eigenvectors, FA, RD, AD, MD and MO [5]. We parcellated the brain regions using ICBM-DTI-81 white-matter labels atlas to extract features of 48 white matter re- gions. These regions were created by hand segmentation of a standard-space average of diffusion MRI tensor maps from the considered 81 subjects [6].We made a vector consisting of features FA, RD, AD, MD, and MO for each region and calculated the Euclidean distance between each pair of regions. It resulted in a SC matrix of size 48x48, which yields 1,128 diagnostic features from the lower or upper

Table 1. Demographic information of the participants. IQ : Intelligence Quotient, PIQ : Performance IQ , VIQ : Verbal IQ, FIQ : Full Scale IQ

	ASD	**TD**	***p*-value (2 sample t -test)**
N (Handedness)	27 (R), 4 (L), 2 (M)	20 (R), 1 (L), 3 (M)	-
Males (Females)	26 (7)	22 (2)	-
Age in years	12.89±3.27	13.39±3.02	0.55
PIQ	103.09±18.18	100.79±14.75	0.60
VIQ	97.21±15.5	105.12±10.63	0.47
FIQ	99.81±14.73	102.79±11.9	0.40

triangular matrix. These features were ranked using the XGBoost feature ranking algorithm [7]. We analyzed the performance of the top 5, 10, 15, 20, 25, and 30 features by 10-fold cross-validation using LR as a classifier.

3. Results and Discussions



(a) **(b)**

Figure 2. (a) Performance of top percentile features (b) Top 20 SC features contributed to the LR classifier

Figure 2 (a) shows the performance of the LR classifier for top features obtained bythe XGBoost feature ranking algorithm. The result shows an increasing accuracy trend for the top 5 features to the top 20 features, then decreases for further increase in the number of features. The classifier shows the highest accuracy of 81% for the top 20 features. We obtained higher classification accuracy than similar studies reported in the literature [8]. This suggests that the SC method proposed in this study was able to capture the microstructure variations in the ASD brain. Figure 2 (b) shows the top 20 connections and their features and importance. The results showed that the connection from the anterior limb of internal capsule L to superior corona radiata R was most dominant in classification. Further, the connection from posterior thalamic radiation L to cingulum L contributed significantly to the classification model.

Few limitations of our study are: we never compared the machine learning model's performance by directly feeding the structural features such as FA, RD, AD, MD, and MO. Furthermore, we have considered the DTI from only one site SDSU, available in the ABIDE database for our analysis. Moreover, we never compared the performance of Euclidean distance-based SC methods with other correlation methods and LR with other machine learning algorithms. In addition to SC, we can include functional connectivity and morphological connectivity from other modalities like fMRI and sMRI and build a multimodal-based diagnostic classification system. Finally, hyperparameter tuning and varying the cross-validation folds can improve the classification performance.

4. Conclusions

In this study, we proposed a framework for the diagnostic classification of ASD using the SC features and machine learning algorithm. We computed the Euclidean distance-based correlation matrix from the structural features obtained from DTI and analyzed the performance using the LR classifier. Our results showed an average 10-fold classification accuracy of 81% using the top 20 features. We found that the features obtained from the anterior limb of internal capsule L to superior corona radiata R regions contributed more to the classification of ASD and TD. Thus, the proposed method may be beneficial for the detection of neurodevelopmental disorders.

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