International Journal of Engineering and Advanced Technology (IJEAT)
ISSN: 2249-8958 (Online), Volume-9 Issue-2, December, 2019

Altered Structural Connectivity in Autism Spectrum Disorder

R.Geetha Ramani, R.Sahayamary Jabarani

Abstract: ***Research in Neurological field has been in great trend in recent days, since the need of detection and treatment of various neuropsychological disorders are in increasing order. Automated approaches for the detection are possible by various technological methods. Autism Spectrum Disorder (ASD) is a one such serious disorder which can be diagnosed in early ages of children. The Emerging technology had contributed the neuro imaging techniques to understand the various basic features and characteristics that cause the disorder. This neuro imaging had lead to a better perspective called connectome analysis which deals network structures (connectome) derived from the neuro images and are used in detection and treatment of the disorder. For these analysis functional and structural connectomes / network of brain are utilized. In this work structural connectomes derived from the Diffusion Tensor Imaging of Typically Developing and Autism Spectrum Disordered had been considered . This connectome / network consists of 264 regions (based on PowerNeuron_264 atlas) and thus 69696 connectivity features (connection between regions). Using the structural connectomes, average connectome analysis had been done and 91 connections had been identified as altered in ASD. There are 112 distinct regions involved in these altered connections and are having varied number of altered connections from one to six. 15 regions among them found to have much alteration since more number of (More than 2) altered connectivity are involved with these regions. To prove the finding , Data mining technique, Support Vector Machine was applied over 42 connectivity features (0.06% of original) out of 91 and are involved with the 15 regions filtered and the classification is done (with 82% accuracy) . Classifier rules are utilized in the diagnosis of ASD . The 15 regions extracted through thisprocess are found to be altered in ASD. These altered regions are related to sensory(touch and taste), memory, movements control, Lexical processing, Consciousness and sleep. This proposed system surely have effective use in the process of high dimensional and complex brain data and the identification of typically developed and autism spectrum disordered brain .This methodology can also be used in detection of other diseases, Role of various Regions, influential regions, etc.,***

Key words: Brain, connectome ,diseases, Neuro images

I. INTRODUCTION

The usage of neuro imaging methodologies had been increased in medical field to reveal hidden and useful information[1]. In particular these methodologies are used in the medical field to provide important, additional and useful information and knowledge to the doctors to handle the patients effectively.

Revised Manuscript Received on December 30, 2019.

* Correspondence Author

***R. Geetha Ramani*,** Department of information science and technology, College of engineering, Guindy, Anna university, Chennai, Tamil Nadu, India. Email:rgeetha@yahoo.com

R, Sahayamary Jabarani, Department of information science and technology, College of engineering, Guindy, Anna university, Chennai, Tamil Nadu, India. Email:sahayageo@yahoo.com

Neurological domain is an important areaof research, which deals about the brain, its structure, functions and the connectivity between brain regions. Since, understanding of Brain's structure and functionalities is highly complex, manual analysis of it is a time consuming task and needs high expertise [2]. Hence computational approaches are sought for analysis of Brain. Brain, being a complex organ, abnormality in the connectivity, functions and structure can lead to malfunctioning and disorders. The common Brain disorders can be Autism Spectrum Disorder (ASD), Epilepsy, Schizophrenia, Parkinson Disease, Multiple Sclerosis etc.,[3]. This work deals with Autism Spectrum Disorder. Autism Spectrum Disorder (ASD) is a neuro developmental condition which impairs the brain's growth and development that damages the ability for communication and interaction[3]. It is a lifelong condition with symptoms that appear in early childhood. Computational approaches are sought for identifying the Typically Developing (TD) Brain from ASD affected brain. For this purpose, the information from brain connectome or network is utilized. The network depicting the connections between brain regions, can be a structural connectome or functional connectome. In this work, structural connectome is used for the detection of altered connectivity in ASD .This work attempts to identify ASD and TD brain by finding the alteration in connectivity features of ASD from TD brain using structural connectome of brain through connectome comparing analysis . The remaining paper is structured as follows: Section II gives the related works briefly in alteration of connectivity in ASD , Section III explains the methodology for detection of the alterations in connectivity featuresof ASD from TD brain, Section IV presents the results of the experiments and section V concludes the paper.

II. RELATED WORK

The detection of altered connectivity in Autism Spectrum Disorder (ASD) and automatic detection of the same is very much utilized by the neurological medical experts. A concise note on the existing works in identification of altered connectivity features and detection of ASD is presented here. The alalysis of functional connectome of brain was done by Zhou et all. Here Extraction of Twenty two quantitative imaging features had been done and fed to various classifiers and their classification performance was assessed through percentage split and cross validation techniques[4].JD Rudie et all, using structural and functional connections author had shown that network organization of brain with respect to structural and functional connections improve the identification of ASD as they clearly show characteristic reduction of local and long-range functional connectivity in ASD and reduced local efficiency and modularity of

functional networks in ASD[5].

Structural connectome features and network features are used as input to SVM classifier to classify ASD and TD subjects, achieving an accuracy of 64%, by Dmitry Petrov et all [6].Another work in 2015, weighted and un weighted brain networks were constructed and performed graph theoretical approaches to analyse the differences between ASD and TD[7]. In subjects with ASD, global efficiency was significantly decreased both in the un weighted and the weighted networks, normalized characteristic path length was significantly increased in the un weighted networks and strength was significantly reduced in the weighted networks. From local analysis, betweenness centrality of the right caudate was significantly increased in the weighted networks and the strength of the right superior temporal pole was significantly decreased in the un weighted networks in subjects with ASD.

Spectral distribution of brain network had been captured through Earth Mover distance based kernel. This kernel improved the classification accuracy of SVM to 71% on a public dataset. This work had been done in 2016[8].Petrov D et all in 2016, a data pre-processing method that utilized geometric and topological connectome normalization was put forth. The work had a claim that an improvement had been done in SVM classification of ASD and TD[9].

Morphometry analysis revealed that the cortical thickness of ASD subjects more than the typically developing. Decision tree classifier was used for Classification and was performed on cortical thickness obtained from structural MRI, white matter connectivity from DTI and neurochemical concentration got from 1H-MRS with an accuracy of 91.90% on 19 ASD and 18 TD subjects[10]. The existing works on analysis of autism data having been presented, the following work presents the identification of altered connectivity features in ASD from structural connectome values.

III. METHODOLOGY

Finding altered connectivity features in ASD from TD using averaging and comparing of structural connectome is being explored in this section. The proposed system architecture is depicted in Fig. 1.

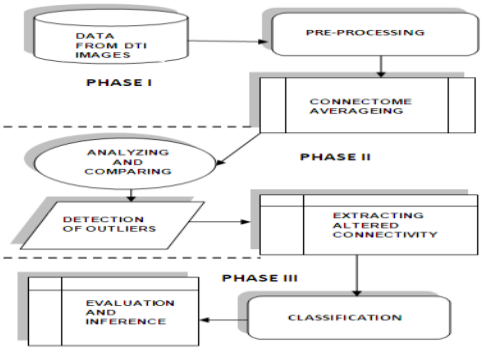

Fig. 1: Proposed System Architecture

This methodology has three phases viz., Phase I- Averaging (Derivation of Average connectivity matrices) Phase II- Extracting(Finding the altered features through analyzing and comparison) and Phase III- Classification and Evaluation. Each phase contains the processes given in the Fig.1.The following sub-sections explains each process.

A. Dataset

The dataset used for this proposed work is from UCLA Multimodal Connectivity Database [11],[12]. The dataset consists of DTI-based connectivity matrices of 75 subjects (42 ASD subjects and 33 TD subjects). These images of DTI scans were obtained on a Siemens 3T Trio. There were sequence of 32 DTI scans with different diffusion-weighted directions (b=1000 s=mm2), three scans with no diffusion sensitization at b=0, and six scans at b=50 s=mm2. The in-plane voxel dimension is 2 2mm with 2-mm thick axial slices, and total scan time was 8 min 1 sec. Tractography was carried out with relaxed constraints: maximum turn angle was set at 50o, and no FA threshold was applied. These Connectivity matrices used for the study were created using parcellation scheme proposed by Power et al. [12]. By this approach 264 brain regions are produced and thus 264X264 connectivity matrices. Following Table I gives the sample regions of the parcellation.

Table -I: Sample Brain Regions Names in PowerNeuron_264 atlas

Sl.No	Region Name
R1	Right Superior Frontal Gyrus
R2	Right Frontal Pole
.	….
R262	Right Occipital Pole
R263	Right Lateral Occipital Cortex inferior division 1
R264	Right Lateral Occipital Cortex inferior division 2

The edge weights were being set with the number of streamlines connecting each pair of regions. Thus, the resulting adjacency matrices were symmetric and weighted, with larger weights indicating more number of streamlines detected between the respective brain regions. Thus 75 subjects with 264X264 connectivity matrix, and each is considered for further process.

B. Data Pre-processing

Pre-processing on the data is carried out to make it suitable and efficient for further processing. For all the 75 subjects used in this work the connectivity matrices are of degree 264X264 . Sample partial matrix on connectivity is shown in the Fig. 2.

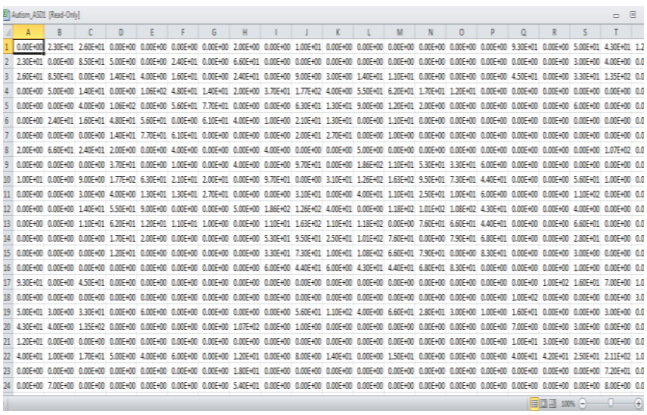

Fig. 2: Sample Connectivity Matrix

The matrices available are weighted, and the upper triangular matrix alone is used for the process, since the value in the upper and lower triangular matrix are the same., thus reducing the feature dimensionality to half (69696 to 34716). The matrix values in the upper triangular are converted into a single row, having 34716 columns. This process is repeated for all the 75 subjects under study, resulted in 75 rows and 34716 columns. The class value ASD or TD is appended to the data as the last column. Sample of pre-processed data is shown in Fig. 3.

Subject	R2-R1	R3-R1	…	R264-R1	…	R264-R263	CLASS
S1	23.00	26.00	…	…	…	61.00	ASD
S2	…	…	…	…	…	…	ASD
…	…	…	…	…	…	…	…
S74	…	…	…	…	…	…	TD
S75	10.00	33.00	…	…	…	65.00	TD

Fig. 3: Sample of Dataset

C .Computing Connectome Average

The 75 subjects out of which 42 are of ASD and 33 are of TD have been considered for analysis.

Let M_i be the matrices represent 42 ASD brain network and $N_j$be the matrices represent 33 TD brain network, where i varies from 1 to 42 and j varies from 1 to 33. Let the values present in the matrix be a_{pq} and $b_{pq}$where p,q varies from 1 to 264.

Average connectivity matrix of ASD (A1)had been found by summing up the each of 69696 features present in each of ASD matrix(M_i)and divide it by 42. In the same way Average connectivity matrix of TD (A2)had been found by summing up the each of 69696 features present in each of TD matrix (N_j) and divide it by 33. With the derived two average connectome matrices for ASD and TD, the comparison had been done in order to find the alteration in the connectivity of ASD .

That is

$$A1=(\sum a_{pq})/42 \quad (1)$$

$$A2=(\sum b_{pq})/33 \quad (2)$$

p,q varies from 1 to 264.

These two average matrices calculated using Micro Soft EXCEL [22]. They are represented as A1(for ASD) and A2(for TD), partially shown in Fig.4,Fig5.

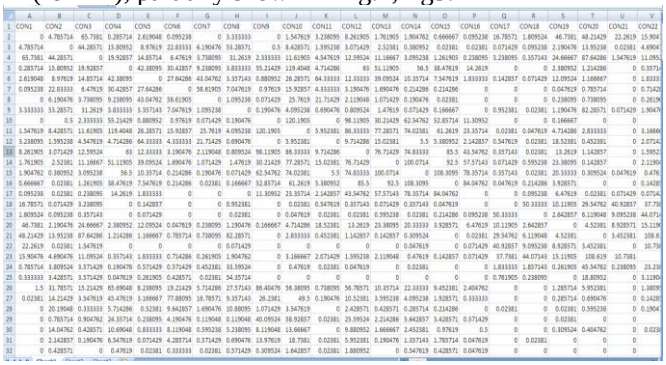

Fig .4Partial view of Average matrix of ASD

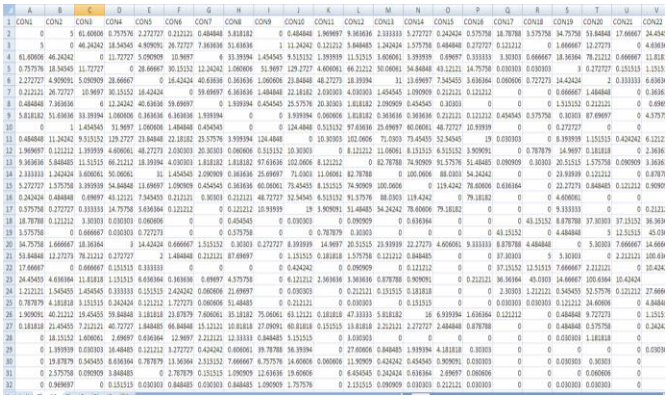

Fig.5. Partial view of Average matrix of TD

D. Analyzing and Comparing of Average matrices

The comparison of average matrices had been done by finding the difference between the average matrices of ASD(A1) and TD(A2) .(A1 minus A2) which produce another 264X264 matrix. Then the distinct difference values are taken from this average difference matrix and examined. There werepositive difference values and as well as negative difference values indicating that there are connectivity features of ASD having greater strength than TD and there are connectivity features of ASD having lower strength than TD.

E. *Detection of outliers*

The positive difference and negative difference values had been taken separately and outliersfor thesevalues are found out using quartile and inter quartile range in order to detect the altered connectivity features[21].

Q1=QUARTILE1(VALUES),
Q3=QUARTILE3(VALUES) THEN

IQR (INTER QURARTILE RANGE) = Q3-Q1 (3)

LL(LOWER LIMIT)=Q1-(IQR*1.5) (4)

UL(UPPER LIMIT)=Q3+(IQR*1.5) (5)

The outliers are the values that are lower than the lower limit and higher than the upper limit.

F. *Extractionand analysis of altered connectivity features*

To extract the altered features of ASDas a first step the outliers are identified .To identify the outliers,Incase of Negative difference values the lower limit is considered and For positive differencevalues the upper limit is used. The outliers are the values lower than lower limit in negative values and higher than upper limit in positive values.The connectivity features having average values with in the outliers (higher than the upper limit of positive difference values and lower than the lower limit of negative difference values) will be considered as altered connectivity features. These altered features are further considered for classification in order to prove their significance. There are 91 features found to be altered in this extraction.

Further the regions involved in these significant connectivity features (91 features) had been analysed for their alteration in ASD. The total number of regions involved in this 91 connectivity features had been found to be 112. These regions are found to be having from one to six altered connections, and they had been segregated according to the number of altered connections (1 to 6).Considering the severity of alteration15 regions had been filtered for having more than 2 altered connectivity. In order to prove the authenticity of the alteration in the 15 regions, the connectivity features involved with these regions with in 91 features are taken into account and again considered for classification and evaluation. There are 42 suchconnectivity features exists.

G. Classification and Evaluation

Classification is defined to be the process of building a model with the training data such that the model predicts the class label of an unlabeled data[14]. Here Support Vector Machine is used for the classification of the subjects as either ASD or TD[13],[15],[16],[18],[19],[20]. With respect to this application, classifier reports the best possible result with 90% accuracy with 91 features and 82% with 42 features. The performance of the classifier is assessed through validation techniques 10-fold cross validation technique, Leave-one-out and accuracy is evaluated[17]. The assessment and performance evaluation of the classification algorithm revealed that this is the better performance with lesser number of features(91 out of 69696and 42 out of 69696) in predicting the class of subjects with ASD and TD. The knowledge base was framed by incorporating the classification rules framed from the algorithm. The inference engine designed was tested with test records whose class label were unknown. Hence the altered features fromproposed system were verified for their alteration in ASD. Also 15 regions that are significantly found to be altered in ASD had been listed. The following section discusses the experiment results.

IV. EXPERIMENTAL RESULTS

The proposed system is performed through various experiments. The experiments were carried out in Microsoft Excel,Matlaband Oracle SQL [22],[23], [24]. The results are presented in the following section.

A. Effect of Averaging

Average of connectivity matrix of ASD subjectsand TD subjectswere calculated and maximum and minimum values are tabulated below in TableII.

Table -II:The Maximum and Minimum Average values of ASD and TD

Nature of Subjects	No. of Subjects	Maximum Average value	Minimum Average value
ASD	42	211.15	0
TD	33	205.06	0

The comparison view of sample average connectivity strength of ASD and TD are shown in Fig.6 and Fig.7

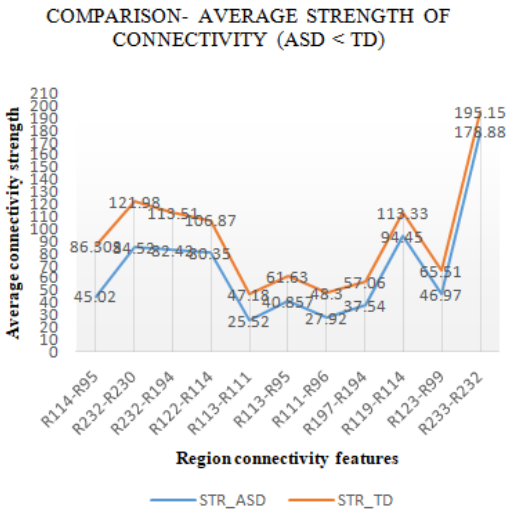

Fig.6. Comparison between Average strength of connectivity – ASD<TD

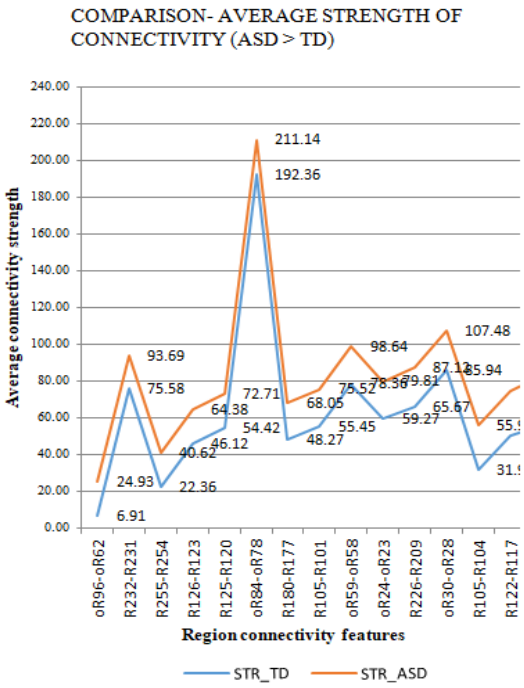

Fig.7. Comparison between Average strength of connectivity – ASD>TD

B. Result of analysis and comparison

Finding the difference in strength of average connectivity features (ASD values minus TD values) had been carried out and it had been varied from 26.53 and -41.27. The distinct difference values are taken and ordered in descending order (lower to higher). The number of distinct positive difference values and distinct negative difference values is tabulated below in TableIII

Table-III : The number of distinct positive and negative difference values

Difference Nature	Number of Distinct Values
Positive	1643
Negative	1381

C. *Outcome of outlier calculation*

The positive difference values and negative values are taken separately and outlier had been calculated for each in order to find out the connectivity features with large difference. The values are tabulated below. Table IV.

Table –IV: The outlier values of positive and negative difference values

Nature of Difference values	Upper limit	Lower limit
Positive	13.50	-3.65
Negative	2.09	-10.74

The values greater than or equal to 13.50 and lesser than or equal to -10.74 are considered as outliers with respect to values considered for processing.

D. *Altered connectivity existence in ASD*

In order to find the altered connectivity in ASD, the connectivity features that has the average difference values less than and equal to -10.74 and greater than and equal to 13.50 had been found. The filtering is done and the results are shown in Table V.

Table No:V The result of filtering of connectivity features depending upon outliers

Filtering criteria	Number of Connectivity features
Extreme average connectivity strength difference-ASD<TD	49
Extreme average connectivity strength difference -ASD>TD	42
Totally altered	91

The list of 49 features (ASD<TD), 42 Features (ASD>TD) and are listed below in table VI and table VII

Table-VI: List of 49 Features

Slno	Diff val	Conn feature	Actual region name where connectivity is between
1	-41.279	R114-oR95	Right Precentral Gyrus 20 and Right Thalamus 1
2	-37.325	R232-R230	Left PlanumTemporale 2 and Left Central Opercular Cortex 4
3	-31.087	R232-R194	Left PlanumTemporale 2 and Left Parietal Operculum Cortex
4	-26.522	R122-R114	Right Precentral Gyrus22 and Right Precentral Gyrus 20
5	-21.658	R113-R111	Right Postcentral Gyrus 19 and Left Postcentral Gyrus 10
6	-20.506	R113-oR95	Right Postcentral Gyrus 19 and Right Thalamus 1
7	-20.374	R111-oR96	Left Postcentral Gyrus 10 and Right Superior Parietal Lobule 3
8	-19.513	R197-R194	Left Postcentral Gyrus 16 and Left Parietal Operculum Cortex
9	-18.881	R119-R114	Right Precentral Gyrus 21 and Right Precentral Gyrus 20
10	-18.539	R123-oR99	Left Precuneous Cortex 1 and Right Postcentral Gyrus 17
11	-18.271	R233-R232	Left PlanumTemporale 3 and Left PlanumTemporale 2
12	-17.924	R152-R150	Left Lingual Gyrus 2 and Left Lingual Gyrus 1
13	-17.377	R243-R235	Right Lateral Occipital Cortex superior division 6 and Right Occipital Pole 2
14	-17.106	R232-R196	Left PlanumTemporale 2 and Left Insular Cortex 3
15	-16.972	R176-R169	Left Inferior Temporal Gyrustemporooccipital part 2 and Left Lateral Occipital Cortex inferior division 3
16	-16.589	oR63-oR61	Right Insular Cortex 5 and Right Insular Cortex 4
17	-15.727	oR12-oR10	Right Cingulate Gyrus anterior division 1 and Left Cingulate Gyrus anterior division 2
18	-15.253	R123-R111	Left Precuneous Cortex 1 and Left Postcentral Gyrus 10
19	-15.143	oR95-oR94	Right Thalamus 1 and Right Superior Frontal Gyrus3
20	-15.024	R127-oR99	Right Precuneous Cortex 2 and Right Postcentral Gyrus 17
21	-14.922	R176-R170	Left Inferior Temporal Gyrus temporooccipital part 2 and Left Lateral Occipital Cortex inferior division 4
22	-14.667	oR66-oR64	Right Parietal Operculum Cortex and Right Insular Cortex 6
23	-14.489	R174-R163	Vermis VI and Right VI
24	-13.974	oR48-oR41	Right Frontal Pole 10 and Right Frontal Orbital Cortex 1
25	-13.504	R113-R108	Right Postcentral Gyrus 19 and Left Postcentral Gyrus 9
26	-13.325	R218-R216	Left Middle Frontal Gyrus 3 and Left Middle Frontal Gyrus 2

27	-13.206	R231-R196	Left PlanumTemporale 1 and Left Insular Cortex 3
28	-13.152	oR63-oR62	Right Insular Cortex 5 and Right Putamen 4
29	-13.015	R259-oR57	Right Central Opercular Cortex 1 and Right Superior Temporal Gyrus anterior division
30	-12.905	R189-R187	Left Middle Temporal Gyrus posterior division 2 and Left Middle Temporal Gyrus posterior division 1
31	-12.803	oR28-oR25	Left Cingulate Gyrus anterior division 4 and Right Cingulate Gyrus anterior division 2
32	-12.682	R263-R262	Right Lateral Occipital Cortex inferior division 3 and Right Occipital Pole 4
33	-12.353	oR70-oR66	Right Postcentral Gyrus 7 and Right Parietal Operculum Cortex
34	-12.165	R123-oR96	Left Precuneous Cortex 1 and Right Superior Parietal Lobule 3
35	-12.019	R147-R139	Left Intracalcarine Cortex 1 and Right Cuneal Cortex 2
36	-11.755	R111-oR99	Left Postcentral Gyrus 10 and Right Postcentral Gyrus 17
37	-11.736	oR63-oR60	Right Insular Cortex 5 and Right Putamen 3
38	-11.675	oR53-oR52	Right Putamen 1 and Right Insular Cortex 1
39	-11.639	R254-R247	Right Lateral Occipital Cortex superior division 9 and Right Lateral Occipital Cortex superior division 7
40	-11.318	oR26-oR10	Left Paracingulate Gyrus 4 and Left Cingulate Gyrus anterior division 2
41	-11.232	R262-R250	Right Occipital Pole 4 and Right Lateral Occipital Cortex inferior division 2
42	-11.216	R206-R104	Left Middle Frontal Gyrus 1 and Left Superior Frontal Gyrus 4
43	-11.188	R208-R104	Left Precentral Gyrus 18 and Left Superior Frontal Gyrus 4
44	-11.115	oR15-oR14	Left Cingulate Gyrus anterior division 3 and Right Paracingulate Gyrus 1
45	-11.076	R235-R138	Right Occipital Pole 2 and Right Cuneal Cortex 1
46	-11.032	oR26-oR25	Left Paracingulate Gyrus 4 and Right Cingulate Gyrus anterior division 2
47	-10.981	R134-R131	Right Precuneous Cortex 6 and Right Precuneous Cortex 3
48	-10.842	R249-R245	Right Occipital Pole 3 and Right Occipital Fusiform Gyrus 2
49	-10.751	R259-oR46	Right Middle Temporal Gyrus posterior division 3 and Right Temporal Pole 2

Table-VII : List of 42 Features

Slno	Diff val	Conn feature	Actual region name where connectivity is between
1	13.714	ooR5-ooR4	Left Superior Frontal Gyrus 1 and Left Paracingulate Gyrus 1
2	13.788	R210-R209	Left Central Opercular Cortex 1 and Left Frontal Operculum Cortex 1
3	13.816	R111-R107	Left Postcentral Gyrus 10 and Left Postcentral Gyrus 8
4	13.911	R110-oR96	Right Precentral Gyrus 18 and Right Superior Parietal Lobule 3
5	14.214	R126-R121	Right Precuneous Cortex 1 and Right Lateral Occipital Cortex superior division 5
6	14.6	oR96-oR60	Right Superior Parietal Lobule 3 and Right Putamen 3
7	14.626	R252-R248	Right Lateral Occipital Cortex superior division 8 and Right Lateral Occipital Cortex inferior division 1
8	14.803	oR69-oR62	Right Superior Parietal Lobule 1 and Right Putamen 4
9	14.831	R181-R108	Left Superior Parietal Lobule 3 and Left Postcentral Gyrus 9
10	14.905	R126-R109	Right Precuneous Cortex 1 and Left Lateral Occipital Cortex superior division 1
11	15.009	R233-R229	Left PlanumTemporale 3 and Left Central Opercular Cortex 3
12	15.165	R189-R186	Left Middle Temporal Gyrus posterior division 2 and Left Middle Temporal Gyrus temporooccipital part
13	15.227	R139-R133	Right Cuneal Cortex 2 and Right Precuneous Cortex 5
14	15.29	R128-R124	Left Cingulate Gyrus posterior division 2 and Left Precentral Gyrus 13
15	15.654	R168-R164	Left VI 2 and Left Occipital Fusiform Gyrus 1
16	16.061	oR11-ooR5	Left Superior Frontal Gyrus 2 and Left Superior Frontal Gyrus 1

17	16.147	R264-R263	Right Lateral Occipital Cortex inferior division 4 and Right Lateral Occipital Cortex inferior division 3
18	16.195	R141-R134	Right Intracalcarine Cortex 9 and Right Precuneous Cortex 6
19	16.212	R127-R126	Right Precuneous Cortex 2 and Right Precuneous Cortex 1
20	16.286	R100-oR97	Right Thalamus 3 and Right Thalamus 2
21	16.294	R147-R144	Left Intracalcarine Cortex 1 and Left Cuneal Cortex 1
22	16.47	R259-R258	Right Middle Temporal Gyrus posterior division 3 and Right Inferior Temporal Gyrus posterior division 2
23	16.563	R108-R107	Left Postcentral Gyrus 9 and Left Postcentral Gyrus 8
24	16.634	R127-R109	Right Precuneous Cortex 2 and Left Lateral Occipital Cortex superior division 1
25	16.831	R232-R199	Left PlanumTemporale 2 and Left PlanumTemporale 4
26	16.857	R255-R248	Right Middle Temporal Gyrus temporooccipital part 2 and Right Lateral Occipital Cortex inferior division 1
27	17.359	oR96-oR69	Right Superior Parietal Lobule 3 and Right Superior Parietal Lobule 1
28	18.019	oR96-oR62	Right Superior Parietal Lobule 3 and Right Putamen 4
29	18.115	R232-R231	Left PlanumTemporale 2 and Left PlanumTemporale 1
30	18.255	R255-R254	Right Middle Temporal Gyrus temporooccipital part 2 and Right Lateral Occipital Cortex superior division 9
31	18.26	R126-R123	Right Precuneous Cortex 1 and Left Precuneous Cortex 1
32	18.29	R125-R120	Left Cingulate Gyrus posterior division 1 and Left Juxtapositional Lobule Cortex 2
33	18.779	oR84-oR78	Right Postcentral Gyrus 13 AND Right Precentral Gyrus 8
34	19.775	R180-R177	Left Superior Parietal Lobule 2 and Left Angular Gyrus
35	20.069	R105-R101	Left Thalamus 1 and Left Precentral Gyrus 7
36	20.279	oR59-oR58	Right Central Opercular Cortex 1 and Right Insular Cortex 3
37	20.537	oR24-oR23	Right Frontal Pole 5 and Right Frontal Pole 4
38	21.452	R226-R209	Left Insular Cortex 5 and Left Frontal Operculum Cortex 1
39	21.537	oR30-oR28	Left Cingulate Gyrus anterior division 5 and Left Cingulate Gyrus anterior division 4
40	24.043	R105-R104	Left Thalamus 1 and Left Superior Frontal Gyrus 4
41	24.173	R122-R117	Right Precentral Gyrus 22 and Left Postcentral Gyrus 12
42	26.539	R113-R110	Right Precentral Gyrus 20 and Right Precentral Gyrus 18

With the analysis of regions involved in theses altered 91 features, There were 112 distinct regions involved in the connectivity representing these features. The regions had been separated according to the number of altered connectivity involved with them. These results are tabulated in Table VIII.

Table -VIII : The result of separation of regions according to number of altered connectivity

Number of Altered connectivity	Number of Regions
One	68
Two	29
Three	9
Four	3
Five	1
Six	2

The involvement more number of altered connectivity indicates the significant alterations in the regions involved. Considering the severity of altered connectivity, regions that establish more than 2 altered connectivity had been taken in to account for further process and There are 15 regions establish more than 2altered connectivity . These regions are tabulated in Table IX.

Table – IX : The regions establish more than 2 altered connectivity

Region	Region Name	Number of altered connectivity
oR62	Right Putamen 4	3
oR63	Right Insular Cortex 5	3
oR95	Right Thalamus 1	3
oR99	Right Postcentral Gyrus 17	3
R104	Left Superior Frontal Gyrus 4	3
R108	Left Postcentral Gyrus 9	3
R114	Right Precentral Gyrus 20	3
R127	Right Precuneous Cortex 2	3
R259	Right Middle Temporal Gyrus posterior division 3	3
R113	Right Postcentral Gyrus 19	4
R123	Left Precuneous Cortex 1	4
R126	Right Precuneous Cortex 1	4
R111	Left Postcentral Gyrus 10	5
R232	Left PlanumTemporale 2	6
oR96	Right Superior Parietal Lobule 3	6

The number of connectivity features involved with these 15 regions are 42 out of 91. These features are listed in Table X below.

Table - X The connectivity features involved with the regions establish more than 2 altered connectivity

Sl.No	Connectivity feature	Actual region name where connectivity is between
1	oR63-oR60	Right Insular Cortex 5 and Right Putamen 3
2	oR63-oR61	Right Insular Cortex 5 and Right Insular Cortex 4
3	oR63-oR62	Right Insular Cortex 5 and Right Putamen 4
4	oR69-oR62	Right Superior Parietal Lobule 1 and Right Putamen 4
5	oR95-oR94	Right Thalamus 1 and Right Superior Frontal Gyrus3
6	oR96-oR60	Right Superior Parietal Lobule 3 and Right Putamen 3
7	oR96-oR62	Right Superior Parietal Lobule 3 and Right Putamen 4
8	oR96-oR69	Right Superior Parietal Lobule 3 and Right Superior Parietal Lobule 1
9	R105-R104	Left Thalamus 1 and Left Superior Frontal Gyrus 4
10	R108-R107	Left Postcentral Gyrus 9 and Left Postcentral Gyrus 8
11	R110-oR96	Right Precentral Gyrus 18 and Right Superior Parietal Lobule 3
12	R111-oR96	Left Postcentral Gyrus 10 and Right Superior Parietal Lobule 3
13	R111-oR99	Left Postcentral Gyrus 10 and Right Postcentral Gyrus 17
14	R111-R107	Left Postcentral Gyrus 10 and Left Postcentral Gyrus 8
15	R113-oR95	Right Postcentral Gyrus 19 and Right Thalamus 1
16	R113-R108	Right Postcentral Gyrus 19 and Left Postcentral Gyrus 9
17	R113-R110	Right Precentral Gyrus 20 and Right Precentral Gyrus 18
18	R113-R111	Right Postcentral Gyrus 19 and Left Postcentral Gyrus 10
19	R114-oR95	Right Precentral Gyrus 20 and Right Thalamus 1
20	R119-R114	Right Precentral Gyrus 21 and Right Precentral Gyrus 20
21	R122-R114	Right Precentral Gyrus22 and Right Precentral Gyrus 20
22	R123-oR96	Left Precuneous Cortex 1 and Right Superior Parietal Lobule 3
23	R123-oR99	Left Precuneous Cortex 1 and Right Postcentral Gyrus 17
24	R123-R111	Left Precuneous Cortex 1 and Left Postcentral Gyrus 10
25	R126-R109	Right Precuneous Cortex 1 and Right Lateral Occipital Cortex superior division 5
26	R126-R121	Right Precuneous Cortex 1 and Right Lateral Occipital Cortex superior division 5
27	R126-R123	Right Precuneous Cortex 1 and Left Precuneous Cortex 1
28	R127-oR99	Right Precuneous Cortex 2 and Right Postcentral Gyrus 17
29	R127-R109	Right Precuneous Cortex 2 and Left Lateral Occipital Cortex superior division 1
30	R127-R126	Right Precuneous Cortex 2 and Right Precuneous Cortex 1
31	R181-R108	Left Superior Parietal Lobule 3 and Left Postcentral Gyrus 9
32	R206-R104	Left Middle Frontal Gyrus 1 and Left Superior Frontal Gyrus 4
33	R208-R104	Left Precentral Gyrus 18 and Left Superior Frontal Gyrus 4
34	R232-R194	Left PlanumTemporale 2 and Left Parietal Operculum Cortex
35	R232-R196	Left PlanumTemporale 2 and Left Insular Cortex 3
36	R232-R199	Left PlanumTemporale 2 and Left PlanumTemporale 4
37	R232-R230	Left PlanumTemporale 2 and Left Central Opercular Cortex 4
38	R232-R231	Left PlanumTemporale 2 and Left PlanumTemporale 1
39	R233-R232	Left PlanumTemporale 3 and Left PlanumTemporale 2
40	R259-oR46	Right Middle Temporal Gyrus posterior division 3 and Right Temporal Pole 2
41	R259-oR57	Right Central Opercular Cortex 1 and Right Superior Temporal Gyrus anterior division
42	R259-R258	Right Middle Temporal Gyrus posterior division 3 and Right Inferior Temporal Gyrus posterior division 2

A. Outcome of Classification and Evaluation

The Support Vector Machine algorithm is applied to classify the subjects as ASD or TD. For the 91 features derived, classifier had been built and performance is evaluated through 10 fold cross validation and leave-one-out. It is seen that the accuracy obtained through classification is 90%. These 91 features can be considered as significant and plays a vital role for the classification of ASD and TD subjects. The error rate and confusion matrix of the cross validation and leave-one-out evaluation is shown in the Fig.8, Fig.9.

Error rate			0.1000			
Values prediction			Confusion matrix			
Value	Recall	1-Precision		ASD	TD	Sum
ASD	0.8780	0.0526	ASD	36	5	41
TD	0.9310	0.1563	TD	2	27	29
			Sum	38	32	70

Fig.8. Error rate and Confusion matrix of the Cross validation

Error rate			0.1067			
Values prediction			Confusion matrix			
Value	Recall	1-Precision		ASD	TD	Sum
ASD	0.8333	0.0278	ASD	35	7	42
TD	0.9697	0.1795	TD	1	32	33
			Sum	36	39	75

Fig.9. Error rate and Confusion matrix of leave-one-out evaluation

Now the 42 features connectivity features involved with 15 regions having more than 2 altered connectivity were considered, to classify the subjects as ASD or TD. The performance of the classification algorithm is evaluated through 10 fold cross validation.

It is seen that the accuracy obtained through classification is 82%. The error rate and confusion matrix is given in Fig.10.

Error rate			0.1857			
Values prediction			Confusion matrix			
Value	Recall	1-Precision		ASD	TD	Sum
ASD	0.8/80	0.1818	ASD	36	5	41
TD	0./241	0.1923	TD	8	21	29
			Sum	44	26	/0

Fig.10. Error rate and Confusion matrix of the Cross validation on 42 features

The 15 regions tabulated in Table. XIare significantly found to be altered in ASD and the regions are related to sensory(touch and taste), memory, movements control, Lexical processing, visual, Consciousness and sleep[25]-[35].

Table –XI: The regions found to be altered

Region	Region Name	Related to
oR62	Right Putamen 4	Regulate movements
oR63	Right Insular Cortex 5	Taste , Sensory
oR95	Right Thalamus 1	Consciousness,Sleep,altertness
oR99	Right Postcentral Gyrus 17	Sensory (Mainly touch)
R104	Left Superior Frontal Gyrus 4	Working memory
R108	Left Postcentral Gyrus 9	Sensory (Mainly touch)
R114	Right Precentral Gyrus 20	Controlling Voluntary Motor Movements
R127	Right Precuneous Cortex 2	Recollection and Memory
R259	Right Middle Temporal Gyrus posterior division 3	Face perception and Language processing
R113	Right Postcentral Gyrus 19	Sensory (Mainly touch)
R123	Left Precuneous Cortex 1	Recollection and Memory
R126	Right Precuneous Cortex 1	Recollection and Memory
R111	Left Postcentral Gyrus 10	Sensory (Mainly touch)
R232	Left PlanumTemporale 2	Lexical processing, Auditory and receptive Language
oR96	Right Superior Parietal Lobule 3	Visual, Sensory

V. CONCLUSION

Autism Spectrum Disorder is a brain disorder affecting interaction and communication. Automated methods are sought to exploit the complex brain network to identify Autism Spectrum Disorder and Typically developing brain. In this work, Structural connectome data of brain is pre-processed and detection of altered connectivity features in ASD had been done through averaging and comparing. This outcome has a lead to detect ASD and TD with a accuracy of82% ,through the classification applied on only 42 features (0.o6% of original) .The 15 regions involved with these features had been found to have significant alterations in ASD.This system could serve in the research related to neurological health, better diagnosis and treatment of the disorder.

REFERENCES

1. AFritjofHelmchen, Brain Research Institute, University of Zurich, Switzerland; Arthur Konnerth, Institute for Neurosciences, Technical University Munich, Germany; Series Editor, Rafael Yuste, Howard Hughes Medical Institute, Columbia University,*Imaging in Neuroscience: A Laboratory Manual.*
2. Bassett, D.S., Bullmore, E.T. *Human brain networks in health and disease*. Curr. Opin. Neurol. 22, 340{347 (2009).
3. Kana, R.K, Uddin, L.Q., Kenet, T., Chugani, D., Mller, , R.A. *Brain connectivity in autism*. Frontiers in human neuroscience 8, 349 (2014).
4. Zhou Y, Yu F, Duong T *Multiparametric MRI Characterization and Prediction in Autism Spectrum Disorder Using Graph Theory and Machine Learning*. PLoS ONE 9(6): e90405(2014).
5. JD Rudie, JA Brown, D Beck-Pancer, LM Hernandez, EL Dennis., *Altered functional and structural brain network organization in autism*, NeuroImage: clinical 2, 79-94,(2013).
6. Dmitry Petrov, Yulia Dodonova, and Leonid Zhukov*Differences in Structural Connectomes between Typically Developing and Autism Groups*,Institute for Information Transmission Problems Bolshoy Karetny 19-1, Moscow, Russia,National Research University Higher School of Economics, Faculty of Computer Science, Kochnovsky 3, Moscow. Russia (2015).
7. Ulrika Roine, Timo Roine, Juha Salmi, Taina Nieminen-von Wendt, Pekka Tani, Sami Leppämäki, Pertti Rintahaka, Karen Caeyenberghs , Alexander Leemans, Mikko Sams,*Abnormal wiring of the connectome in adults with high-functioning autism spectrum disorder*.Molecular autism, 2015.
8. Yulia Dodonova, Mikhail Belyaev, Anna Tkachev, Dmitry Petrov, Leonid Zhukov, *Kernal classification of connectomes based on earth mover's distance between graph spectra.* MICCAI-BACON 16 Workshop,arXiv(1611.08812) (2016)
9. Petrov, D., Dodonova, Y., Zhukov, L., Belyaev, M.: *Boosting Connectome Classification via Combination of Geometric and Topological Normalizations. Pattern Recognition* in Neuroimaging Proceedings (2016, accepted).
10. Libero LE, DeRamus TP, Lahti AC, Deshpande G, Kana RK. *Multimodal neuroimaging based classification of autism spectrum disorder using anatomical, neurochemical, and white matter correlates*. Cortex; a journal devoted to the study of the nervous system and behavior. 2015;66:46-59 doi:10.1016/j.cortex.2015.02.008.
11. Jesse A. Brown, Jeffrey D. Rudie, Anita Bandrowski,John D. Van Horn, Susan Y. Bookheimer. *The UCLA Multimodal Connectivity Database: A web – based platform for connectivity matrix sharing and complex network analysis (2012).* Frontiers in Neuroinformatics, 2012;6:28.doi: 10.3389/fninf.2012.00028.
12. Power, J.D., Cohen, A.L., Nelson, S.M., Wig, G.S., Barnes, K.A., Church, J.A., Vo- gel, A.C., Laumann, T.O., Miezin, F.M., Schlaggar, B.L., Petersen, S.E. *Functional net- work organization of the human brain.* Neuron 72, 665{678 (2011)
13. Shomona Gracia Jacob,R. Geetha Ramani and P.Nancy, *"Feature Selection and classification in breast cancer datasets through data mining Algorithms"*, Proceedings of IEEE International Conference on Computational Intelligence and Computing Research(ICCC' 2011).pp661-667, Kanyakumari,India,December 15-18,2011.
14. R Geetha Ramani, Lakshmi Balasubramanian, Shomona Gracia Jabob, *Automatic prediction of diabetic retinopathy and glaucoma through image processing and data mining techniques*, Proc. of Int. Conf. on Machine Vision and Image Processing Pg.163-167(2012).
15. ShomonaGraciaJacob,R. GeethaRamani and P.Nancy, "*Efficient Classifier for classification of Hepatitis C virus clinical data through data mining algorithms and techniques*",Proceedings of the international conference on Computer Applications, Techno Forum Group, Pondicherry,India, January 27-31.2012.
16. Cristianini, J. Shawe-Taylor, and P. Sykacek Bayesian classifiers are large margin hyperplanes in a Hilbert space.In J. Shavlik, editor, Machine Learning: Proceedings of the Fifteenth International Conference, pp.109–117. Morgan Kaufmann, 1998.

17. Hastie, T., Tibshirani, R., Friedman, J. The elements of statistical learning. Springer (2001)
18. Jiawei Han, MichelineKamber. Data Mining Concepts and technique. Second Edition, 2000.
19. Shomona Gracia Jacob and R. Geetha Ramani, "Discovery of Knowledge Patterns in clinical data through data mining algorithms: multi-class categorization of breast tissue data", International journal of Computer Applications, vol.32(7), pp. 46-53,2011.
20. R. Geetha Ramani and K.Sivaselvi, Data mining Technique for indentification of Diagnostic Biomarker to predict Schizophrenia Disorder,978-1-4799-3975-10.1109/ICCIC.2014.7238525(2014).
21. Sang Kyu Kwak[1] and Jong Hae Kim , Statistical data preparation: *management of missing values and outliers.Korean J Anesthesiol*. 2017 Aug; 70(4): 407–411 Published online 2017 Jul 27. doi: 10.4097/kjae.2017.70.4.407
22. Microsoft Excel 2010 Product Guide
23. MATLAB Language Reference COPYRIGHT by The MathWorks, Inc
24. Oracle® SQL Developer User's Guide
25. Gabriels RL, Agnew JA, Miller LJ, Gralla J, Pan Z, Goldson E, Ledbetter JC, Dinkins JP, Hooks E (2008) *Is there a relationship between restricted, repetitive, stereotyped behaviors and interests and abnormal sensory response in children with autism spectrum disorders?* Res Autism SpectrDisord 2:660-670.
26. Uddin LQ, Supekar K, Lynch CJ, Khouzam A, Phillips J, Feinstein C, Ryali S, Menon V (2013) *Salience network-based classification and prediction of symptom severity in children with autism.* JAMA Psychiatry 70:869-879.
27. Koshino H, Kana RK, Keller TA, Cherkassky VL, Minshew NJ, Just MA (2008) *fMRI investigation of working memory for faces in autism: visual coding and underconnectivity with frontal areas.*Cereb Cortex 18:289-300.
28. Mostofsky SH, Powell SK, Simmonds DJ, Goldberg MC, Caffo B, Pekar JJ (2009) *Decreased connectivity and cerebellar activity in autism during motor task performance*. Brain 132:2413-2425.
29. Jones TB, Bandettini PA, Kenworthy L, Case LK, Milleville SC, Martin A, Birn RM (2010) *Sources of group differences in functional connectivity: an investigation applied to autism spectrum disorder*. Neuroimage 49:401-414.
30. Kleinhans NM, Richards T, Sterling L, Stegbauer KC, Mahurin R, Johnson LC, Greenson J, Dawson G, Aylward E (2008) *Abnormal functional connectivity in autism spectrum disorders during face processing*. Brain 131:1000-1012.
31. Di Martino A, Kelly C, Grzadzinski R, Zuo XN, Mennes M, Mairena MA, Lord C, Castellanos FX, Milham MP (2011) *Aberrant striatal functional connectivity in children with autism*. Biol Psychiatry 69:847-856.
32. Mosconi MW, Kay M, D'Cruz AM, Seidenfeld A, Guter S, Stanford LD, Sweeney JA (2009) *Impaired inhibitory control is associated with higher-order repetitive behaviors in autism spectrum disorders*. Psychol Med 39:1559-1566.
33. Militerni R, Bravaccio C, Falco C, Fico C, Palermo MT (2002) *Repetitive behaviors in autistic disorder*. Eur Child Adolesc Psychiatry 11:210-218.
34. Clery H, Andersson F, Bonnet-Brilhault F, Philippe A, Wicker B, Gomot M (2013) *fMRI investigation of visual change detection in adults with autism*. NeuroimageClin 2:303-312.
35. Sungji Ha1 , In-Jung Sohn1,2, Namwook Kim1,2, HyeonJeong Sim1 and Keun-Ah Cheon1,2* 1 Department of Psychiatry, Institute of Behavioral Science in Medicine and Yonsei Autism Laboratory, Yonsei University College of Medicine, Seoul 03722, 2 Division of Child and Adolescent Psychiatry, Severance Children's Hospital, Yonsei University College of Medicine, Seoul 03722, Korea *Characteristics of Brains in Autism Spectrum Disorder: Structure, Function and Connectivity across the Lifespan*ExpNeurobiol. 2015 Dec;24(4):273-284. pISSN 1226-2560 • eISSN 2093-8144

AUTHORS PROFILE

R.GeethaRamani, Professor,Department of information science and technology, College of engineering, Guindy, Anna university, Chennai, Tamil Nadu, India. Doctorate from Pondicherry University, her area of expertise are Data Mining and evolutionary Algorithms. Published more than 50 research papers in reputed journals. Presented more than 50 papers in international level conferences. Guided 8 P.hD. scholars and presently guiding 5 scholars.

R.SahayamaryJabarani, P.hD. Scholar**,** Department of information science and technology, College of engineering, Guindy, Anna university, Chennai, Tamil Nadu, India**.** Presently Working as software developer in Office of the Controller of Examinations , Anna university, Chennai, Tamil Nadu. Completed the Master Degree in Engineering through Anna University .Presently perusing research under the guidance of Dr.R.GeethaRamani.