Altered Structural Connectivity in Autism Spectrum Disorder

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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 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 this process 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

1. 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.

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 features of 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 analysis of functional connectome of brain was done by Zhou et al. 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 al, 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

Revised Manuscript Received on December 15, 2019.

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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 al [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 normaliztion 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 H-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.

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.

| Sl.No | Region Name |
|-------|-------------|
| R1    | Right Superior Frontal Gyrus |
| R2    | Right Frontal Pole |
| R3    | 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.
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 | ...     | ...       | ASD   |
| S2      | ...   | ...   | ...     | ...       | ASD   |
| S74     | 10.00 | 33.00 | ...     | ...       | TD    |
| S75     | 10.00 | 33.00 | ...     | ...       | TD    |

**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 ($A_1$) 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 ($A_2$) 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

$$A_1 = \frac{\sum_{p,q} a_{pq}}{42}$$  \hspace{1cm} (1)

$$A_2 = \frac{\sum_{p,q} b_{pq}}{33}$$  \hspace{1cm} (2)

$p,q$ varies from 1 to 264.

These two average matrices calculated using Microsoft Excel [22]. They are represented as $A_1$ (for ASD) and $A_2$ (for TD), partially shown in Fig. 4, Fig. 5.

**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 ($A_1$) and TD ($A_2$). ($A_1$ minus $A_2$) which produce another 264X264 matrix. Then the distinct difference values are taken from this average difference matrix and examined. There were positive 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 outliers for these values are found out using quartile and inter quartile range in order to detect the altered connectivity features [21].

$$Q_1 = \text{QUARTILE1(VALUES)}$$

$$Q_3 = \text{QUARTILE3(VALUES)}$$

Then

$$\text{IQR} = \text{INTER QUARTILE RANGE} = Q_3 - Q_1$$ \hspace{1cm} (3)

$$\text{LL(LOWER LIMIT)} = Q_1 - (1.5 \times \text{IQR})$$ \hspace{1cm} (4)

$$\text{UL(UPPER LIMIT)} = Q_3 + (1.5 \times \text{IQR})$$ \hspace{1cm} (5)

The outliers are the values that are lower than the lower limit and higher than the upper limit.
F. Extraction and analysis of altered connectivity features

To extract the altered features of ASDs a first step the outliers are identified. To identify the outliers, in case of Negative difference values the lower limit is considered and For positive difference values 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 alteration, 15 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 such connectivity 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 69696 and 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 from proposed 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, Matlab and Oracle SQL [22],[23], [24]. The results are presented in the following section.

A. Effect of Averaging

Average of connectivity matrix of ASD subjects and TD subjects were calculated and maximum and minimum values are tabulated below in Table II.

| 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](image)

![Fig.7. Comparison between Average strength of connectivity – ASD>TD](image)
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 -1.27. 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 Table III.

| Difference Nature | Number of Distinct Values |
|-------------------|---------------------------|
| Positive          | 1643                      |
| Negative          | 1381                      |

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

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.

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

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

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.

| 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.

| 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 Gyrustemporoccipital 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 |
Table VII: List of 42 Features

| Sno | Diff val | Conn feature | Actual region name where connectivity is between |
|-----|----------|--------------|-------------------------------------------------|
| 1   | 13.714   | oR5-oR4     | Left Superior Frontal Gyrus 1 and Left Paracingulate Gyrus 1 |
| 2   | 13.788   | R210-R209   | Left Central Opercular Cortex 1 and Left Frontal Opercular 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 Precentral 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 5 and Right Lateral Occipital Cortex superior division 1 |
| 8   | 14.803   | oR69-oR62   | Right Superior Parietal Lobule 3 and Right Postcentral Gyrus 4 |
| 9   | 14.831   | R181-R108   | Left Superior Parietal Lobule 3 and Left Postcentral Gyrus 9 |
| 10  | 14.905   | R126-R109   | Right Precentral Cortex 1 and Left Lateral Occipital Cortex superior division 1 |
| 11  | 15.009   | R233-R229   | Left PlanumTemporale 3 and Left Central Opercular Cortex 3 |

Left Inferior Temporal Gyrus temporooccipital part 2 and Left Lateral Occipital Cortex inferior division 4
Right Parietal Operculum Cortex and Right Insular Cortex 6
Vermis VI and Right VI
Right Frontal Pole 10 and Right Frontal Orbital Cortex 1
Right Postcentral Gyrus 19 and Left Postcentral Gyrus 9
Left Middle Frontal Gyrus 3 and Left Middle Frontal Gyrus 2
Left PlanumTemporale 1 and Left Insular Cortex 3
Right Insular Cortex 5 and Right Putamen 4
Right Central Opercular Cortex 1 and Right Superior Temporal Gyrus anterior division
Left Middle Temporal Gyrus posterior division 2 and Left Middle Temporal Gyrus posterior division 1
Left Cingulate Gyrus anterior division 4 and Right Cingulate Gyrus anterior division 2
Right Lateral Occipital Cortex inferior division 3 and Right Occipital Pole 4
Right Postcentral Gyrus 7 and Right Parietal Operculum Cortex
Left Precuneus Cortex 1 and Right Superior Parietal Lobule 3
Left Intracalcarine Cortex 1 and Right Cuneal Cortex 2
Left Postcentral Gyrus 10 and Right Postcentral Gyrus 17
Right Insular Cortex 5 and Right Putamen 3
Right Putamen 1 and Right Insular Cortex 1
Right Lateral Occipital Cortex superior division 9 and Right Lateral Occipital Cortex superior division 7
Left Paracingulate Gyrus 4 and Left Cingulate Gyrus anterior division 2
Right Occipital Pole 4 and Right Lateral Occipital Cortex inferior division 2
Left Middle Frontal Gyrus 1 and Left Superior Frontal Gyrus 4
Left Precentral Gyrus 18 and Left Superior Frontal Gyrus 4
Left Cingulate Gyrus anterior division 3 and Right Paracingulate Gyrus 1
Right Occipital Pole 2 and Right Cuneal Cortex 1
Left Paracingulate Gyrus 4 and Right Cingulate Gyrus anterior division 2
Left Parietal Operculum Cortex and Right Superior Temporal Lobule 3
Right Occipital Pole 3 and Right Occipital Fusiform Gyrus 2
Right Middle Temporal Gyrus posterior division 3 and Right Temporal Pole 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 2 altered connectivity . These regions are tabulated in Table IX.

### 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                 |

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 – 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 4       |
| 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 Gyrus 3|
| 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-oR59            | Right Superior Parietal Lobule 1 and Right Superior Frontal Gyrus 4 |
| 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 Gyrus 22 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.
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 | 0.1067 |
|-------------|---------|
| Values prediction | Confusion matrix |
| Value | Recall | 1-Precision | ASD | TD | Sum |
| ASD | 0.9233 | 0.0278 | ASD | 35 | 7 | 42 |
| TD | 0.9977 | 0.1795 | TD | 1 | 32 | 33 |
| Sum | 36 | 39 | 75 |

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

The 15 regions tabulated in Table XI are 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, alertness |
| 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 Precuneus Cortex 2 | Recollection and Memory |
| r259   | Right Middle Temporal Gyrus posterior division 3 | Face perception and Language processing |
| r113   | Right Postcentral | Sensory (Mainly touch) |

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 of 82% through the classification applied on only 42 features (0.06% 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.

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