# Analysis of Bipolar Disorder Using fMRI

**Wiselin Jiji** ( jijivevin@yahoo.co.in )
Dr Sivanthi Aditanar College of Engineering https://orcid.org/0000-0002-6304-1892
**Muthuraj A**
Dr Sivanthi Aditanar College of Engineering
**Catherine Praiseye Vijayan**
Dr Sivanthi Aditanar College of Engineering
**Rajesh A**
VSSC: Vikram Sarabhai Space Centre

**Research Article**

**Keywords:** Bipolar disorder, Independent Component Analysis (ICA), Hierarchical Modular Analysis (HMA), classification.

**Posted Date:** June 28th, 2022

**DOI:** https://doi.org/10.21203/rs.3.rs-889832/v1

## Abstract

In this work, we have analysed bipolar disorder using fMRI based on brain regional activity measurements. In this research work, we have located the eights regions as per the literature review which are strongly affected brain regions because of BPD. For those regions, the below operations are carried out. Initially functional points are identified using independent component analysis and their connectivity has been established using correlation coefficients. Then located the activated points using Hierarchical Modular Analysis based on the strength of the interregional connectivity. Followed by constructing network between the activated points of each brain regions. Property of network parameters like centrality page rank and centrality degree, centrality closeness, assortativity and clustering coefficients are extracted. Finally, adaboost classifier consist of three weak classifiers, KNN, GDA and naïve bayes are experimented. It was found that this work had given 94.2% accuracy comparatively better than earlier research works.


## Introduction

Bipolar disorder is the sixth leading cause of disability in the world (WHO). Bipolar disorder, a serious mental health disorder is characterized by periods of excitability or euphoria (mania or hypomania) alternating with periods of severe depression. In regards to records in advanced countries, about 2,40,000 in Australia, 7,25,000 withinside the UK, 3,90,000 in Canada, 8,10,000 in Iran, and nearly 10,00,000 in Germany have bipolar disorder (approx.). Bipolar disorder impacts as a minimum 1% of the populace, is related to accelerated mortality, and is a few of the pinnacle 10 maximum disabling ailments global. Currently, based on NIMH statistics report, the Prevalence Rate for bipolar disorder is approximately 1.1% of the population over the age of 18, or in other words, at any one time as many as 51 million people worldwide suffer from bipolar disorder. The aim of this work is to analyse fMRI based on the interconnectivity within the brain activated functional points.

## Related Works

Clark L et.al [6] reported that studies using functional brain imaging indicate that the deficits may be associated with neural system comprising the prefrontal and anterior cingulate cortex, as well as subcortical limbic regions including the amygdala and ventral striatum.

William R. Marchand, et.al [16] results indicated that cortical midline structures (CMS) circuit dysfunction persists in the euthymic state and thus may represent trait pathology. Euthymic bipolar patients had faded activation in response to the affective stimuli in each cortical and subcortical brain regions when compared with healthy subjects (Gin S Malhi, et.al., [8]). In precise, patients had much less activation withinside the left ventral prefrontal cortex suggesting a ability trait deficit. Patients have been slower to react than healthy controls, but did not fluctuate with respect to accuracy. Strakowski. S., et.al., [21] study results support the hypothesis that dysfunctional anterior limbic networks are present in euthymic bipolar patients. Specifically, compared with the healthy subjects, patients showed increased activation in limbic and paralimbic areas as well as ventrolateral prefrontal regions.

Attenuated activation of the IFG or ventrolateral prefrontal cortex exists, (Chen C-H et.al., [4]) which was consistent across emotional and cognitive tasks and particularly related to the state of mania, and enhanced limbic activation, shows abnormal frontal-limbic activation in Bipolar Disorder (BD). Mani N. Pavuluri et.al., [15] results demonstrate overactivity of the pregenual anterior cingulate and amygdala as well as reduced activation at the dorsal convexity of the prefrontal cortex (PFC) in the Ventrolateral prefrontal cortex (VLPFC) and Dorsolateral prefrontal cortex(DLPFC) areas during processing of words with negative emotions. This limbic overactivity could be due to reduced top–down control from the VLPFC and/or to intrinsic limbic abnormalities. Hilary P. Blumberg et.al., [10] findings endorse the presence of dysfunction withinside the subcortical portions of the fronto striatal circuits in adolescents with bipolar sickness. Gruber SA, Rogowska J, et.al., [9] findings suggest differential processing strategies of bipolar patients and support the theory of altered frontal systems in these patients during the performance of reasoning tasks.

Bipolar disorder can be conceptualized, in neural circuitry terms, as parallel disorder in prefrontal cortical (specially ventrolateral prefrontal cortical)-hippocampal-amygdala emotion-processing and emotion-regulation circuits bilaterally, (Phillips ML, et.al., [18]) together with an “overactive” left-sided ventral striatal-ventrolateral and orbitofrontal cortical reward-processing circuitry, resulting in characteristic behavioural abnormalities associated with bipolar disorder: emotional lability, emotional dysregulation, and heightened reward sensitivity. In the Mania group, it is found that cortical volume and area decreased in each of the dorsolateral prefrontal cortex (DLPFC) and the inferior frontal cortex (Christoph Abe et.al., [5]). In contrast no detectable change is found in DLPFC and inferior frontal cortex cortical volume in the No-Mania group.

Bipolar disorder is associated with a trait abnormality in left ventral prefrontal cortex (Hilary P Blumberg, et.al., [3]). Additional ventral prefrontal abnormalities can be related to unique acute mood states. When compared with healthy controls and Major Depressive Disorder (MDD) patients, (Lawrence NS et.al., [12]) BD patients proven accelerated subcortical and ventral prefrontal cortical responses to each positive and negative emotional expressions. Pavuluri MN et.al., [17] findings document a disturbance in affective neurocircuitry in pediatric bipolar disorder. Reduced activation in ventrolateral prefrontal cortex would possibly reflect diminished top-down control that leads to the determined exaggerated activation in amygdala and paralimbic areas.

Teng. S et.al., [22] study determined the alteration in resting-state connectivity associated with the striatal-thalamic circuit for bipolar patients. The extensively different functional connectivity turned into withinside the striatal-thalamic circuit and among the circuit and different brain areas inclusive of the middle and posterior cingulate cortex in addition to the para hippocampus. The dorsal caudate - posterior parietal cortex (DC-PPC) connectivity is a critical circuitry in the oxytocinergic modulation of dopaminergic reward systems, and dysfunctional dorsal caudate - executive control network (DC-ECN) circuitry implicates a maladaptive neuroplasticity in BD II patients, specifically (Wei, SY et.al., [24]). Other regions, along with cerebellum, are easily overlooked, however may also have vital regulatory roles in the corticostriatal circuitry in BD II.

The cortical thinning was present in multiple prefrontal cortices in bipolar disorder (Lyoo IK et.al., [13]). Greater responsiveness to fear with hippocampal activation in patients possibly reflects recollection of traumatic events associated with past experiences of illness or simply the use of a more mnemonic (hippocampal) as opposed to affective (amygdala) approach when performing the task (Malhi GS et.al., [14]). It is viable that, prefrontal-subcortical network dysfunction that relegates neural processing to limbic regions has been impaired in bipolar disorder patients.

In this work, it is hypothesized that the analysis of bipolar disorder can be provided based on the regional brain activity measurements using fMRI of bipolar patients and Healthy Control.

# Methodology

The block diagram for the proposed work is given in Fig. 1. We have concentrated on eight brain regions for this research i.e. frontal lobe, temporal lobe, lentiform nucleus, insular, thalamus, caudate nucleus, parietal and occipital regions. Interconnected activity within 8 regions followed by feature extraction and classification operation is performed.

Data Set Description

The input fMRI images were taken from the OpenNEURO which is open science neuro informatics database storing datasets from human brain imaging studies research. The subjects taken for study include 49 patients with Bipolar Disorder and 130 in Healthy control where the subjects were in Resting State. In Bipolar, 22 female patients and 27 male patients were taken in which 16 patients are between the age 20 and 30 and 17 are between 31 and 40 and the other 16 patients are between 41 and 50 years of age. The healthy control is also of 60 female patients and 70 male patients in which 75 patients are between the age 20 and 30, 28 between 31 and 40 and the other 27 is between 41 and 50 years of age. The images are 4-dimensional images in 64 x 64 with 34 slices with each case’s fMRI having 152 sets at resting state. A sample 2D slice of 4D is as shown in Fig. 2 and Fig. 3 for the input Healthy Control and BPD respectively.

Initially, we have contacted Radiologist Dr. Moses Arunsingh. S, Reg No. 84180, TamilNadu National Medical College, to make our Region of interest for the below brain regions frontal lobe, temporal lobe, lentiform nucleus, insular, thalamus, caudate

nucleus, parietal and occipital regions respectively which is in the table 1 and the brain regions taken for analysis is given in Fig. 4.

# Determination of Functional Connectivity

The functional points are selected in the brain region based on independent component analysis (ICA) on the input data using Fast ICA algorithm [1]. As per literature, using ICA, we have computed 90 [20] functional points. The algorithm type used in Fast ICA is kurtosis which is the classical measure of non gaussianity. The kurtosis of y is classically defined by

$$kurt(y) = E\left\{y^4\right\} - 3(E\{y^2\})^2$$

1

Finally, resultant matrix containing 90 independent components scaled to variance 1 of the input are computed. Then the functional connectivity is calculated between each pair of points 8 by using Pearson's correlation [22], resulting in a n | n correlation matrix for every participant which is represented as a correlation map in Figs. 5 and 6 for BPD and Healthy Control respectively.

# Hierarchical Modular Analysis

The Functional Connectivity are further analysed by Hierarchical modular analysis (HMA) to determine the activated functional points based on the functional connectivity. In order to determine the modules with high to low interregional connectivity, HMA is done to cluster the n functional points into several modules based the strength of the interregional connectivity in the activated functional points with reference to the work proposed by Teng, et.al., [22]. Figures 7 and 8 depicts BPD and Healthy Control data set respectively and the activated functional points are depicted in different colours based on the clustered modules.

These clustered Functional Points are further used to determine the regional activity measurements.

# Feature extraction

The activated functional points which are obtained using HMA are taken for each region. In order to construct a network for each region to their obtain features for further classification, a graph is constructed as a network for the activated points in each region. The network plot is given in Table 2 in which for each region, the network is formed only for the activated functional points in it's respective region.

Using the network of each region, the network metrics are attained which are used to derive the network association of the individual brain region's functional points (Rutvi, et.al[19]). The network metrics are calculated for the following parameters such as centrality page rank[2], centrality degree[2], clustering coefficient[25], assortativity[25], centrality_closeness[25] for each region and then mean and standard deviation for page rank, degree, closeness and clustering coefficient are calculated.

Centrality Page rank

$$C_{PR} = (1 - aAD^{-1})^{-1}1 = D(D - aA)^{-1}$$

2

Where, D is a diagonal matrix, I is an N x N identity matrix, a is weight on the edges from vertex *v*.

# Centrality degree

$$C_D(i) = k_i = \sum_{i \neq j} A_{ij}$$

3

Where, A is a matrix with vertices *i, j* where $i \neq j$

Clustering coefficient

$$C_{\text{clustering}}(v) = \frac{1}{d(v).\,(d(v)-1)} \sum_{r,\,s \in N(v)} A_{rs}$$

4

Where, $d(v)$ is the degree of vertex *v*, $N(v)$ is set of all nodes that are a distance 1 from a vertex v and A is the matrix.

# Assortativity

$$\rho D = \frac{\sum_{jk} jk(e_{jk} - q_j q_k)}{\sigma_q^2}$$

5

Where, $e_{jk}$ refers to the joint excess degree probability for nodes with excess degrees *j* and *k*. $q_k$ is a normalized distribution of a randomly selected node, given by $q_k = \frac{(k+1)\,P_k}{\sum_j P_j}$ and $\sigma_q$ is the standard deviation of the distribution $q_k$.

# Centrality_closeness

$$C_{closeness}(v) = \frac{1}{\sum_{u \in V} d(v,\,u)}$$

6

Where, $d(u,\,v)$ is the distance to all the other nodes in the network.

With these network metrics and the number of activated points in each region, the analysis report is generated as a feature datafile and is given for the classification.

# Classification

We evaluated Adaboost classifier [7] which includes 3 classifiers GDA (Gaussian Discriminant Analysis), KNN (K- Nearest Neighbours), Logistic Regression and Naive Bayes for our work and implemented and automated using MATLAB (v.9, Mathworks, Inc.) software. Boosting is a “greedy” algorithm that in the end combines weak classifiers right into a strong classifier, and always accepts the extra classifier that most strongly reduces the classification error at that precise iteration. The values of KNN parameters used in this work are Nearest neighbours: 30; In GDA and Naïve Bayes, the parameters are set to default values.

## Discussion And Results

The proposed work was trained using Adaboost and performance of the algorithm was compared with an earlier work. The analysis was carried out with 49 bipolar and 130 healthy control fMRI Images. The performance was measured on 1.19 GHz Intel® core™ i51035G1 CPU with 8 GB of RAM running Microsoft Windows 10 20H2. Table 3 represents the input data set used in this work.

Table 3: Input data of both bipolar and healthy control

| Total Participants | Total Participant | Male | Female | Age 20 – 30 | Age 31 – 40 | Age 41-50 |
|---|---|---|---|---|---|---|
| Healthy | 49 | 27 | 22 | 16 | 17 | 16 |
| BPD | 130 | 70 | 60 | 75 | 28 | 27 |

We carried out a study and selected the 90 functionally defined points using Independent Component Analysis (ICA). For these points functional connectivity is obtained by calculation of 90 x 90 correlation map as in Fig. 9. The warm colours represent the positive correlations whereas the cool colours represent the negative correlations between functional points. The 90 points is represented in x axis(left-right) and in y axis (top-bottom) and the correlation value is utmost positive for the points with itself and thus they form maximum correlation for itself ie., in the main diagonal and the plot is mirrored in left and right of the main diagonal as the correlation coefficient from point a to b and b to a(say) is same.

The modular structure of brain functional connectivity is calculated for the correlation matrix which is signified in Fig. 10.

This modular pattern is obtained by reordering functional points in the correlation matrix according to maximizing the strength of connectivity close to the main diagonal of the correlation map.

For the activated functional points, regional activity measures are taken based on the network metrics that has been calculated based on the 8 parameters for the 8 regions in each dataset and the number of activated points in each region is also estimated which are given in the Table 4.

Table 4: Network metrics for feature parameters for 8 regions for an input data

| | Page Rank Mean | Page rank Std | Centrality Degree Mean | Centrality Degree Std | Clustering Coefficient | Assortativity | Centrality Closeness Mean | Centrality Closeness Std. | No. of activated points |
|---|---|---|---|---|---|---|---|---|---|
| R1 | 0.015625 | 0.016793 | 2.0625 | 4.327377 | 0.1875 | 0.393398 | 0.00052 | 0.00109 | 20 |
| R2 | 0.015625 | 0.015918 | 3.75 | 6.546537 | 0.25 | 0.436436 | 0.000945 | 0.001649 | 128 |
| R3 | 0.015625 | 0.017182 | 1.125 | 2.80306 | 0.140625 | 0.350382 | 0.000283 | 0.000706 | 41 |
| R4 | 0.015625 | 0.016144 | 3.28125 | 5.977388 | 0.234375 | 0.426956 | 0.000827 | 0.001506 | 113 |
| R5 | 0.015625 | 0.017109 | 0.65625 | 1.887459 | 0.109375 | 0.314576 | 0.000165 | 0.000476 | 25 |
| R6 | 0.015625 | 0.015866 | 0.1875 | 0.731925 | 0.0625 | 0.243975 | 0.000047 | 0.000184 | 8 |
| R7 | 0.015625 | 0.016896 | 0.46875 | 1.468924 | 0.09375 | 0.293785 | 0.000118 | 0.00037 | 18 |
| R8 | 0.015625 | 0.017192 | 0.875000 | 2.333333 | 0.125000 | 0.333333 | 0.000220 | 0.000587 | 32 |

Using the above 9 features obtained based on the region-based activity, the classification of Bipolar is achieved. The classification was completed with Adaboost classifier. In An AdaBoost classifier[24], we have used Logistic Regression as base estimator. In this work, we have used n_estimators as 50 and learning rate as 1. The misclassified training samples get more weights, and the test error keeps decreasing even after 700 iterations. In Logistic Regression, Bias value as -1.0059, Lambda value as 3.1674e-05 and Delta Gradient value as 1.4582 and the performance and the efficiency in determining the results was tested based on the cross-validation procedure of the input dataset and the proposed work is compared with the earlier work of Juan I. Arribas, et. al., [11] which is represented in Table 5.

Table 5: Performance measures of proposed work and work[11] for Bipolar Analysis.

| | *Accuracy* | *Sensitivity* | *Specificity* | *Precision* | *Recall* | *F_measure* | *Gmean* |
|---|---|---|---|---|---|---|---|
| *Proposed Work* | 0.94233 | 0.98421 | 0.98224 | 0.94047 | 0.98789 | 0.91625 | 0.90931 |
| *Work [11]* | 0.80323 | 0.89423 | 0.89225 | 0.87166 | 0.89104 | 0.84506 | 0.85619 |

Each feature is analysed with the performance measures (Umi Mahdiyah, et.al, [23]). In identification of bipolar disorder, the efficiency and the performance are measured based on the accuracy, sensitivity, specificity, precision, recall, F_measure and Gmean. Results show that the Adaboost algorithm produces results that are optimal in performance when compared to Juan I. Arribas, et. al., [11]. During testing phase, we achieved 98.42% on sensitivity, 98.22% on specificity and 98.79% on recall and the accuracy of the proposed work is 94.2% and is more accurate when compared to work of Juan I. Arribas, et. al., [11] which has accuracy around 80% and the AUC curve in terms of sensitivity and specificity gives 89% in cross – validation over the test set which is given in chart in Fig. 11.

## Conclusion

The proposed work performed diagnosis based on the regional brain activity measurements using fMRI for bipolar or normal control. In this work, we have concentrated 8 brain regions which are usually affected by BPD as per literature. Our work has produced better accuracy of 94.23% when compared to earlier work. This work can be extended for Parkinson and Alzheimer diseases too.

## Declarations

Funding: Indian Council for Medical Research, New Delhi.(HRD Fellowship-II (2) /2014-15) dated 09 Oct 2014.

Conflicts of interest/Competing interests: We have **no conflicts of interest** to disclose.

Availability of data and material (data transparency): Data available on request from the authors.

Code availability (software application or custom code): software application

## References

1. Aapo, Hyvärinen, Oja, E., & Networks, N. Independent Component Analysis: Algorithms and Applications, Volume 13, Issues 4–5(2000). Pages 411–430, ISSN 0893–6080, https://doi.org/10.1016/S0893-6080(00)00026-5.
2. Fornito, A., Zalesky, A., & Bullmore, E. T. Chap. 5 - Centrality and Hubs, Fundamentals of Brain Network Analysis, Academic Press(2016). Pages 137–161, ISBN 9780124079083, https://doi.org/10.1016/B978-0-12-407908-3.00005-4.
3. Blumberg, H. P., Leung, H. C., Skudlarski, P., Lacadie, C. M., Fredericks, C. A., Harris, B. C. … Peterson, B. S. (2003 Jun;60(6):601-9). A functional magnetic resonance imaging study of bipolar disorder: state- and trait-related dysfunction in ventral prefrontal cortices. Arch Gen Psychiatry. doi: 10.1001/archpsyc.60.6.601. PMID: 12796223.
4. Chen, C-H., Suckling, J., Lennox, B. R., Ooi, C., & Bullmore, E. T.. A quantitative meta- analysis of fMRI studies in bipolar disorder https://doi.org/10.1111/j.1399-5618.2011.00893.x
5. Christoph Abé, C. J., Ekman, C., Sellgren, P., Petrovic, M., Ingvar, M., & Landén (November 2015). Manic episodes are related to changes in frontal cortex: a longitudinal neuroimaging study of bipolar 9disorder 1, Brain, Volume 138, Issue 11, Pages3440–3448, https://doi.org/10.1093/brain/awv266
6. Clark, L., & Sahakian, B. J. (2008). Cognitive neuroscience and brain imaging in bipolar disorder. *Dialogues Clin Neurosci*, 10(2), 153–163. doi:10.31887/DCNS.2008.10.2/lclark
7. Douglas, P., Sam Harris, K., & Yuille, A., Mark S. Cohen,Performance comparison of machine learning algorithms and number of independent components used in fMRI decoding of belief vs. disbelief, NeuroImage, Volume 56, Issue 2, 2011, Pages544–553, ISSN 1053–8119,https://doi.org/10.1016/j.neuroimage.2010.11.002.

8. Gin, S., Malhi, J., Lagopoulos, P. S., Sachdev, B., & Ivanovski, Ron Shnier, An emotional Stroop functional MRI study of euthymic bipolar disorder 2005, https://doi.org/10.1111/j.1399-5618.2005.00255.x
9. Gruber, S. A., Rogowska, J., & Yurgelun-Todd, D. A.. Decreased activation of the anterior cingulate in bipolar patients: an fMRI study. J Affect Disord. 2004 Oct 15;82(2):191–201. doi: 10.1016/j.jad.2003.10.010. PMID: 15488247.
10. Hilary, P., Blumberg, M. D., Andrés Martin, M. D., Joan Kaufman, P. D., Hoi-Chung Leung, P. D., Pawel Skudlarski, P. D. … Peterson, M. D. (2003). Frontostriatal Abnormalities in Adolescents With Bipolar Disorder: Preliminary Observations From Functional MRI, https://doi.org/10.1176/appi.ajp.160.7.1345
11. Juan, I., Arribas, V. D., Calhoun, & Adali, T. "Automatic Bayesian Classification of Healthy Controls, Bipolar Disorder, and Schizophrenia Using Intrinsic Connectivity Maps From fMRI Data," in IEEE Transactions on Biomedical Engineering, vol. 57, no. 12, pp. 2850–2860, Dec(2010). doi: 10.1109/TBME.2010.2080679.
12. Lawrence, N. S., Williams, A. M., Surguladze, S., Giampietro, V., Brammer, M. J., Andrew, C. … Phillips, M. L.. Subcortical and ventral prefrontal cortical neural responses to facial expressions distinguish patients with bipolar disorder and major depression. Biol Psychiatry. 2004 Mar 15;55(6):578 – 87. doi: 10.1016/j.biopsych.2003.11.017. PMID: 15013826.
13. Lyoo, I. K., Sung, Y. H., Dager, S. R., Friedman, S. D., Lee, J-Y., Kim, S. J. … Renshaw, P. F. (Regional cerebral cortical thinning in bipolar disorder. Bipolar Disord 2006). : 8: 65–74. ª Blackwell Munksgaard, 2006
14. Malhi, G. S., Lagopoulos, J., Sachdev, P. S., Ivanovski, B., Shnier, R., & Ketter, T.. Is a lack of disgust something to fear? A functional magnetic resonance imaging facial emotion recognition study in euthymic bipolar disorder patients. Bipolar Disord. 2007 Jun;9(4):345 – 57. doi: 10.1111/j.1399-5618.2007.00485.x. PMID: 17547581.
15. Mani, N., Pavuluri; Megan Marlow, O. C., Erin, M., Harral; John, A., & Sweeney (2008). An fMRI study of the interface between affective and cognitive neural circuitry in pediatric bipolar disorder.,162(3),244–255. doi:10.1016/j.pscychresns.2007.10.003
16. Marchand, W. R., Lee, J. N., Johnson, S., Gale, P., & Thatcher, J. (2014). Abnormal functional connectivity of the medial cortex in euthymic bipolar II disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 51, 28–33
17. Pavuluri, M. N., O'Connor, M. M., Harral, E., & Sweeney, J. A. (2007). Affective neural circuitry during facial emotion processing in pediatric bipolar disorder. Biol Psychiatry. Jul 15;62(2):158 – 67. doi: 10.1016/j.biopsych.2006.07.011. Epub 2006 Nov 9. PMID: 17097071.
18. Phillips, M. L., & Swartz, H. A. (2014). A critical appraisal of neuroimaging studies of bipolar disorder: toward a new conceptualization of underlying neural circuitry and a road map for future research. *Am J Psychiatry*, 171(8), 829–843. doi:10.1176/appi.ajp.2014.13081008
19. Rutvi Prajapati & Isaac Arnold Emerson. (2020). Global and regional connectivity analysis of resting-state function MRI brain images using graph theory in Parkinson's disease. *International Journal of Neuroscience*10.1080/00207454.2020.1733559,https://doi.org/10.1080/00207454.2020.1733559
20. Shirer, W. R., Ryali, S., Rykhlevskaia, E., Menon, V., & Greicius, M. D. (2012). Decoding Subject-Driven Cognitive States with Whole-Brain Connectivity Patterns. *Cerebral Cortex*, 22, 158–165
21. Strakowski, S., Adler, C., Holland, S., et al. (2004). A Preliminary fMRI Study of Sustained Attention in Euthymic. *Unmedicated Bipolar Disorder. Neuropsychopharmacol 29*, 1734–1740. https://doi.org/10.1038/sj.npp.1300492
22. Teng, S., Lu, C-F., Wang, P-S., Li, C-T., Tu, P-C., et al. (2014). Altered Resting-State Functional Connectivity of Striatal-Thalamic Circuit in Bipolar Disorder. *PLoS ONE*, 9(5), e96422. doi:10.1371/journal.pone.0096422
23. Umi Mahdiyah, M., & Isa Irawan (2015). Elly Matul Imah,Integrating Data Selection and Extreme Learning Machine for Imbalanced Data, Procedia Computer Science, Volume 59, Pages 221–229, ISSN 1877 – 0509, https://doi.org/10.1016/j.procs.2015.07.561.
24. Wei, S. Y., Tseng, H. H., Chang, H. H., et al. (2020). Dysregulation of oxytocin and dopamine in the corticostriatal circuitry in bipolar II disorder. *Transl Psychiatry 10*, 281. https://doi.org/10.1038/s41398-020-00972-6
25. Wan, Z., Mahajan, Y., Kang, B. W., Moore, T. J., & Cho, J. H. "A Survey on Centrality Metrics and Their Network Resilience Analysis," in IEEE Access, vol. 9, pp. 104773–104819(2021). doi: 10.1109/ACCESS.2021.3094196.

# Tables

Table 1-2 are available in supplementary section.

# Figures

**Figure 1**

Proposed Architecture

**Figure 2**

*Input Image (Healthy Control)*

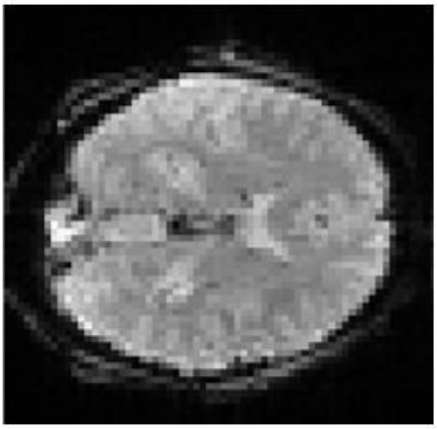

**Figure 3**

Input Image (BPD)

**Figure 4**

Regions taken for analysis

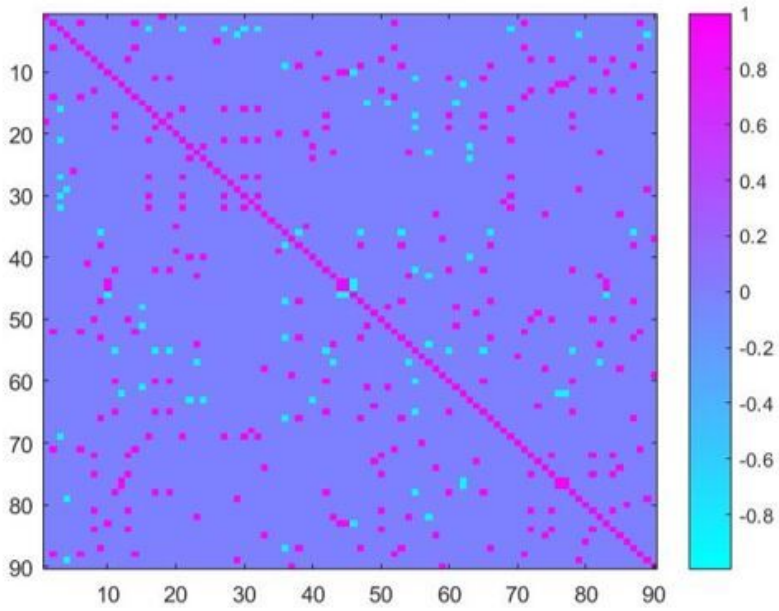


**Figure 5**

Correlation map for the 90 functional points (BPD)

**Figure 6**

Correlation map for the 90 functional points (Healthy Control)

**Figure 7**

Output Image (BPD)

**Figure 8**

Output Image (Healthy Control)

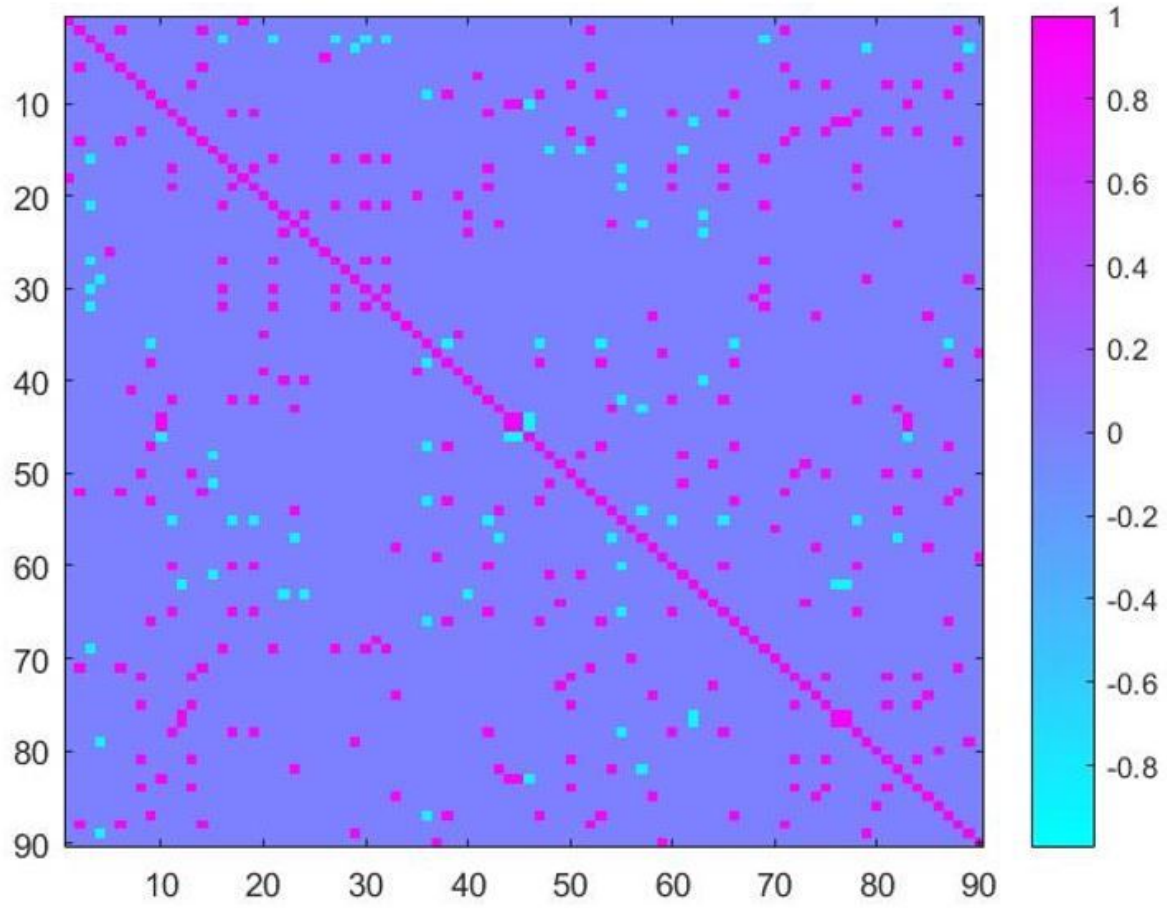


**Figure 9**

Correlation map for the 90 functional points

**Figure 10**

Modular structure of the correlation matrix

**Figure 11**

Performance comparison chart of Bipolar analysis with Work [11]

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tables.docx