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Classification of Autism Spectrum Disorder using Resting State-Functional Magnetic Resonance Imaging and Artificial Neural Network

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Abstract
Autism Spectrum Disorder (ASD) represents a growing challenge in public health, characterized by irreversible neurodevelopmental abnormalities. Despite a rising prevalence, the underlying aetiology and neural substrates of ASD remain incompletely understood. Resting state-functional Magnetic Resonance Imaging (rs-fMRI) has emerged as a valuable non-invasive tool for probing the organization and cognitive functions of the brain by capturing hemodynamic changes. This study explores the relationship between Functional Connectivity (FC) alterations, measured by rs-fMRI, and the manifestation of ASD-related brain disorders. In this paper, we propose a hybrid approach employing an InfoMax Independent Component Analysis (ICA) algorithm and Artificial Neural Network to distinguish between the ASD subjects and Healthy Controls (HCs). Initially, rs-fMRI datasets are preprocessed using Statistical Parametric Mapping (SPM). Further, these datasets are processed using InfoMax ICA to extract the distinct features such as fractional Amplitude of Low-Frequency Fluctuations (fALFF) and Dynamic Range and visualize the FC alterations by region mapping. In addition to this, the number of activated voxels for each brain regions are estimated to observe the neural abnormalities. Finally, the extracted features are fed as input to train, test and validate the ANN classifier. The efficacy of the proposed network is evaluated using the Autism Brain Imaging Data Exchange (ABIDE) dataset and an accuracy of 75.3 percentage is achieved.

Keywords: Resting state-functional Magnetic Resonance Imaging, Autism Spectrum Disorder, Functional Connectivity, InfoMax Independent Component Analysis, Artificial Neural Network, Fractional Amplitude of Low-Frequency Fluctuations, Dynamic Range

1. Introduction

Brain disorders encompass a diverse range of conditions, each with unique implications for individuals, families, and societies on a global scale. These disorders can affect cognitive function, behavior, and

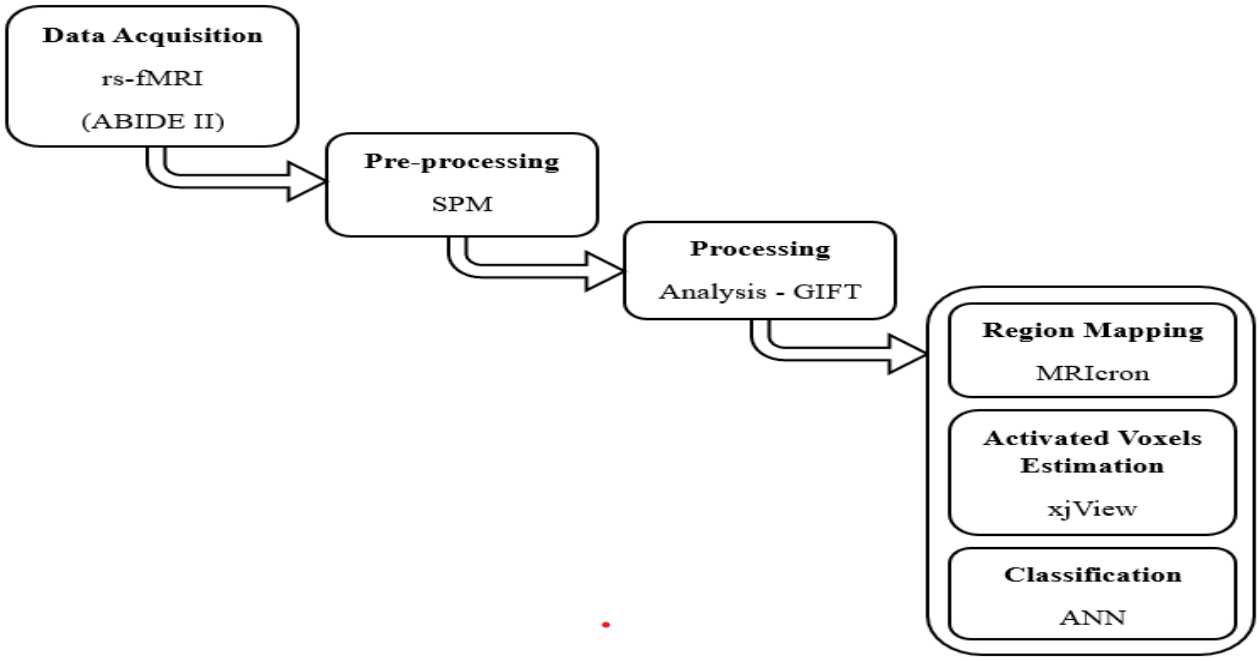
emotional well-being. The impact varies widely, depending on the specific disorder, but common themes emerge. At an individual level, those affected by brain disorders may experience challenges in cognition, memory, motor function, or mental health. The severity and nature of symptoms vary, ranging from mild to debilitating. Individuals often require tailored medical interventions, rehabilitation, and support services to manage their condition effectively.

One of the major brain disorders is ASD. ASD is a complex developmental disorder marked by challenges in social interaction, communication difficulties, and repetitive behaviour patterns. Symptoms vary widely among individuals, encompassing difficulties in social interaction, communication challenges, and repetitive behaviours [3]. The rs-fMRI plays a vital role in investigating brain network activity. Brain network activity during the resting state has been investigated in subjects with ASD and typical development in numerous studies [2, 7, 13]. In this work, the advantages of rs-fMRI and machine learning algorithm are combined together to classify ASD from HC as it aids in early diagnosis and treatment which thereby can reduce the severity of the disorder. ABIDE II datasets were utilized for this study.

2. Methodology

The proposed methodology is depicted in the block diagram shown in Figure 1.

Figure 1: Block Diagram



2.1 Data Acquisition

The Autism Brain Imaging Data Exchange (ABIDE) initiative consists of aggregated functional and structural brain imaging data collected from various laboratories to understand the neural bases of autism or ASD. It includes ABIDE I and ABIDE II [6, 10]. A total of 77 subjects are taken from the ABIDE II dataset, in which 46 subjects are ASD and 31 subjects are HCs.

2.2 Pre-processing

The rs-fMRI images generally have the challenges such as non-alignment of individual slices with each

other, motion blur, different brain sizes and noise that can cause error during processing. Hence, fMRI images are pre-processed by SPM12 to remove these defects [9]. The pre-processing steps involve realign, normalize and smoothening. Realign comprises two processes, estimate and reslice. This process helps counteract the motion caused by the subjects during scan. Here, the resliced images have been normalized with respect to the avg152T1 template with voxel size set to 3x3x3 mm^3 to ensure that each voxel for each subject corresponds to the same part of the brain. Then, the normalized images are smoothened using a spatially stationary Gaussian filter in which the kernel size is determined by the Full Width Half Max (FWHM). The FWHM was set to 10x10x10 mm^3.

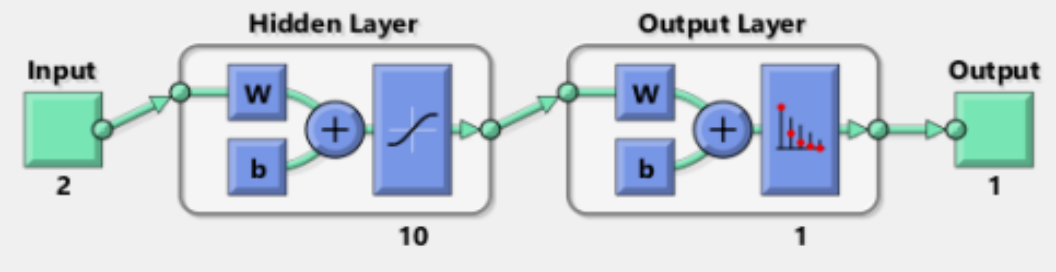
2.3 Processing

Independent component analysis (ICA), a multivariate approach, has been utilized to analyze brain imaging data and to understand its' functional connectivity. ICA is performed using the Group ICA Of fMRI Toolbox (GIFT) to extract features from the pre-processed fMRI images. In GIFT, standard ICA is performed, and 20 components are extracted from each image using the infomax algorithm [14]. GIFT outputs a spectral summary containing the Dynamic Range, fALFF and the Peak Coordinates for each of the 20 components. Region Mapping is performed using MRIcron. In MRIcron, the template was set to AAL3v1.nii.gz and the peak coordinates are entered in and the regions corresponding to the entered coordinates are obtained for both autistic and healthy subjects [1]. The number of activated voxels for each regions are estimated using xjView [5].

2.4 Classification

ANN was implemented using the neural pattern recognition tool in MATLAB to classify the subjects as ASD and HC [12]. The dynamic range and fALFF values obtained from GIFT for each subject individually are given as inputs and a binary value corresponding to each category is set as target. The ANN consists of a two-layer feed-forward network, with sigmoid hidden and softmax output, classifies vectors arbitrarily well, given enough neurons in its hidden layer. The architecture of the ANN is shown in Figure 2. The network was trained with scaled conjugate gradient backpropagation. The number of hidden neurons was set to 10 and the 70% of the inputs were used for training, 15% for validation and 15% for testing.

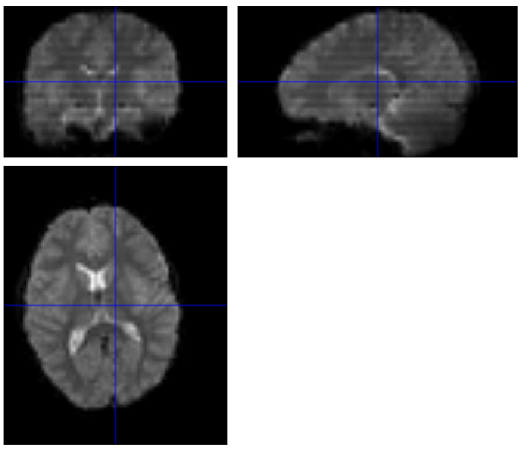
Figure 2: ANN Architecture



3. Results and Discussion

The raw fMRI image before preprocessing is shown in the Figure 3.

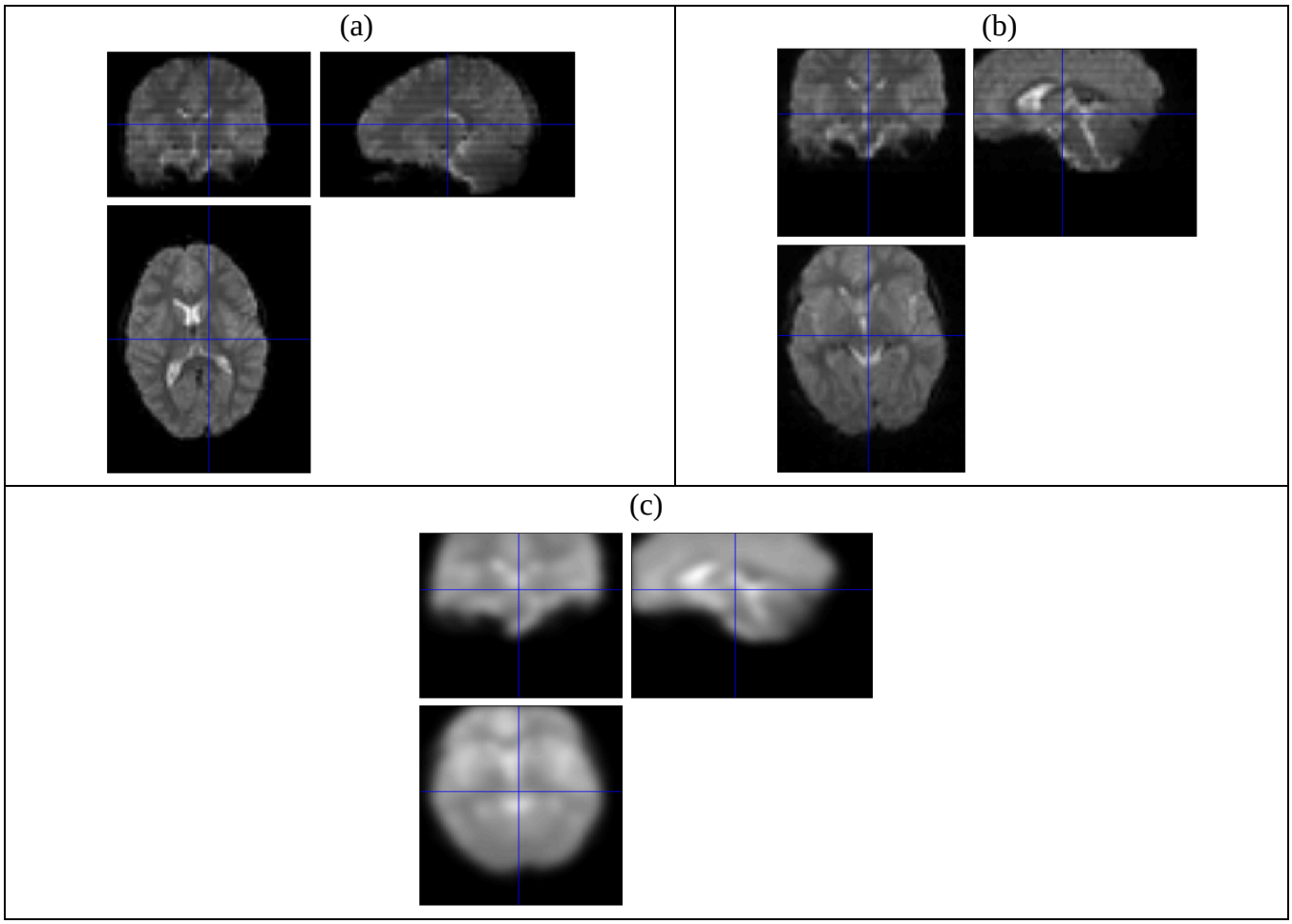
Figure 3: Raw fMRI Image



3.1 Preprocessed fMRI images

The preprocessed fMRI datasets after undergoing the process of realign, normalize and smooth are obtained and shown in the Figure 4.

Figure 4: Preprocessed fMRI images - (a) Realigned fMRI Image, (b) Normalised fMRI Image, (c) Smoothened fMRI Image



3.2 Analysis of fMRI images

The output obtained for the first component when ICA was performed to a group containing all the subjects having ASD is displayed in Figure 5. Figure 6 shows the average Functional Network Connectivity (FNC) correlations of each component with each of the other components. MRIcon maps the brain region for the entered coordinates. xjView estimated the number of activated voxels for each brain region in the selected cluster. The brain regions that were activated and predominant for both healthy and ASD subjects are listed in Table 1. It is observed that there are 9 regions that were common for both ASD and healthy subjects. The activated voxels in these regions of HC are mostly higher than the ASD subjects which indicates that there is abnormal brain activity in these regions of ASD subjects. These regions are mainly associated with frontal lobe, parietal lobe and cingulate gyrus which are involved in decision-making, planning, problem-solving, impulse control, mathematical reasoning, visuospatial processing, object manipulation, processing and regulating emotions, forming and retrieving memories.

Figure 5: GIFT Output for the First Component

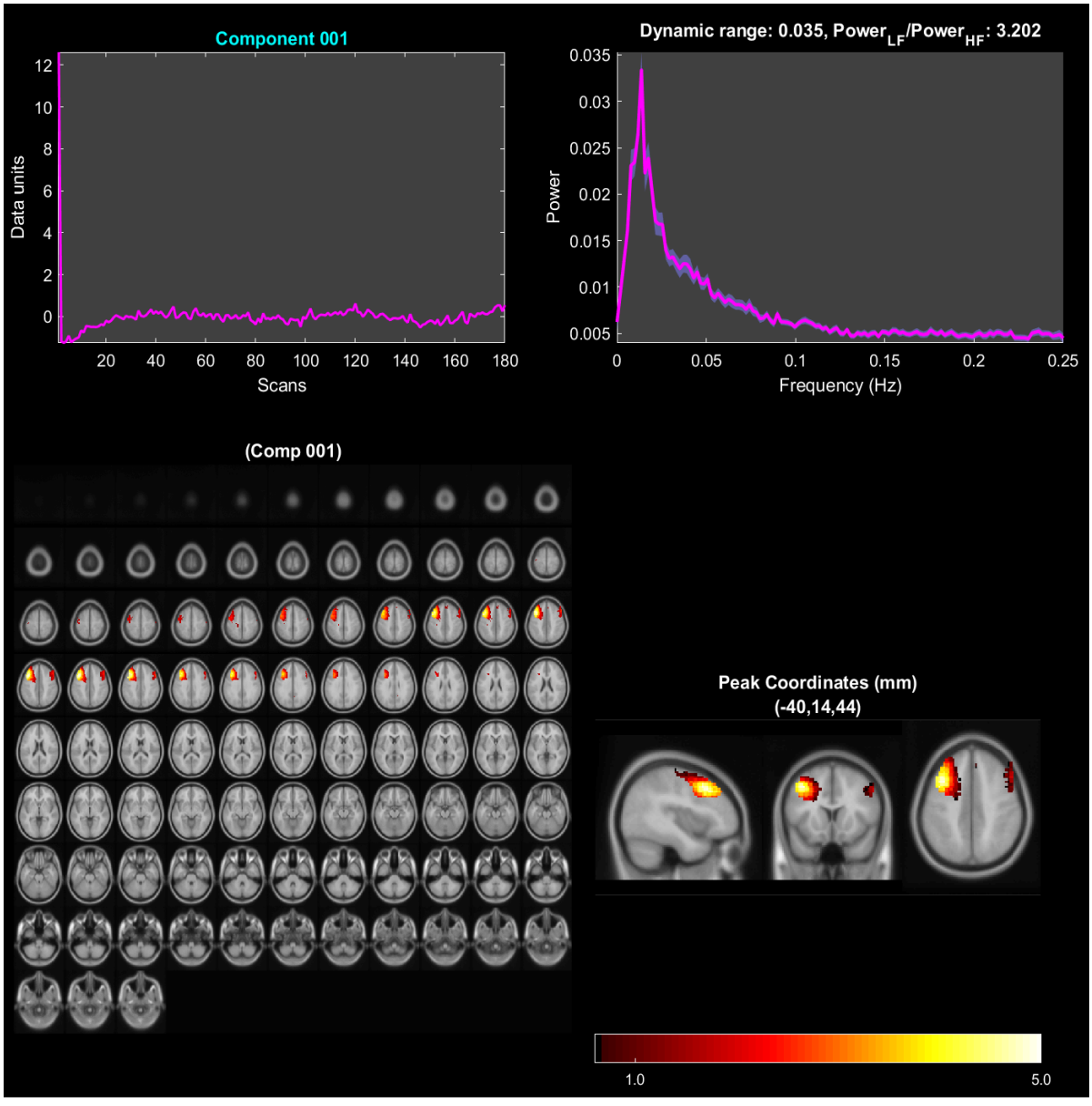


Figure 6: Autistic Subjects' Average FNC Correlations

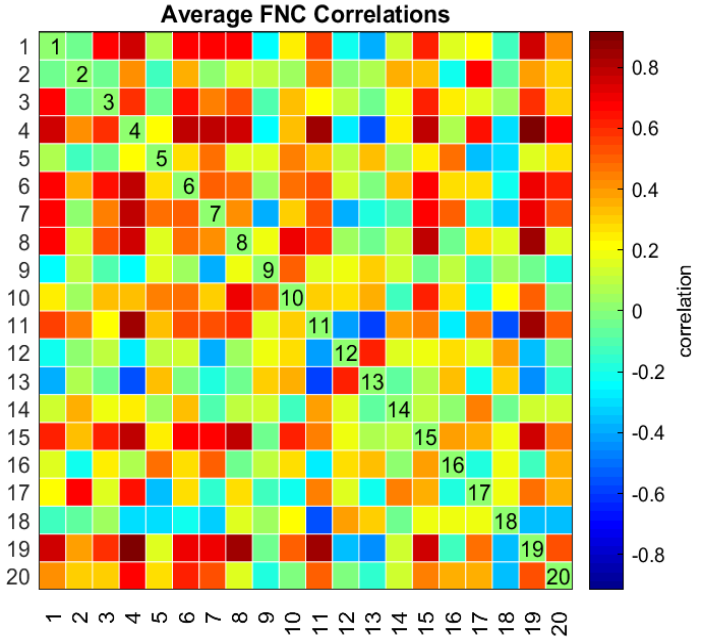


Table 1: Common Regions in ASD and HC subjects

S.No.	Regions	ASD/HC	Peak Coordinates	Dynamic Range	fALFF	Activated Voxels
1	Frontal_Mid_2_L 5	ASD	(-40,14,44)	0.035	3.202	592
		HC	(-46,28,44)	0.039	6.148	760
2	Paracentral_Lobule_R 74	ASD	(0,-26,76)	0.038	4.482	178
		HC	(0,-38,74)	0.046	12.283	222
3	Frontal_Mid_2_R 6	ASD	(44,38,44)	0.039	4.819	804
		HC	(44,14,40)	0.034	2.827	818
4	Cingulate_Mid_L 37	ASD	(0,-20,40)	0.041	3.483	481
		HC	(0,14,40)	0.035	2.567	506
5	Supp_Motor_Area_R 16	ASD	(2,4,80)	0.037	5.023	630
		HC	(6,28,82)	0.038	3.812	630
6	Cingulate_Mid_R 38	ASD	(0,-26,26)	0.035	2.731	535
		HC	(2,-32,50)	0.042	4.346	585
7	Frontal_Inf_Tri_R 10	ASD	(38,22,28)	0.034	2.384	56
		HC	(38,22,26)	0.037	2.739	65
8	Frontal_Sup_Medial_L 19	ASD	(-4,20,40)	0.035	2.433	286
		HC	(-6,32,38)	0.035	3.9	345
9	Precuneus_R 72	ASD	(8,-44,52)	0.04	5.216	158
		HC	(2,-52,58)	0.046	8.213	497

Table 2: Regions in ASD subjects

S.No.	Regions	Peak Coordinates	Dynamic Range	fALFF	Activated Voxels
1.	Precuneus_L 71	(0,-56,34)	0.04	4.602	229
2.	Postcentral_R 62	(48,-22,58)	0.036	4.561	370
3.	SupraMarginal_R 68	(36,-40,34)	0.035	3.813	40
4.	Paracentral_Lobule_L 73	(0,-28,62)	0.049	10.648	359

Table 3: Regions in HCs

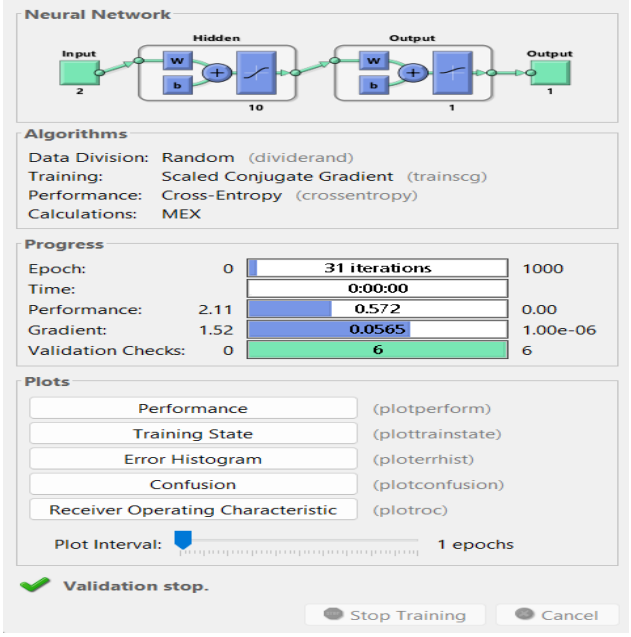
S.No.	Regions	Peak Coordinates	Dynamic Range	fALFF	Activated Voxels
1.	Precentral_R 2	(50,8,50)	0.043	7.044	821
2.	Angular_L 69	(-40,-62,38)	0.039	3.534	66
3.	Supp_Motor_Area_L 15	(0,-2,70)	0.042	6.64	589
4.	Postcentral_L 61	(-48,-28,56)	0.044	5.895	808
5.	Parietal_Inf_L 65	(-30,-62,40)	0.041	7.65	432

From Table 2, it can be inferred that the activated voxels are very less in Right Supramarginal gyrus (SMG) when compared to other predominant regions of ASD. The abnormal or reduced activity in this region is associated with a low capacity for sympathy, empathy, and language in ASD [4, 8, 11]. These results clearly differentiate ASD from that of HC. The other predominant regions in HCs are listed in Table 3.

3.3 ANN Classifier

The ANN Classifier are trained for 31 epochs, at which all 6 validation checks are completed. The performance of the trained ANN is 0.572 and the gradient is 0.0565. These values obtained are shown in the Figure 7.

Figure 7: ANN Classifier - Algorithms and Progress



The ANN gives the lowest cross-entropy and the best validation performance of 0.53562 at the 25th epoch. This can be observed from the graph shown in Figure 8. The ANN has 6 validation checks, on completing which the neural network completes training. The neural network trains for 31 epochs and the gradient is 0.056 at the 31st epoch which can be observed in the Figure 9. The total error range is divided into 20 smaller bins here and the obtained error histogram plot is shown in Figure 10. From the confusion matrix obtained in Figure 11, the overall efficiency of the ANN classifier is about 75.3 percentage. Receiver operating characteristic (ROC) curve obtained for the ANN classifier is as shown in the Figure 12. Thus, the ANN Classifier was able to correctly classify between autistic and healthy subjects with an overall accuracy of 75.3 percentage.

Figure 8: ANN - Performance Plot

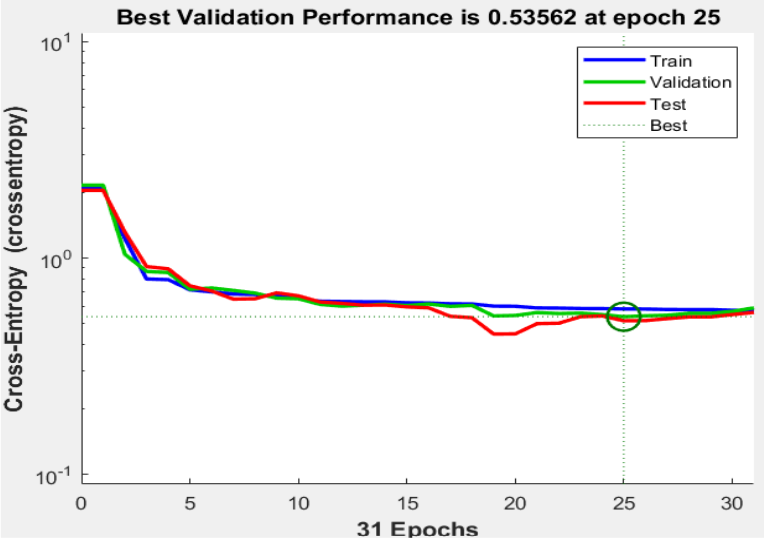


Figure 9: ANN - Gradient Plot and Validation Checks

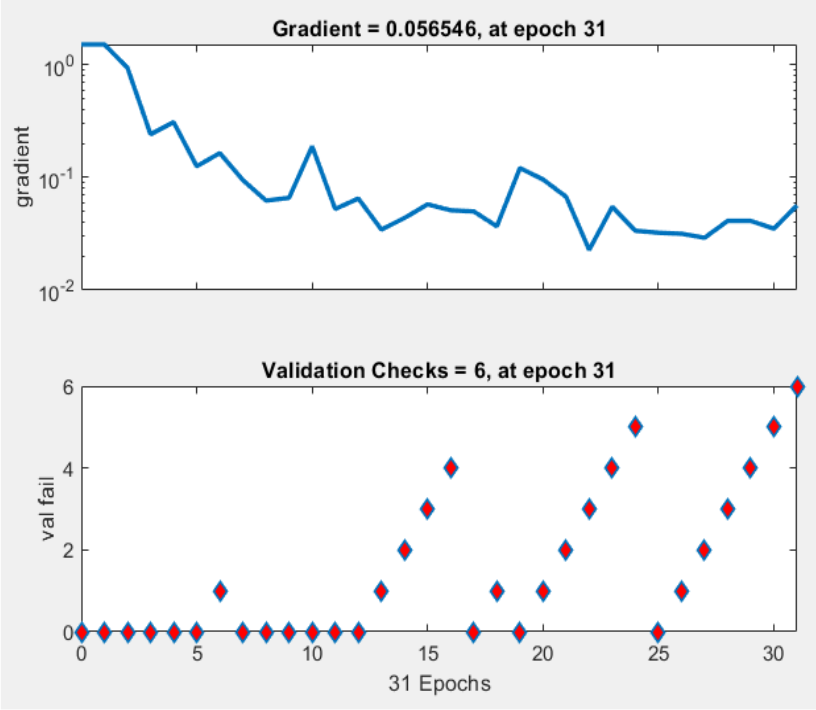


Figure 10: ANN - Error Histogram

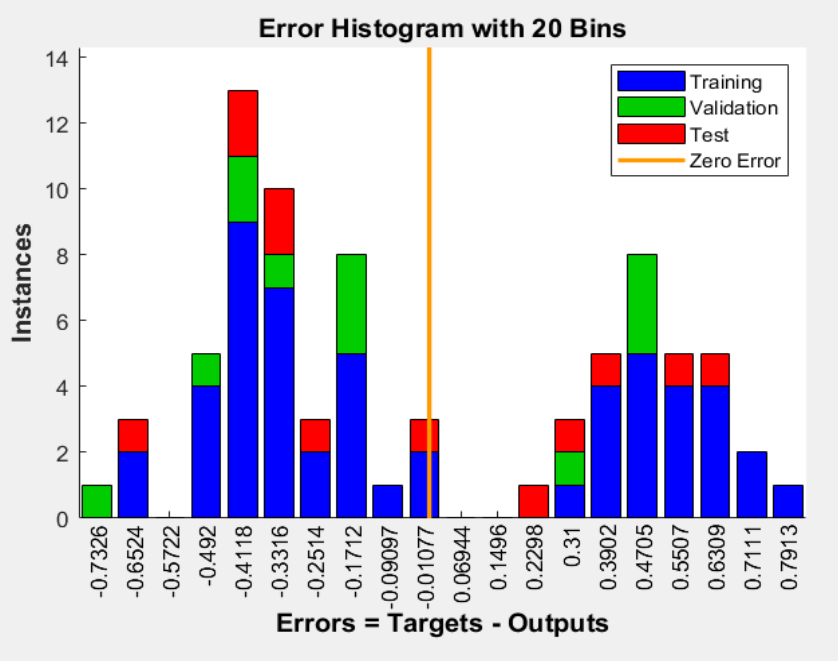


Figure 11: ANN - Confusion Matrix

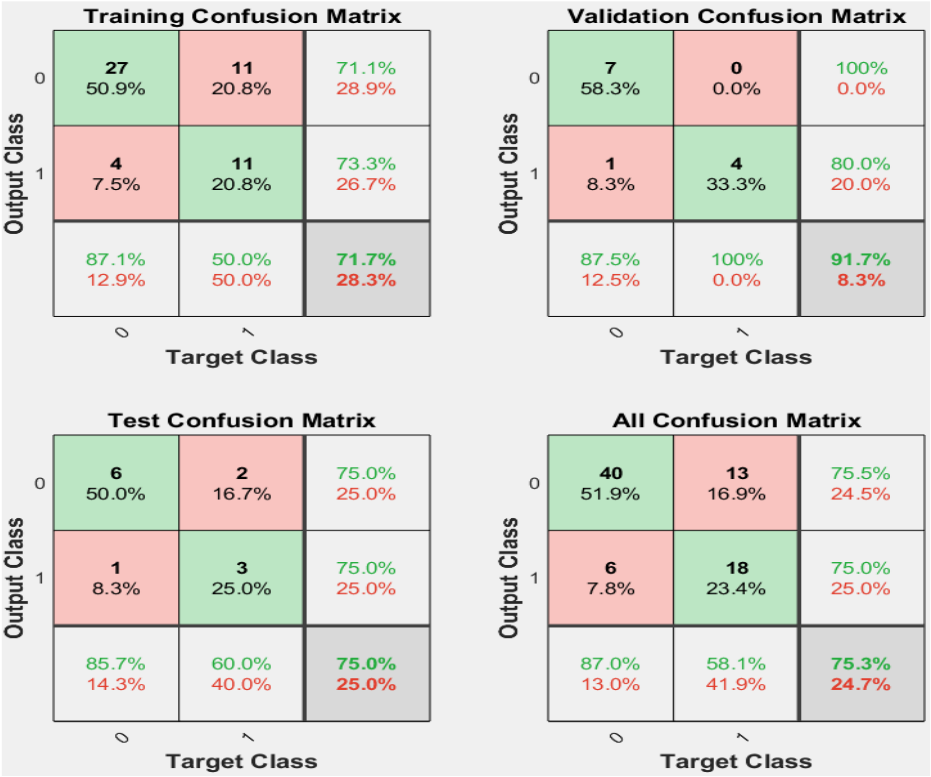
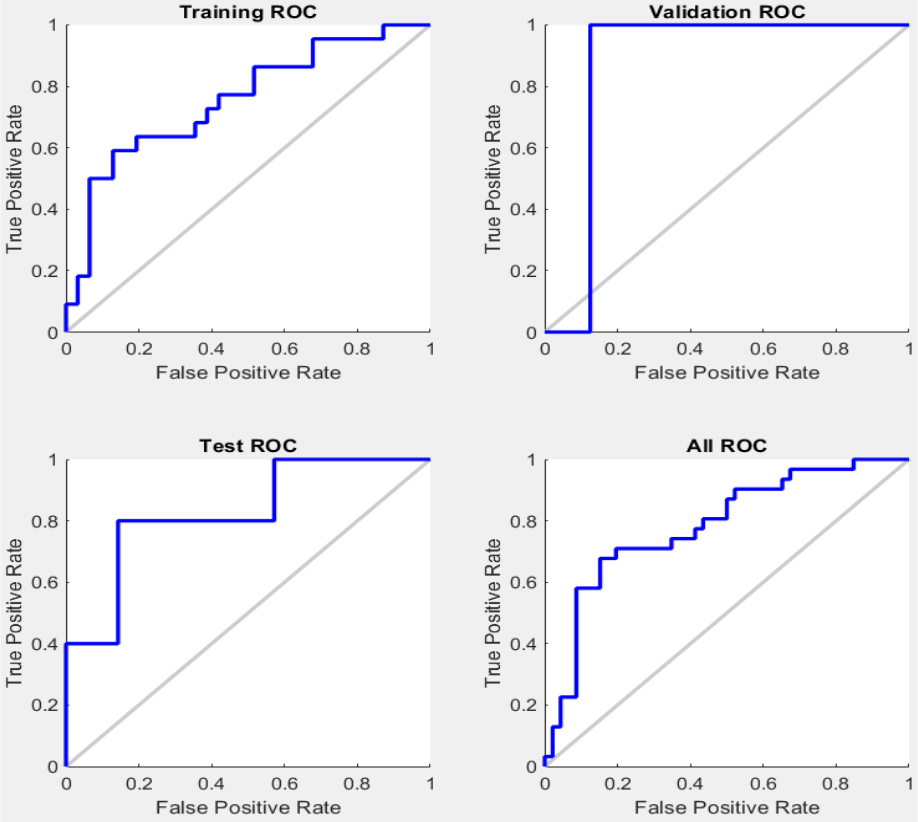


Figure 12: ANN - ROC Curve



4. Conclusion

Thus, the modelled ANN explores the interactions among subjects by incorporating details such as dynamic range and fALFF. This comprehensive approach not only enhances biomarker identification but also delves into the complex relationships embedded within the dataset. The classification process, executed with precision using the ANN, significantly contributes to a thorough understanding of the underlying patterns and nuances present in the provided data. The efficiency of the model is obtained to be 75.3 percentage which is on par with the existing machine learning algorithms. Also, the number of activated voxels for autistic subjects are less compared to healthy subjects which inturn justifies that there is abnormal brain activity in regions related to cognitive behavior, in case of ASD subjects. These experimental results imply that the proposed network has great potential in the application of computer-aided diagnosis based on medical images.

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