

AI-Based Feature Extraction Approaches for Dual Modalities of Autism Spectrum Disorder Neuroimages

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Abstract: High-dimensional data, lower detection accuracy, susceptibility to manual errors, and the requirement of clinical experts are some drawbacks of conventional classification models available for Autism Spectrum Disorder (ASD) detection. To address these challenges and explore the affiliated information from advanced imaging modalities such as Magnetic Resonance Imaging (MRI) in structural MRI (sMRI) and resting state-functional MRI (rs-fMRI), the study applied an Artificial Intelligence (AI) approach. In this context, AI is used to automate the feature extraction process, which is crucial in the interpretation of medical images for diagnosis. The work aims to apply AI-based techniques to extract the features and identify the impact of each feature in the Autism diagnosis. The morphometric features were extracted using sMRI images and rs-fMRI scans were employed to fetch functional connectivity features. Surface-based, region-based, and seed-based analyses are performed for the whole brain, followed by feature selection techniques such as Recursive Feature Elimination (RFE) with correlation, Principal Component Analysis (PCA), Independent Component Analysis (ICA), and graph theory are implemented to extract and distinguish features. The effectiveness of the extracted features was measured as classification accuracy. Support Vector Machine (SVM) with RFE is the best classification model, with 88.67% accuracy for high-dimensional data. SVM is a supervised learning model that outperforms other classification models due to its capability to handle high-dimensional data with a larger feature set. Medical imaging modalities provide detailed insights and visual differences related to various cognitive conditions that must be recognized accurately for efficient diagnosis. The study presented an empirical analysis of various Feature extraction approaches and the significance of the extracted features in high-dimensional data scenarios for Autism classification.

Keywords: Autism Spectrum Disorder, Artificial Intelligence, Feature Extraction, MRI, Structural MRI, Functional MRI

Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that restricts the natural development of children by affecting their communication and social behavior (Genovese and Butler, 2020). Autism occurs in the very early stages of life and children with autism are characterized by repetitive behavior, restricted interaction, and communication. This symptomatic variation makes it challenging for autistic individuals to perform routine tasks (Huang *et al.*, 2017; Randall *et al.*, 2018). Early diagnosis of ASD is essential to minimize the adverse

consequences to the patients and help the professionals and caretakers plan therapies and treatment plans (McCarty and Frye, 2020). However, the accurate diagnosis of autism can be challenging due to the varying symptoms and attributes (Jacob *et al.*, 2019). Continuous and persistent occurrence of a diverse range of symptoms is difficult to diagnose accurately. At present, multiple tools and observational measures are available to assess ASD-related behaviors. For example, the Autism Diagnostic Observation Schedule (ADOS) is widely used for diagnosis (Adamou *et al.*, 2018), while other instruments—such as the Autism Observation Scale for Infants (AOSI) (Reid *et al.*, 2024), the Social Orienting

Continuum and Response Scale (Mosconi *et al.*, 2009), and the Early Social and Communication Scales (Wetherby *et al.*, 2021) serve as research tools to observe early indicators of ASD but are not diagnostic in nature. Diagnosis requires manual efforts and expertise, which vary based on the experience, information given by the parent, and the individual's behavior, as well as observations. Physicians use clinical biomarkers for the early diagnosis of ASD. However, these biomarkers are insufficient for the early identification of ASD since the patterns of the disease vary for each individual. Recent studies have successfully employed computer-aided techniques using various data modalities, such as Electroencephalogram (EEG) signals and MRI to understand ASD (Tawhid *et al.*, 2021; Sivasangari *et al.*, 2022; Ismail *et al.*, 2016). Moreover, advances in imaging techniques such as structural MRI (sMRI) and resting state functional MRI (rs-fMRI) have resulted in the precise identification of ASD. Several research has been presented that utilize MRI modalities to identify ASD (Hashem *et al.*, 2020; Li *et al.*, 2017; Dekhil *et al.*, 2017). Despite the advancements, it is still uncertain whether the structural and functional abnormalities are sufficient in distinguishing between individuals with ASD and those who are neurotypical. While both sMRI and rs-fMRI can accurately identify brain pattern changes and connectivity, Artificial Intelligence (AI) based models for ASD classification have yet to be fully developed. Furthermore, to achieve accurate ASD diagnosis, it is crucial to explore and distinctly define disease-related features that capture complex brain patterns. This research aims to harness the benefits of AI by developing a framework that incorporates a feature extraction mechanism to enable accurate and efficient diagnosis of ASD.

The core contributions of the paper are:

- Empirical analysis of dual neuroimaging modalities performing the preprocessing, feature extraction, dimensionality reduction, and comparative analysis of structural features for classification
- The classification algorithms applied to the structural features and proposed to be applied to rs-fMRI features

The research is based on a high-dimensional scenario, which is most suitable for studies aimed to explore the insights of a specific condition, but the dataset availability is limited. The study aimed to achieve higher classification using AI methodologies suitable for limited datasets having a huge number of features, such as high-resolution medical images. The hypothesis for the study was to investigate the impact of a large feature set coupled with a low volume of data on classification accuracy and the successive clinical implications.

Related Work

Inaccurate or late diagnosis might cause severe damage and can result in perilous circumstances. Hence,

it is essential to develop efficient techniques for consistent definition and detection of the symptoms of ASD with high accuracy. Recent studies have implemented AI techniques to extract complex and multivariate patterns from neuroimaging data for diagnosing ASD (Chen *et al.*, 2020; Ferrari, 2021). In addition, feature extraction plays a significant role in providing valuable information about the disease and advanced diagnostic tools such as fMRI and rs-fMRI provide relevant information about the brain (Mohi ud Din and Jayanthi, 2023). Recent research proposed a deep multimodal approach, which combines the information acquired from rs-fMRI with a deep learning model to automate ASD diagnosis (Tang *et al.*, 2020). This approach achieved a classification accuracy of 74%, a recall rate of 95%, and an F1 score of 0.805 in distinguishing ASD individuals from neurotypical individuals. Another study proposed an informative biomarker for ASD diagnosis using rs-fMRI data, where static and dynamic connectivity were determined and used as inputs for the classifier to select essential features (Karampasi *et al.*, 2021). These features comprised demographic and motion data, which were critical in identifying ASD cases. The classification accuracy achieved by the model was 76.63% with static and dynamic connectivity being key factors. The authors Koc *et al.* (2023) implemented sMRI and resting-state MRI (rsMRI) data to detect ASD. For the experimentation, the authors utilized two-dimensional rs-fMRI images that were transformed into 3D sMRI images for analysis. The data was collected from the ABIDE dataset and the fusion of sMRI and rs-fMRI data enabled the Hybrid Convolutional Recurrent Neural Network (HCRNN) model to achieve a phenomenal accuracy of 96% in classifying ASD. A Convolutional Neural Network (CNN) combined with rs-fMRI modality was applied by Mahadevaswamy and Manjunath (2022) for detecting autism. The CNN was trained using the scan images obtained from rs-fMRI, which yielded an accuracy of 97%. The effectiveness of feature selection and extraction was validated, and a comprehensive explanation was provided. In the work presented by Lamani *et al.* (2023); Hazim Hamed and Albahri (2023). It implies that feature extraction is a crucial process that helps the AI models to identify the patterns or characteristics in the data to differentiate individuals with ASD from Normal Control (NC). Multi-level feature extraction has a more significant role in enhancing the accuracy of AI models such as neural networks given by Alam *et al.* (2023). Although AI models, along with sMRI and rs-fMRI, are more effective in automating the ASD detection process, there are specific challenges due to complicated structures and inconsistent biomarkers. Most of the existing work does not consider the biological diversity of individuals and less cognitive functional individuals with severe ASD symptoms are often neglected, which affects the generalization capacity of the models.

Materials and Methods

The material applied for the research is the neuroimaging modalities of autistic and normal subjects. Data for the experimental analysis was collected from a multisite data repository known as ABIDE containing rs-fMRI and sMRI images. The ABIDE II was a set of 1114 scans with a balanced combination of 521 ASD and 593 control subjects and greater phenotypic characterization. The dataset applied in the presented work belongs to the University of California Los Angeles (UCLA). The dataset information is available at http://fcon_1000.projects.nitrc.org/indi/abide/, which specified that the data repository has followed all the protocols released by the US Health Insurance Portability and Accountability Act (HIPAA) as well as approved by the regional Institutional Review Board to collect the data.

The scans obtained from sMRI and rs-fMRI were preprocessed to achieve artifact and noise-free images for feature extraction. The research implements a five-stage process for detecting ASD. The flowchart displayed in Fig. (1a), the detailed execution of the steps given in Fig. (1b). The first step was to collect the data as input from the ABIDE dataset, which consisted of images obtained from sMRI and rs-fMRI scans. The second step was the preprocessing stage, wherein the input images were processed and a regression model was created. In the third step, feature extraction from sMRI containing the Gray Matter (GM), White Matter, and Cerebro Spinal Fluid (CSF) volumes of brain regions, Total Intracranial Volume (TIV), and surface thickness. Features for the rs-fMRI scan images are extracted using Functional Connectivity analysis (FC), graph theory, and ICA, followed by PCA in the fourth step. The extracted features are applied to various AI classification models to validate the significance of extracted features for autistic subjects.

The Graph theory approach was employed to calculate the correlation coefficients between every voxel in the brain and to categorize them. Based on the correlation, a thresholding level was identified using which the redundant edges from the brain images are eliminated and only relevant brain regions are considered for detecting ASD. Figure (1a-b) depicts the whole methodology applied to the current work.

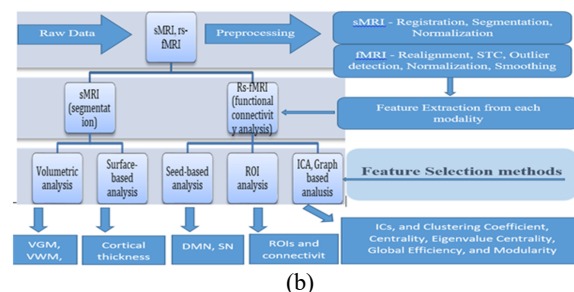
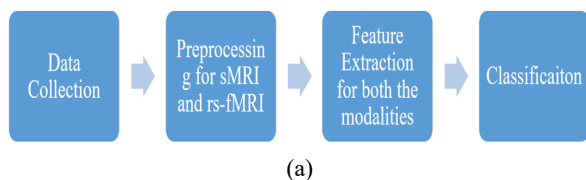


Fig. 1: (a) Flow chart for the complete analysis; (b) Methodology flow chat

Data Preprocessing

Preprocessing was performed to remove external noise, such as physiological and thermal noise, and prevent the influence of uncertainties. The MATLAB, Statistical Parametric Mapping (SPM), and the Functional Connectivity (CONN) toolbox were applied to perform preprocessing. The preprocessing was executed individually on sMRI and rs-fMRI with different steps. The functional scans are processed in six different steps, which are as follows: (i) Functional realignment and unwarp (ii) Slice-timing correction, (iii) Outlier identification (iv) Direct segmentation and normalization, and (vi) Functional smoothing (Nieto-Castanon, 2020). The preprocessing steps for sMRI scans are registration, segmentation, and normalization. The original images, the pipeline of the preprocessing stages, and the preprocessed images are displayed in Fig. (2).

Realignment: The MRI data was realigned with a 6-parameter rigid-body affine transformation and least squares approach. The image co-registration was performed with the first image of the scan of the session considering it as a reference scan. Further, the scans were resampled using the b-spline interpolation so that the data the resampled data can be applied for motion and magnetic susceptibility interactions.

Slice Timing Correction (STC): The slice acquisition was in interleaved mode and Repeat Time (TR) was 3, which was a comparative larger and needed to be corrected to remove any time difference effects on the slices. The temporal misalignment between different slices of the functional data was corrected using the STC process (Parker *et al.*, 2017). The STC involves correcting and shifting the slices using slice Acquisition Time (TA) for the first slice of the TR parameters to ensure temporal alignment.

Outlier detection: Possible outlier scans are detected using Artifact detection Tools (ART). A frame-wise displacement was determined at each time step by creating a bounding box of dimension 140×180×115 mm across the brain. The time series for each subject transformed into MNI template space using 12°C of Freedom linear affine transformation. The distorted BOLD signals and filtered signals with the outlier are shown in Fig. (3).

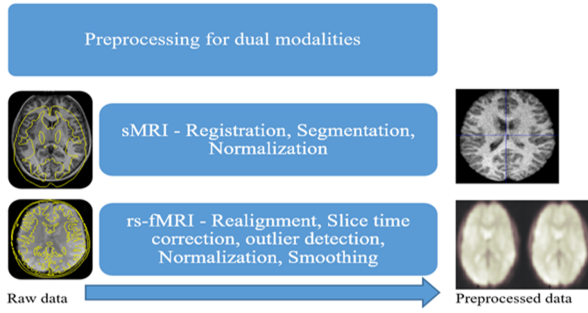


Fig. 2: Methodology flow chat

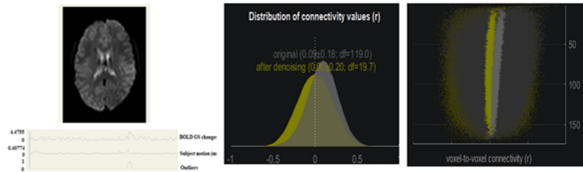


Fig. 3: Outlier detection-sample output for single image demising

Structural segmentation and normalization: The functional and structural data are normalized into a standard default Tissue Probability Map (TPMT1-152) template (Pecco *et al.*, 2022). The segmentation was performed on the sMRI scans to achieve GM, WM, and CSF tissue types followed by resampling to 2 mm isometric voxels. The normalization was performed using forward deformation and B-Spline interpolation algorithms. The voxel size and resolution need to be adjusted to enhance the quality of normalized scans, the image voxel size was considered for resampling.

Functional smoothing and filtering: The functional scan smoothening was achieved with an eight-mm Full Width Half Maximum (FWHM) Gaussian kernel with a spatial convolution, to maximize the Signal-To-Noise Ratio (SNR) to minimize the impact of residual variations in both functional and anatomical scans across different subjects. The 'F' statistic is a ratio of the mean square between and within a group. The noise removal for low-frequency ranges or drift high pass filter was applied to the fMRI scans. The brain activity signals can be as slow as noise but not below the range of 0.008 Hz which is equivalent to a cycle below 125 sec. To preserve the significant signals and to remove the noise high pass filter was applied to the time series ranging from 0.008 Hz and 0.09 Hz. The range of filtered signal was estimated to be from 13.6-40.2. The average ratio for the de-noised signal was 35.6 for all individuals.

Feature Extraction and Feature Selection

The data applied in the current work is high-dimensional data with a small set of images, such scenarios are challenging and known as the curse of dimensionality. Several methodologies were applied under the trial-and-error strategy. Least Absolute

Shrinkage and Selection Operator (LASSO), FeatureWiz, and RFE applied to sMRI scans for feature extraction. To perform the whole brain analysis, ICA was applied to rs-fMRI scans for feature extraction. PCA algorithm applied to rs-fMRI scans for dimensionality reduction. Functional Connectivity maps and features were observed using Graph theory.

Recursive Feature Elimination (RFE)-sMRI

RFE is an ML-based wrapper-type feature selection methodology that applies ML methods to evaluate the significance of a feature. RFE is a recursive elimination process to reach a predefined count of features. Correlation analysis was performed to remove the highly correlated and redundant features. To achieve the most significant features, RFE was performed using Random Forest (RF), Support Vector Machine (SVM), and Logistic Regression (LR).

Seed-Based Connectivity Maps (SBC)-rs-fMRI

The spatial pattern of functional connectivity was observed from seed or Region of Interest (RoI)/seed to each voxel in the brain using the 32 HPC-ICA network ROIs. The FC is determined using Fisher-transformed bivariate correlation coefficients obtained using the weighted General Linear Model (GLM). The z-score for transforming the coefficients into a score is defined using Eq. (1):

$$z = 0.5[\ln(l + r) - \ln(l - r)] \quad (1)$$

where, z is the z-score, r is the correlated coefficient and $\ln$ is the natural log.

The coefficients are determined for each seed and target voxel, as shown in Eq. (2):

$$r(x) = \frac{\int S(x, t) R(t) dt}{(\int R^2(t) dt \int S^2(x, t) dt)^{\frac{1}{2}}} \quad (2)$$

where, R is the average BOLD time series within an ROI, r is the spatial map of pearson correlation coefficients and Z is the SBC map of Fisher-transformed correlation coefficients for the ROI.

ICA-rs-fMRI

ICA performed a whole-brain analysis and extracted 40 statistically Independent Components (ICs) to analyze the communication between brain regions. A Singular Value Decomposition (SVD) on the z-score normalized BOLD signal (subject-level SVD) is performed for each feature. Mathematical representation is given in Eq. (3):

$$X = AS \quad (3)$$

where, X is the observed data matrix with dimensions' $n \times m$, n is the number of observations (samples) and m is the number of variables (features). S represents the matrix of independent source signals with dimensions' $n \times m$ and A

is the mixing matrix with dimensions' $n \times m$. GICA3 back projection is used to compute the ICA maps associated with the same brain regions for each subject separately.

Graph Theory

A graph theory is applied to determine the correlation between the features and to estimate the correlated coefficients. In the graph, the nodes denote the regions and the edges are the connections. A threshold value is defined to remove the redundant edges or regions; only relevant regions are considered. Graph theory produces two essential features: Clustering coefficient, betweenness centrality, eigenvalue centrality, global efficiency, and modularity.

Results and Discussion

The most commonly used methods to analyze MRI data modalities are GLM, FC analysis, Voxel-Based Morphometry (VBM), and Surface-Based analysis (Ecker *et al.*, 2017; Nickl-Jockschat *et al.*, 2012; Müller, 2014). The study aimed to achieve the most significant features to optimize the classification accuracy for autistic neuroimages. Due to high dimensional data, dimensionality reduction was challenging to achieve. The selected features are discussed in detail and the classification accuracy for the sMRI scans is compared and evaluated using ML methodologies.

Structural Features

Morphological aspects for sMRI scans are - Gray matter volume within a particular region, Cortical thickness, that is, the average distance between the outermost (the pial surface) and the innermost layer of GM, and the surface area of the cortex. Curvature is the local folding pattern of the cortex, which is calculated by calculating the Gaussian curvature at every point on the cortical surface. Computational Anatomy Toolbox-CAT12, applied to perform volumetric and surface analysis to the sMRI images. VBM calculates and compares the GM volume between both groups at the voxel level. The GM Volume (GMV), Total Brain Volume (TBV), and Total Intracranial Volume (TIV) are extracted as significant features for classification. Cortical thickness and surface area differences are measured using surface-based analyses. Surface-based analyses involve the reconstruction of the cortical surface and alignment of the surfaces across the subjects, followed by statistical analyses to calculate the differences in the cortical thickness or surface area between groups. The segmented regions GM (green), WM (pink), and CSF (blue) are shown in Fig. (4).

RFE applied to all the 134 regions defined in the neuromorphometry atlas. Best performing features were

observed as right caudate, left caudate, right cerebral WM, left cerebral WM, left lateral ventricles, left ventral dorsal caudate, left anterior cingulate gyrus, left central operculum, right occipital pole, Left superior parietal lobule. For WM analysis the volume variations are observed in the right cerebellum white matter, right cerebral white matter, right OCP occipital pole, Left INF LAT vent, right pallidum, right GRE gyrus rectus, brain regions where most of them are common for both GM and WM, but notable changes in WM was found in right Pallidum and Right GRE gyrus rectus.

Functional Connectivity Analysis for fMRI

SBC for individual subjects was implemented to measure the connectivity between seed and voxels. Figure (5a) depicts a default mode connectivity map for a single subject. Group-level analysis executed with GLM and voxel-level assumptions is performed using multivariate parametric statistical analysis. The cluster (set of adjacent voxels) evaluation and cluster-level implications are obtained using the parametric statistics. The selected clusters for group-level analysis are shown in Fig. (5b). The clusters are obtained using p-value, $p < 0.001$ voxel-level threshold, and a familywise corrected p-FDR < 0.05 for cluster-size threshold.

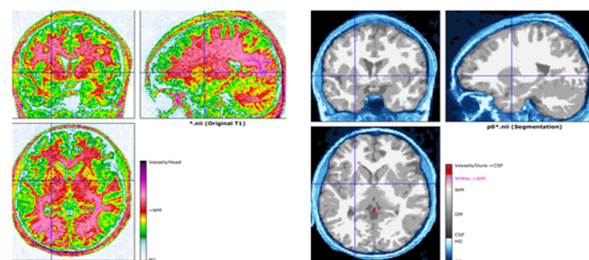
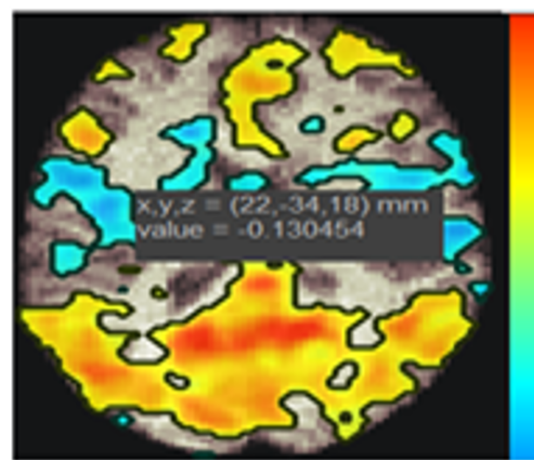


Fig. 4: Gray matter, white matter, and CSF



(a)

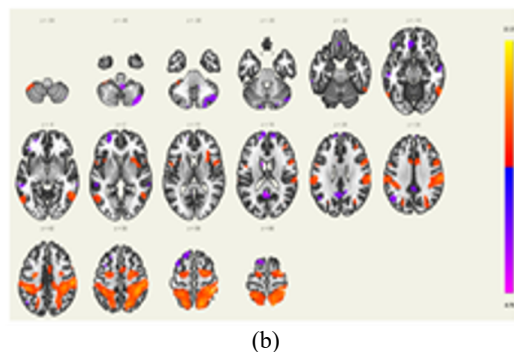


Fig. 5: (a) First level SBC analysis for autistic brain; (b) Group level SBC analysis for autistic brain

The ROI approach was performed on the 32 ROIs to observe the connectivity patterns among individual subjects and between groups. The ASD group has 13 subjects and the NC group has ten subjects.

The matrix display for the first-level analysis is displayed in Fig. (6a) and the group-level analysis is presented in Fig. (6b). Regions with the network strength are shown in the circular representation and different colors, where each color has a predefined strength, are shown in Fig. (6c). A 2D matrix display was generated to understand the network strength of all subjects better. Figures (7a-b) represent the upper triangle connectivity of the brain regions and connectivity strength for ASD and NC groups, respectively. The matrix displayed an observable difference in the network pattern among the groups.

The selected graph theory features are global efficiency and clustering coefficient. The graph theory results for ASD and NC datasets are displayed in Figs. (8a-b), respectively.

The ROIs selected are analyzed concerning the threshold value of 0.15, eliminating the redundant edges and nodes. If the clustering coefficient is 0.94, the graph states that 94% of the neighboring nodes are connected to the selected ROI. Results of the experimental analysis show that using the coefficients for all ROIs, the proposed approach effectively distinguishes the connectivity between the brain regions for both groups.

ML Classification strategies were applied using structural feature sets to assess the significance of the features. The ML models were selected using high-dimensional data based on the existing neuroimaging results. GM volumes for neuromorphometry regions are considered as features. Four ML models, including RF, LR, Gradient Boost, and Naïve Bays, were implemented with 40, 30, 25, 20, 15, and 10 features. The features for Naïve Bays are selected using select best and the chi-square test. Classification accuracy of 80% was achieved with Naïve Bays using the features selected with a chi-squared test. The highest classification accuracy of 88.67% was achieved using SVM and RFE.

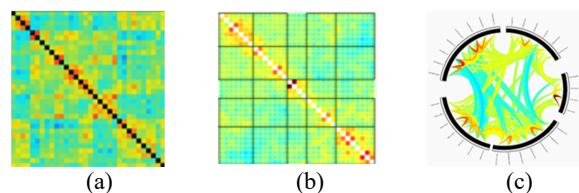


Fig. 6: (a) ROI analysis for a single subject; (b) ROI analysis group ASD; (c) ROI functional connectivity analysis

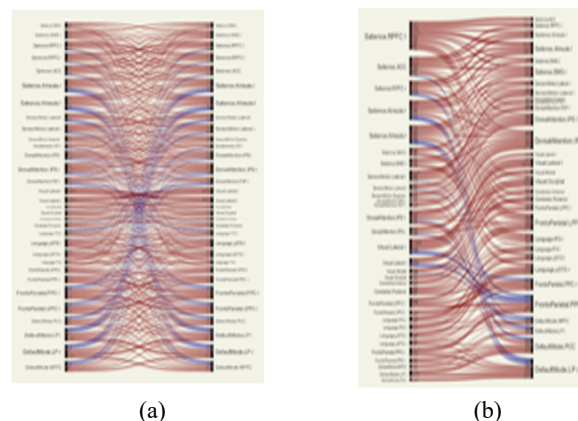


Fig. 7: (a) Connectivity matrix for ASD; (b) Connectivity matrix for NC

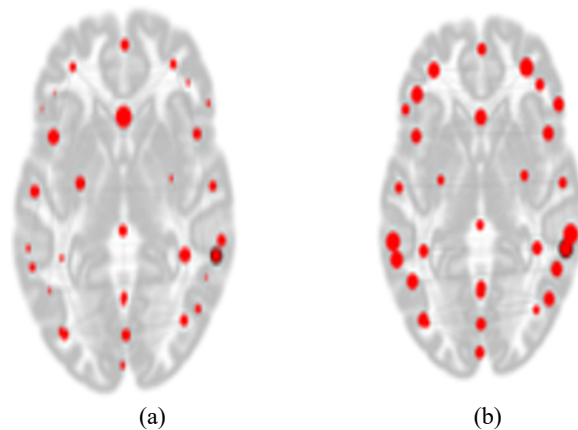


Fig. 8: (a) Results of graph theory for ASD; (b) Results of graph theory for NC

The comprehensive explanation of the features achieved by both imaging modalities proved the significance of features for specific analysis. The VBM and SBM analysis for sMRI provide the structural information for the disorder and are useful for exploring spatial differences. In contrast, the features extracted from rs-fMRI images, such as functional connectivity measures and network information, helped to study the brain's functional activities during the resting state.

SVM with RFE performed better than other classifier methods. The features collected with different methods were assessed using the classification accuracy achieved by distinct AI models. SVM has outperformed in multiple medical imaging studies because it can handle large volume data. RFE feature extraction works well with a low volume of data and a huge amount of features.

Based on the achieved resulting images, it is confirmed that neuroimages in distinct modalities are noisy and attenuated by external signals such as mechanical fluctuations, physical movements, and other physiological effects. The pre-processing pipelines are implemented with multiple methodologies and achieved higher quality images for further analysis, which needs to be performed for classification and region of interest for autism disorder. The results and the visual analysis of pre-processed images displayed the signal changes in the extracted time series for each voxel present in the number of frames of an MRI scan. The original scans and the pre-processed scans provide a huge set of information but the noisy or raw images contain inaccurate information, which needs to be filtered using specific strategies to extract the data without noise. Medical image pre-processing is a crucial step to achieve a higher accuracy rate. In the study, a comprehensive comparison was performed on the neuroimaging dataset modalities and presented the various levels of denoising. The deliverables of the work are the strategies and the results for future research works in the field of cognitive disorders using neuroimaging scans.

Conclusion

Autism is a condition with a cluster of comorbid conditions with no definite symptoms or biomarkers. In the current scenario, most of the work in autism detection is diverted to neuroimaging research. The study presented a comprehensive analysis of feature extraction strategies for dual modalities of autistic brains. Successful implementation of highly recommended methods for structural and functional images was performed. The result section discussed the features and classification accuracy for 23 images. Work with high-dimensional data is complicated and challenging due to the curse of dimensionality, overfitting, and poor generalization, but the presented work has achieved 88.67% accuracy. The contribution of the work is to present the best-performing feature extraction techniques for autism detection with less or high-dimensional data. The present work performed feature extraction for sMRI and rs-fMRI. The research aims to implement the functional features for the classification and discover the model to solve the current challenges. The future enhancement of the work suggested is including more data for analysis. The Deep Learning model is restricted to data limit and needs a large dataset; it can be another advancement to the current work.

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Author's Contributions

Meenakshi Malviya: Conceptualization and design, data acquisition, implementation, data interpretation and analysis, draft preparation and manuscript writing.

Chandra J: Research planning and study organization, results interpretation and critical review.

Nagendra N: Implementation, manuscript design, writing, formatting and editing.

Ethics

This article is original and contains unpublished material. The corresponding author confirms that all co-authors have read and approved the manuscript, and that there are no ethical issues involved.

Conflict of Interest

The authors have no competing interests to declare that are relevant to the content of this article.

Data Availability Statement

The data used in this study are part of the Autism Brain Imaging Data Exchange (ABIDE) II project https://fcon_1000.projects.nitrc.org/indi/abide/abide_I.html.

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