

Autism spectrum disorder diagnosis support model using InceptionV3

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Abstract - Autism spectrum disorder (ASD) is one of the most common neurodevelopment disorders that severely affect patients in performing their day-to-day activities and social interactions. Early and accurate diagnosis can help decide the correct therapeutic adaptations for the patients to lead an almost normal life. The present practices of diagnosis of ASD are highly subjective and time-consuming. Today, as a popular solution, understanding abnormalities in brain functions using brain imagery such as functional magnetic resonance imaging (fMRI), is being performed using machine learning. This study presents a transfer learning-based approach using Inception v3 for ASD classification with fMRI data. The approach transforms the raw 4D fMRI dataset to 2D epi, stat map, and glass brain images. The classification results show higher accuracy values with pre-trained weights. Thus, the pre-trained ImageNet models with transfer learning provides a viable solution for diagnosing ASD from fMRI images.

Keywords - epi images, fMRI, Inceptionv3, stat map images, transfer learning

I. INTRODUCTION

The current motivation of psychiatric neuroimaging research is to identify objective biomarkers to diagnose neurological disorders like Autism Spectrum Disorder (ASD) and Attention deficit hyperactivity disorder (ADHD). Recent advances in the field of biomedical imaging and deep learning provide efficient diagnostic and treatment processes to identify different brain-based disorders [1][2][3]. This paper proposes a novel technique for automatic identification of ASD by applying Transfer Learning (TL) on Functional Magnetic Resonance Imaging (fMRI) data.

ASD is identified as a common multifactorial neurological disorder that affects the development of the brain, causing numerous disabilities. ICD-10 WHO (World Health Organization) [3] and DSM IV APA (American Psychiatric Association) [5], have specified main features in human interactions and behaviour of the patients, which can be used to diagnose ASD. Individuals diagnosed with ASD typically suffer from speech and communication difficulties, issues in social interaction, and lack of eye

contact [2].

In 2018, the Centers for Disease Control and Prevention (CDC) in USA have shown that the ratio of Autism patients to the general population is 1 to 59. This is twice as grater as the ratio reported in 2004, which was 1 to 125 [6]. Generally, there is a higher tendency of males being diagnosed with ASD than females, where the reported ratio is 4 to 1. According to the WHO report, it is estimated that 1 in 160 children has an ASD, worldwide. The study conducted in 2009 found that the prevalence of ASD among 18–24-month children is 1.07% in Sri Lanka [7].

Diagnosing ASD is a subjective and difficult task since there is no specific medical test. Usually, symptoms of ASD begin to appear before the age of 3 and it can prevail throughout the entire lifetime of a person, even if the severity may decline over time. Physicians and clinicians diagnose ASD by observing the patient's behaviour and development, considering the child's family history, genetic details, the progress of the development, and the skills they have in their lifestyle [2]. Current diagnostic processes may be carried out by involving several professionals from different disciplines with special skills t to identify the ASD-specific characteristics **Error! Reference source not found.** Lack of experience and training may lead to misdiagnosis of the children suffering from ASD. Research shows that early detection of ASD can lead to better results, enabling various ways to minimizing the symptoms and maximizing abilities [1].

The exact cause behind ASD is still unknown. A recent hypothesis in neurology has identified unusual neural activities in the brain of ASD patients. The cause has been discovered as the irregularities in neural patterns, disassociation, and anti-correlation of cognitive function between different regions, that affect the global brain network [9]. Thus, the fMRI data can be used to identify the abnormal neural pattern between brain regions to identify ASD.

The novelty of the paper was in carrying out a study to investigate the adaptation of pre-trained ImageNet weights on the Inception v3 model to classify ASD form controls using raw fMRI data. The Inception v3 model forms layers in parallel, whereas other models arrange layers in stacks. Thus, the Inception v3 model consists of a lesser number of parameters and generally provides higher accuracy compared to other models like VGG16, ResNet50. Therefore, the proposed approach uses Inception v3

architecture as the backbone deep learning technique. Most of the past research has used already preprocessed fMRI images like C-PAC (Configurable Pipeline for the Analysis of Connectomes) or various techniques [1] to preprocess fMRI images. In these studies, they have used features like functional connectivity (FC), specific brain regions related to ASD [10][11] to recognize ASD. The proposed method converted the raw 4D fMRI image to 2D epi images, stat map images, and glass brain images, while considering the sagittal, coronal, and axial views of brain volumes. The Inception v3 model was trained with and without ImageNet weights to investigate the weight transferring of different target domains. Thereafter, Section II gives a brief introduction to the background. Section III explains the workflow and the methodology followed by the research. Section IV discusses the model evaluation and, finally, Section V concludes the paper.

II. BACKGROUND

Functional MRI is a non-invasive technique that measures brain activities by detecting variations associated with blood flow [12]. It identifies high neural activity based on the fact that cerebral blood flow and neural activity are correlated, so that blood flow is high in the brain where neurons are highly active. The functional relationship that occurs in different brain regions at resting or task-negative state is measured by resting-state fMRI. It allows the observer to identify the abnormalities of the brain function easily due to the absence of added task-related brain functions. [13][14]. Thus, it is one of the popular techniques used in the identification of neuro-developmental disorders by observing the associations between brain function and phenotypic features [3][14].

Machine Learning (ML) is used to perform recurring and tedious tasks using feature extraction methods on raw data or with the features learned by other machine learning models. However, some issues associated with the medical image database have caused some limitations of using ML. For instance, the incompleteness by missing parameters and the lack of publicly sufficient labelled databases [16]. Furthermore, the performance of ML in medical image classification is far from the practical standard while the feature extraction and selection are time-consuming. The trending branch of ML, Deep learning (DL), can autonomously extract the prominent features from the raw input data, through a hierarchical sequence of non-linear transforms. DL is being used to identify patients with normal groups and it is further enhanced as a model to foresee the risk of developing disorders and predicting responses to different treatment procedures [11][14]. The fundamental goal of applying DL to neuroimage analysis is to remove the cumbersome and ultimately limiting feature selection process.

Moreover, Convolutional Neural Networks (CNNs), which are prevalent Deep Neural Networks (DNN), have shown significant performance in image classification [10][17][18]. DL models that use CNN are highly accurate because CNN extracts and learns features directly from images during the training process of the network.

As a result of the small sample size and high dimensionality of the fMRI dataset and the lack of interpretability of DL models, the application of whole-brain fMRI data is still limited [19]. Generally, a small number of ASD patients undergo fMRI scans as most seek

different other types of diagnosis for the moment. This leads to the unavailability of large sample datasets. However, many fMRI samples (volumes) are recorded for a single subject. These volumes can contain hundreds of dimensions, known as voxels. That results in lesser samples, but many dimensions in fMRI datasets. Thus, DL methods, as well as traditional machine learning methods, struggle in the learning curve, resulting in overfitting. In that case, TL is the key solution to this challenge.

Transfer learning is a way of gaining and storing knowledge from solving a problem of one task and applying it to a different but related task. It has become a popular concept in recent years and has been applied in a diverse set of domains. Pretraining is the first phase of TL in which, the network is trained using a large dataset consisting of highly varied labels/categories, representing many different areas. Then, the pre-trained network is 'fine-tuned' using a specific dataset from a field of interest. With this two-stage method, the high resource and time-consuming pre-training operation can be conducted only once, and then the results can be used in many different areas by fine-tuning.

In the field of medical image analysis, the current trend is to fine-tune an existing model with its architecture, with its pre-trained weights. ResNet [20], and Inception [21][22] are the few popular pre-trained DL models, which are trained on ImageNet datasets that are extensively applied in medical TL applications [23]. However, there is a considerable difference between ImageNet classification and medical image analysis in various ways.

In medical imaging problems, large images are represented a bodily region of interest which are used to identify the nature of the disease by recognizing the variations. On the other hand, in natural image datasets such as in ImageNet, the entire subject can be found within an image [23]. Further, ImageNet is a large dataset consisting of more than a million images that are smaller in size, while those of medical imagery is larger in size, but the number of images in the dataset is small. In addition, ImageNet is being trained for thousands of classes, while medical images are classified into few classes, less than 20, for instance. Moreover, the higher layers of the ImageNet architecture consist of many parameters, hence, is not the finest model for medical image classification.

Many CNN-based methods have been proposed to solve the problem of diagnosis of ASD using fMRI data, which remain unsolved and challenging. Related studies have addressed different approaches of pre-trained CNN networks like VGG 16, ReNet50, and Inception v3 with ImageNet weights with different input images. Husna et al. have applied a DL method from CNN variants of VGG-16 and ResNet-50 to identify ASD patients and extract the robust characteristics from fMRI. An accuracy of 63.4% and 87.0% has been achieved respectively [24].

In order to detect ASD, Dominic et al. have used a pre-trained InceptionResNetV2 model with TL on the augmented dataset. This has been generated by converting 4D resting-state fMRI into 2D data, where a validation accuracy of 57.75% has been achieved [25]. Ahmed et al. have developed an image generator, which developed single volume brain images from preprocessed fMRI images that are available in ABIDE dataset. The images were classified using ensemble classifiers which are combined with four different types of pre-train networks DenseNet, ResNet, Inception v3, Xception, and a CNN. The study has used

VGG16 as a feature extractor and gets an overall accuracy of around 82.7% [26].

Chen et al. have developed a VGG19 based CNN model with TL which provides 74.5% accuracy. The model predicts the cognitive assessment of infants using a brain structural connectome constructed by Diffusion tensor imaging (DTI) [27]. A deep multimodal proposed by Tang et al. have used two types of connectome data offered by fMRI scans. In Phase, I, the feature extractors, multilayer perceptron (MLP) and ResNet-18 were separately trained as independent networks. In phase II, an end-to-end model was obtained by combining MLP and ResNet-18 model with four fully connected layers as their output layer. The resulting multimodal network has been trained from scratch and classification accuracy of 74% has been achieved [28].

In another point of view, a few studies have used EEG signals and thermal images to diagnose ASD using machine learning-based classification techniques [29]. **Error! Reference source not found.** Haputhanthri et al. have utilized a correlation-based feature selection method to select relevant features and the necessary number of EEG channels. They have achieved an accuracy level of 93% by using Random Forest and Correlation-based Feature Selection **Error! Reference source not found.** The Accuracy of both logistic regression and multi-layer perceptron classifiers was able to be increased to 94% by integrating EEG and thermographic features [29].

III. DESIGN AND METHODOLOGY

A. Dataset

The Autism Imaging Data Exchange (ABIDE I/ II) dataset was used to carry out the proposed study [30] [31]. ABIDE is an online sharing consortium that provides Resting state fMRI (rsfMRI) data of ASD and controls participants' data with their phenotypic information. The ABIDE datasets consist of 17 different imaging sites. Out of the total dataset, a sample group aged between 0-12 is selected.

The sample dataset consists of 69 ASD individuals and 69 matched controls belonging to Kennedy Krieger Institute (KKI) data. The proposed ASD identification workflow is involves data preparation by converting 4D data to 2D images, feature extraction, followed by TL using pre-trained DNN model (InceptionV3), and evaluation as shown in Fig. 1.

B. 4D to 2D image transformation

The 4D fMRI image was transformed to a 2D image set, by slicing it along the sagittal, coronal, and axial directions. NIFTI is a file format for neuroimaging. As illustrated in Fig. 2, the 4D NIFTI image consists of a series of 3D volumes along the 4th axis; the time. The shape of the 4D image is identified and a series of 2D brain images is formed, considering the 3D brain volumes. As an example, the shape of the 4D image is 128, image converter creates 128 2D images from each volume. Three types of plotting functions epi, stat_map, and glass_brain were used to create three different types of 2D images from the raw fMRI images. A random slice from the sagittal, coronal, and axial direction was formed using the cut_coods parameter [26]. A total of 138 fMRI images in the proportion of 69 ASD

samples and 69 TD were converted to 20500 sample 2D images and saved in .png format.

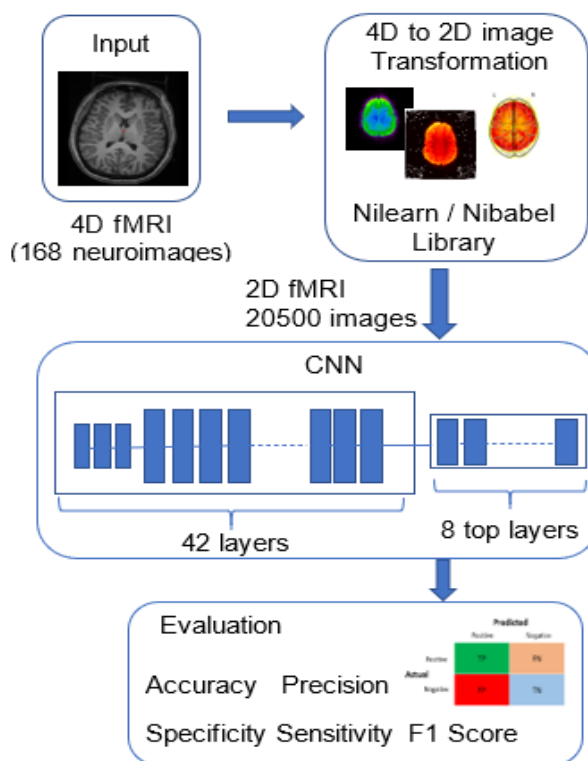


Fig. 1. ASD identification process

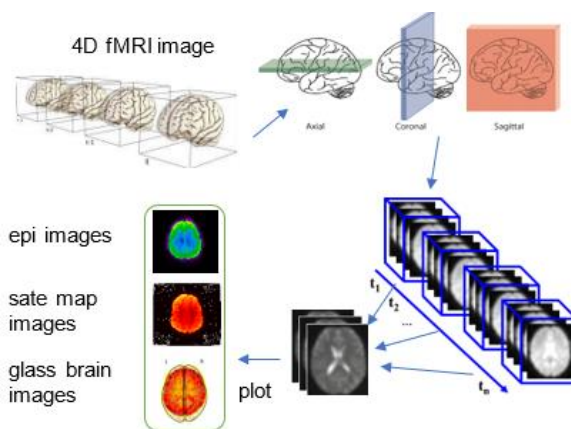


Fig. 2. Process of converting 4D fMRI image to 2D images

C. Transformed 2D image types

Three types of image plotting methods were used to train the neural network. Epi images are Echo-Planar Imaging. This is the type of sequence used to acquire functional or diffusion MRI data. Statistical images or stat maps plot cuts of a region of interest (ROI)/mask image of frontal, axial, and lateral. Epi images and stat images are 2D visualization images. The glass brain images represent the 3D view of the brain while plotting 2D projections of an ROI/mask image.

D. Augmentation

The training dataset was artificially increased using a data augmentation module, so that the training of the network was benefitted with a higher variation of input data.

For this purpose, Keras-based ImageDataGenerator was used by defining the image augmentation parameters such as batch size (32), rescale (1./255), transformations (shear, zoom, rotation). Here, the rescale parameter 1./255 transforms every pixel value from range [0, 255] -> [0,1], since 255 is the maximum pixel value. These augmentation methods increase the specificity and the sensitivity of medical images in the classification task. This may reduce network overfitting and support the model to generalize properly. Augmented epi images are shown in Fig. 3.

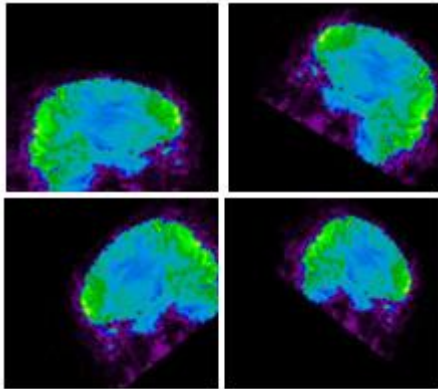


Fig. 3. Augmented epi images

E. Transfer learning settings with CNN

Inception v3 [32] model was selected as the CNN model to train the nine different image datasets using the TL approach. Inception v3 model pertained with ImageNet dataset (Natural images), which consist of 1.28 million training images, 100 k testing images, and 50 k validation images to classify 1000 classes. InceptionV3 model, layers are often connected in parallel instead of being stacked on top of one another and it is 42 layers deep. It comprises several inception modules that contain convolutions, average pooling, max pooling, dropouts, and fully connected layers. SoftMax is used to compute the loss. It employs techniques like regularizations, parallelized computations, dimension reduction, and factorized convolutions to optimize the network and enhance the model adaptation. The Inception v3 model was modified to adapt them to our classification task shown in Fig 4.

The InceptionV3 model deployed without the top layers and append new layers to the top layer. CNN was trained in two distinct ways and those are named MED1 & MED 2.

MED1: Initialize the Inception v3 by ImageNet weights and overlay with TP1 top layers

MED2: Initialize the Inception v3 by random weights and overlay with TP1 top layers

Fig. 4 (a) illustrates the Inception v3 model with TL settings and modifications. The classification was done by

setting the last dense layer to the softmax function. The models were trained by adjusting the hyperparameters. ADAM optimizer was selected with a 0.0001 learning rate. The dataset was randomly split into the sample ratio of 70:15:15. The implementation was done in python using Keras libraries

TP1 top layer block which is shown in Fig. 4 (b) is a combination of global average pooling layers, three dropout layers, three dense layers and one flatten layer. Here, GAP states the global average pooling layer, FL denotes the flatten layer, DEANs specifies the dense layer and DL states the dropout layer. Further, to reduce overfitting of the model L2 regularization was applied.

F. Statistical analysis

The CNN pre-trained model was evaluated using five statistical measurements, Accuracy (A), Recall (R) or Sensitivity, Precision (P), Specificity (S), and F1 score (F) [11] [15] [33]. The model identifies ASD subjects exactly as ASD is known as True Positive (TP) while the model which identifies TD subjects as TD is given as True Negative (TN). Further, the models which identify the ASD subjects as TD and TD subjects as ASD are referred to as False Negative (FN) and False Positive (FP), respectively.

Accuracy is defined as the closeness of a measured value to a known value, specified as the percentage of correctly classified samples. It can be calculated using the equation depicted in (1).

$$\text{Accuracy} = (\text{TP} + \text{TN}) / (\text{TP} + \text{TN} + \text{FP} + \text{FN}) \times 100\% \quad (1)$$

Precision describes how often the model provides an accurate prediction for positive class as shown in (2). That is the ratio of the correctly ASD positive labelled to all ASD positive labelled.

$$\text{Precision} = \text{TP} / (\text{TP} + \text{FP}) \times 100\% \quad (2)$$

Recall, also called sensitivity or true positive rate (TPR) is described as the percentage of correctly classified ASD subjects from all ASD subjects. The recall is calculated using (3).

$$\text{Recall (Sensitivity)} = \text{TP} / (\text{TP} + \text{FN}) \times 100\% \quad (3)$$

Equation (4) explains how the specificity or true negative rate is calculated as the number of correct negative predictions divided by the total number of negatives. It is the percentage of correctly classified control subjects from all control subjects:

$$\text{Specificity} = \text{TN} / (\text{TN} + \text{FP}) \times 100\% \quad (4)$$

The F1-score or balanced F-score is determined as the harmonic mean precision and recall. It focuses on the analysis of positive class. A high value for F1 suggests that the model performs better on the positive class. F1 score is calculated using Equation (5).

$$\text{F1 score} = (2 \times \text{Precision} \times \text{Recall}) / (\text{Precision} + \text{Recall}) \quad (5)$$

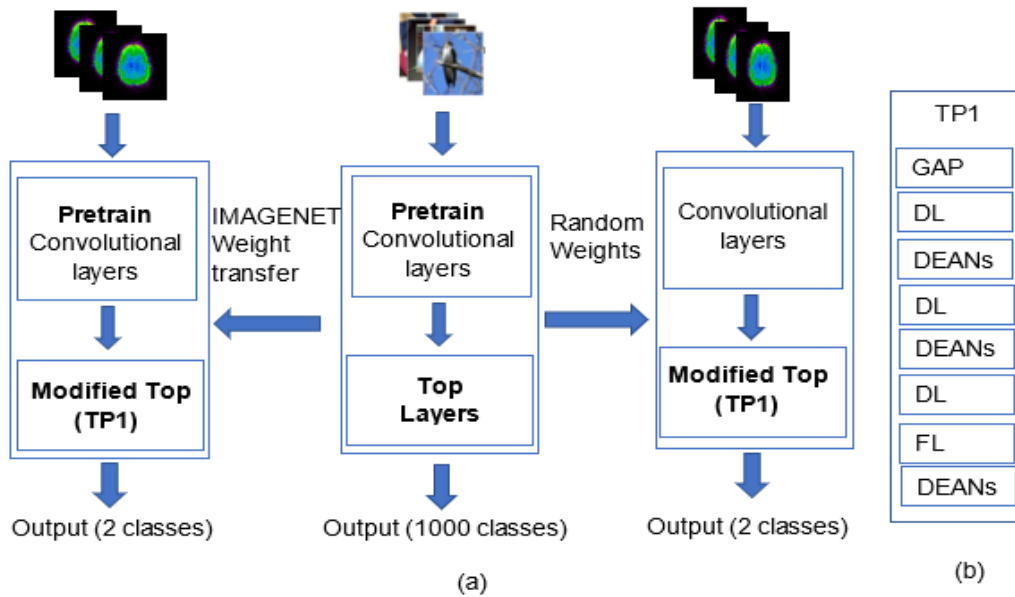


Fig. 4 (a) Transfer learning process of MED1 and MED2 (b) TP1 top layer

IV. MODEL EVALUATION

A. Experiment results

Inception v3 classification performance was calculated using the two methods MED1 and MED2. Each method, trained with nine different data sets, belongs to three different image plotting types. The performance of the model was measured with the test set, which is 15% of the data set.

All of the image types showed a similar and statistically significant performance in MED1 shown in Table I. The highest accuracy, sensitivity, specificity, precision, and F1 score was obtained by the axial view of glass brain images. On the other hand, in the accuracy metric, stat map Sagittal view obtained the lower result with 97.04%, followed by stat map Coronal view and stat map Axial view with 96.59%, 96.65% respectively.

The accuracy of all categories of MED2 was between 57% to 74%. The highest accuracy was observed in the Coronal view of epi images, which is 73.79%. The lowest accuracy value of 57.31% was observed in the Sagittal view of stat map images. There is a significant difference in Sensitivity (R), Specificity (S) in all types of image categories. In every category, the percentage of specificity is less than the percentage of sensitivity except in the glass brain sagittal view. That implies the fact that the percentage of correctly classified ASD is greater than the percentage of correctly classified Controls. The percentage value of the F1 score is around 74% in epi images and 70% in stat map images. The higher value of F1 shows that the MED2 model performs better on the positive class than the negative class.

There are only a few studies conducted on the effects of TL from ImageNet architectures. Most of the time this architecture does not provide the best performance on medical image datasets due to the lower capacity of data [23]. This is because when it comes to TL, two most important factors considered are the size of the new dataset (small or big) and its similarity to the original dataset.

In this research, the fMRI images lie in a different domain when compared to the ImageNet dataset. Not only that, when the size of the datasets are compared, the ImageNet dataset has a huge number of images than the fMRI image dataset. Nevertheless, it is observed in this study, that there is a clear impact on the ImageNet weights in ASD subject identification. The overall results demonstrate that the MED1 has a significantly higher performance than the MED2, in all image categories used to identify ASD subjects from controls. MED1 method, the Inception v3 model used the ImageNet weights as the initial weights for the training network. Even if ImageNet weights are trained using millions of Natural images, still it is possible to transfer those ImageNet weights to medical imaging, due to the properties of CNN, like gradual feature extraction in subsequent layers.

Lower layers identify basic features like lines and points, middle layers detect partials of objects, where top layers learn to recognize an entire object. Since any type of image consists of low-level features (points & lines) it is possible to start from a common low-level layer and then introduce specific higher-level layers according to the domain. Thus, the weights trained using ImageNet pre-trained dataset can be used as the initial weights to extract the basic feature of any type of image. Inception v3 model trained using these weights, achieved around 98% accuracy in epi images, 97% in stat map images, and 98% in glass brain images with equally high sensitivity, specificity, precision, and F1 score.

In contrast, in the MED2 the weights are initialized randomly, and the network starts learning from scratch by adjusting the weights. Inception v3 is a larger CNN with 42 convolutional layers, with 24 million parameters which need a large number of images to converge the network. When compared with the ImageNet, the size of the epi images, stat map images, and glass brain images were lesser, but still, the learning percentage of the network was between 58% to 70%, from the given data to identify ASD subjects from Control subjects.

TABLE I. PRECISION (P), RECALL OR SENSITIVITY(R), SPECIFICITY (S), F1 SCORE (F1), ACCURACY (A) OF MED1 AND MED2 METHODS

Image type	Display mode														
	Sagittal (x) %					Coronal (y) %					Axial (z) %				
	P	R	S	F1	A	P	R	S	F1	A	P	R	S	F1	A
MED1 (with ImageNet pre-trained weights)															
Epi images	97.82	97.31	97.87	97.56	97.69	96.96	98.23	96.97	97.59	98.59	98.25	99.27	99.26	98.89	98.76
Stat map	97.66	96.38	97.62	97.01	97.04	97.81	97.10	97.80	97.45	96.59	97.62	95.67	97.65	96.89	96.65
Glass brain	97.77	98.02	97.78	97.91	97.90	98.03	97.91	98.03	97.96	97.97	98.60	99.12	98.56	98.85	98.84
MED2 (with raw images)															
Epi images	59.40	97.57	34.40	73.84	65.79	71.55	78.25	69.39	74.50	73.79	65.62	84.02	56.44	73.60	70.18
Stat map	54.54	86.72	28.01	66.96	57.31	53.75	99.60	14.71	69.83	57.06	56.66	90.49	30.13	69.68	60.45
Glass brain	76.19	60.27	81.37	67.30	70.89	59.91	99.56	31.95	74.80	66.07	59.92	98.92	32.76	74.63	65.85

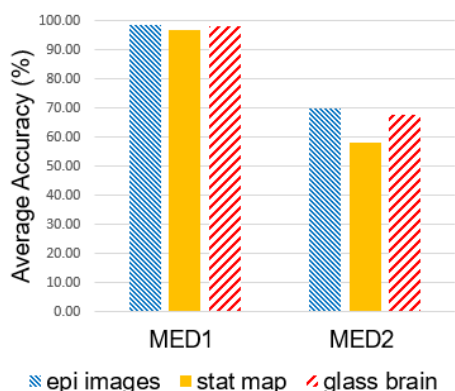


Fig. 5 Average accuracy of MED1 and MED2

Training a deep CNN network from scratch with random initialization of weights is a challenging task which consumes time. The accuracy can be increased using TL and pre-trained models, in a shorter period, compared to models trained from scratch.

The study examines three different types of unprocessed images, epi images, stat map images, and glass brain images. The epi images and stat map images represent the 2D visualization of Sagittal, Coronal and Axial view of 4D fMRI images while glass brain images represent the 3D visualization. According to Fig. 5, the highest average accuracy value of 98% was observed in epi images and glass brain images respectively from MED1. MED2 method also produced higher accuracy values, which were observed in epi images and glass brain images. Overall, epi image produced the best results, while stat map images yielded relatively poor results for both MED1 and MED2.

B. Comparison with the existing studies

The underlined research investigates methods to use TL to classify ASD utilizing unprocessed fMRI data by transforming the 4D image to a series of 2D images. Table II compares the proposed study with few other similar studies. Most studies carried out to identify ASD, have been conducted using natural imagery like facial images due to the domain similarity. But very few have investigated TL methodology with fine-tuning, using fMRI images to the target task. The study conducted by Husna et al. has achieved a higher accuracy of 87% using ResNet50, but the model suffers from overfitting [24]. It is a best practice to apply Regularization and data augmentation to avoid model overfitting [16].

Moreover, the epi image based InceptionResNetV2 model trained by Dominic et al. has obtained less accuracy due to a lesser number of sample images and model overfitting [25].

TABLE II. COMPARISON WITH RELATED STUDIES

Study	Features considered	Techniques	Accuracy %
[24]	2D images	VGG-16	63.40
		ResNet-50	87.00
[25]	epi images	InceptionResNetV2	57.75
[26]	stat map images, glass brain images	ensemble classifiers	82.70
[27]	DTI images	VGG19 based CNN	74.50
[28]	ROI correlation Matix	Combined model (MLP and ResNet-18)	74.00
Proposed study	epi images,	Inception v3	98.35
	stat map images,		96.76
	glass brain images		98.24

In contrast, this study has proposed a model with data augmentation as well as Regularization to avoid overfitting. Ahmed et al. have designed ensemble classifiers combining four different types of pre-trained networks. These include DenseNet, ResNet, Inception v3, Xception which are used to classify ASD from controls using various preprocessing pipelines. They have been able to achieve 82.7% accuracy with stat map and glass brain images [26]. In the context of this study, the images were created from raw fMRI images which imply the fact that preprocessing normalizes the images by reducing noise, together with fine features of the image. This study has gained better results compared to related studies.

C. Future research directions

The method was only applied to the KKI site of the ABDIE dataset. To implement a universal model to identify ASD subjects, it needs to experiment with all other sites of the ABDIE dataset. Combining the ABDIE site data may increase the number of sample points to train a deep CNN from scratch, which may benefit the creation of a universal set of weights for identifying ASD. Ultimately it is highly advantageous if the model can be enhanced to develop a universal set of weights to analyze and diagnose all ailments related to the brain. The underlined method opens up a new way of developing a computation model to identify ASD subjects using raw images. Furthermore, it decreases the computational cost compared to other studies which are

beneficial to develop an efficient computational model with necessary improvements.

V. CONCLUSION

Technology enhanced decision support systems facilitate the analysis of medical images. The study has introduced a transfer learning-based approach to identify ASD using fMRI images. We have shown that the ImageNet based pre-train models can be used to increase the performance in the medical image domain. The classification accuracy of the pre-train Inception v3 model with ImageNet weights was observed to be 98% in epi all image categories. This concludes that it can transfer the pre-trained weights with ImageNet to a highly diverse medical image domain with high accuracy, with a smaller number of sample data.

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