ADHD Identification using Convolutional Neural Network with Seed-based Approach for fMRI Data

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ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a highly prevalent psychiatric disorder with persistent patterns of inattention, hyperactivity and impulsivity behaviors among children. The perilous factor lies underneath is that often these children are commonly entangled with learning difficulties which tend to lead frustration when they reach adulthood. This study presents an effective approach for ADHD identification at an early stage by using functional Magnetic Resonance Imaging data for the resting-state brain. The proposed methodology is based on seed correlation which computes the functional connectivity between seeds and all other voxels within the brain. The classification is done using Convolution Neural Network based on extracted seed correlations from different Default Mode Network (DMN) regions. The proposed method using correlation on DMN regions has shown significant accuracies between 84% and 86% to be used with CNN for the identification of ADHD.

CCS Concepts

• Applied Computing → Life and medical sciences→ Computational biology → Imaging

Keywords

ADHD, fMRI, seed correlation, DMN, CNN, ADHD-Care_v1.

1. INTRODUCTION

ADHD is a common behavioral pattern of inattention, hyperactivity and impulsivity with a comparatively higher rate compared to normal people [1]. At present, 7% of the world population has been diagnosed with ADHD, including 6.4 million children in the United States between the ages of 7 and 14. ADHD is a common neurodevelopmental mental disorder at a young age, it affects 5-10% of the child population to have a poor quality of life and lifetime impairment [2].

The higher rate of ADHD children will continue to have clinical symptoms even to their adulthood by displaying destructive elements as a result of lack of proper therapies [2]. Hyperactivity may also lie in various other fields such as creativity and curiosity, where inattentive and impulsive children have trouble in focusing their attention and impulsively act immediately without thinking.

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Hence, there is a high risk of developing these behaviors and symptoms into comorbid disorders with lack of proper treatments such as to conduct disorder, obsessive-compulsive disorder, and other learning-related difficulties [3].

Recent researches [3][4] have also shown that abnormalities in different brain areas such as the anterior cingulate posterior cingulate cortex and ventromedial prefrontal cortex as the main factors for this disorder. Regional homogeneity analysis [5], has shown that there are significant differences in the activity in the cerebellum, motor cortex and temporal lobe in ADHD positive subjects. The diagnosis of ADHD indicates that these areas are mandatory when functional Magnetic Resonance Imaging (fMRI) data is being analyzed. Thus, fMRI data provides effective features to identify different brain activities as responses to various neural activities for the identification process of ADHD.

The lack of well-defined techniques to diagnose ADHD in clinical practice, has motivated the research on accurate identification of ADHD using fMRI data [2]. Many related studies [3][6] for classifying ADHD are based on electroencephalogram (EEG), fMRI, and eye movement data using different classification approaches. This study addresses the ADHD identification based on seed correlation approach using fMRI data. The classification process is based on Convolution Neural Network (CNN) and relevant features are extracted based on seed correlations. We consider Default Mode Networks (DMN) including DMN region MNI coordinates for the Medial Prefrontal Cortex (MPC), Posterior Cingulate cortex (PCC), Left Temporoparietal junction (LT), Right Temporoparietal junction (RT) and classify the derived data using CNN to derive an accurate classifier with fMRI data. This study is obtained higher accuracy, specificity and sensitivity values for major DMN regions compared to the existing studies [5].

The structure of the paper is as follows. Section 2 describes the background of the study with related work. Section 3 and Section 4 explains the design and implementation process, respectively. Section 5 evaluates the results and Section 6 draws the conclusion.

2. BACKGROUND

2.1 Overview of ADHD

Children with ADHD tend to experience severe realities that could lessen their self-confidence and may eventually lead to severe depression and other related issues. Hence, early intervention of ADHD is important. A recent statistic has shown that 40 % of the ADHD diagnosed subjects tend to pursue the disorder into their adulthood [2]. The common symptoms of this disorder may lead to issues in socializing, productivity and learning compared to normal groups. The victims may also affect with other non-psychiatric disorders such as allergies, asthma, gastrointestinal and seizure depending on their mental state and severity of the disorder [3].

2.2 fMRI Data

fMRI is an efficient approach in determining brain activity by detecting the changes in blood oxygen level in the brain that occurs as responses to several neural activities [7]. In Magnetic Resonance Imaging (MRI), an intense field of magnetic is used to capture the biological tissue images. Different types of tissues can be detected depending on the pulse sequence used in MRI such as tumor images, bone damages, defects in blood vessels, etc [7]. But these structural studies are not capable of revealing sensitive physiological changes occur in a short time with related to brain activations. fMRI studies [8][9] were introduced to overcome this limitation by identifying different patterns of brain activation which occurs as a response to various mental processes. Thus, links the mental functionalities with the brain activations [7].

Several studies have used neural networks for the fMRI image classification together with other feature reduction approaches such as applying masks, feature selection approaches such as PCA, ICA for unsupervised learning [8].

2.3 Default Mode Network

ADHD is related to Default Mode Network (DMN) on activities that are required effortful engagement. DMN is defined as a broad brain network in neuroscience, which is interacted with highly correlated brain regions and distinct with other brain networks [5]. Main three DMN subdivisions are the ventral medial prefrontal cortex, posterior cingulate cortex, dorsal medial prefrontal cortex, and adjacent precuneus plus the lateral parietal cortex. Additionally, the entorhinal cortex is an associated area of DMN.

Some studies have identified that dysregulations of DMN can be a significant element in neurobiological justifications for the identification of deficits in ADHD subjects [5][10]. Similarly, ADHD subjects have shown difficulties in suppressing default mode activity on tasks which demands attention. However, ADHD subjects are unable to expand the required effort in challenging energetically and suboptimal tasks such as lack of motivation and over or under activation, to suppress interference of DMN in performance optimization [10].

2.4 Analysis of Seed-based Correlation

The Seed based correlation denotes the correlation between seed voxel or region of interests and all other individual voxels in the brain area. It estimates the relationship between seed regions defined based on different anatomical locations and other brain regions. Connectivity is calculated based on the time series of seed voxels as a correlation of time series for all the remaining voxels within the brain. The behavior of seed ROI is defined in average BOLD signal and correlated with voxel BOLD time series in another brain region that defined as a Fisher-transformed bivariate correlation between brain regions [11].

The ROIs with exceeding coefficients are considered regions, which are functionally connected to the defined seed region. Single expert-selected voxel, geometric voxel set, and whole-brain regions are the typical ROI selection mechanisms used in seed correlation. The single seed ROI is much simpler as it uses a single voxel as the seed points for the interpretation of the correlation. Seed Correlation Analysis is mainly used in studying the functional connectivity of fMRI data to explore the DMN regions [5]. Furthermore, this approach is also used in different other clinical applications [8]. The seed-based correlation coefficients between seed and given voxel between can be defined in (1).

$$C_{SB}(x1, x2) = \frac{\sum_{t=1}^{T} S(x,t)\, R(t)}{\sqrt{\sum_{t=1}^{T} R(t)^2 \sum_{t=1}^{T} S(x,t)^2}} \tag{1}$$

S(x, t) denotes the BOLD time series within voxel x which mainly places to zero-mean and the R(t) represents the BOLD time series of seed ROI which is also centers to zero. Z(x) will be the Fisher-transformed correlation coefficient as shown in (2).

$$Z(x) = r(x) \tag{2}$$

2.5 Related Techniques

Most of the features considered to classify ADHD are ReHo, fALFF, ALFF, RSN, etc. [9][12][13]. Peng et al. [14], has shown that fALFF as the best feature for the ADHD classification in terms of accuracy. In another study, Miao et al. [12] have addressed different combinations of ALFF, RSN, and ReHo. They have shown that ALFF and ReHo provide more information for the classification with limited accuracy and a combination of ALFF, ReHo and RSN were able to achieve 67% accuracy. Among the feature selection techniques, Miao and Zhang [12], have shown that VA-Relief performs well compared to other selection methods such as minimum redundancy maximum relevance (mRMR) technique.

The early research on the classification of ADHD using machine learning approaches included using Support Vector Machine (SVM) classifiers and extreme machine learning approaches. The work presented by Kropotov et al. [15], have used event-related potentials (ERP) signals with ICA as the feature extraction method. They have gained 92% accuracy with 10-fold cross-validation using SVM classifier. Moreover, with the use of EEG data fed into SVM classifier for adult ADHD classification, 73% accuracy has obtained by considering different scenarios on the resting state [13].

Further, the use of ELM algorithm on structural MRI data has provided a precise objective clinical identification for ADHD. Peng et al. [14], has applied both the learning algorithm of SVM and ELM to experiment on the most accurate and high performing learning algorithm for the ADHD classification and ELM was identified as the most suitable technique with 90.18% accuracy, while hierarchical ELM (H-ELM) classifier has shown a high accuracy with nested cross-validation and a kappa score of 0.57. Another classification approach is presented by Solmaz [16], using a Bag of Words method for resting-state fMRI data to compute the correlation between voxel pairs for a given area. Applying to the SVM as the classier, they were able to obtain a 65% accuracy.

Deep learning approaches to classify ADHD have been directed in many different areas covering deep belief networks (DBN), deep Bayesian Networks (BN), Convolution Neural Networks (CNN), artificial neural networks (ANN) [5][9][17][18]. A study on the frequency domain features of fMRI to identify ADHD with respective to the DMN areas has obtained 51.47% accuracy in the visual cortex, 54.41% in the prefrontal cortex and 54.60% in the cingulate cortex, respectively [5]. Also, they have identified the classification accuracy improved with the number of hidden layers applied. Another method proposed by Hao [17], has used both DBN and Bayesian network as deep Bayesian network, which incorporates dimensionality reduction using DBM and Bayesian network to extract the features of relationships. This method has resulted in 63.33% accuracy using the SVM classifier.

The neural network approaches are emerging in the field of image classification rapidly. Deshpande et al. [18], has proposed a deep artificial neural network (ANN) to classify ADHD and subtypes, where several possible topologies were compared under different criteria to select the best neural network architecture. They were able to obtain accuracy for ADHD classification as 90% and 95% for the subtypes. Fully Connected Cascade Artificial Neural Network (FCC ANN) was selected as a well-performing classifier.

A decision support system to classify neurological disorders using learning models is proposed in [19]. They have used pre-processed resting state fMRI data with a set of learning classifiers resulted in 0.86 F1-score. The correlation between the regions of interests was measured using correlation, partial correlation and tangent functional connectivity measures. In another study [20], the resting-state networks were obtained from Independent Component Analysis (ICA) and functional information was extracted using spatial maps that are specific for each subject. The variant of ICA was also used in isolating connectivity patterns for ADHD based on statistical patterns to differentiate between control and clinical groups [20]. ICA was combined with Fisher's Linear Discriminant for characterization of inter classes of ADHD using resting-state fMRI data. The suggested methodology was well suited with fMRI data for connectivity patterns characterizing disorders, as it does not need prior information on spatial patterns in source signals. Multidimensional Scaling was used to denote the brain network with a graph to measure the activity levels of brain voxels using fMRI data. Histogram of oriented gradient (HOG) features has been used along with machine learning techniques for classifying different psychiatric disorders. The HOG feature descriptors were obtained for both MRI and fMRI data which was given accuracies of 69.6% and 65% for ADHD and Autism classification [21].

Convolutional Neural Networks (CNN) has been identified as one of the best classifiers for neuroimaging data. Zou et al. [9] have shown that even a combination of structural and functional data together with extracted features for each type, was able to showcase a state-of-art accuracy outperforming the other classifier such as LDA, SVM, etc. CNN has been applied for both fMRI image classification and identification of disorders such as Autism, as a diagnosis support for cognitive impairments System Design [8]. Furthermore, k-Nearest Neighbor (kNN), Gaussian Naïve Bayes (GNB) Classifier and Linear Discrimination Classifier (LDC) also can be used to Identify ADHD using fMRI data [13].

3. SYSTEM DESIGN

We have designed the system of ADHD Identification using fMRI data which is known as ADHD-Care version 1. As shown in Fig. 1, fMRI data from ADHD 200 - Global Competition [22] was utilized. The data are preprocessed using normalization, motion correction, slice timing correction, band-pass filtering, and the co-registration. Under the spatial normalization of fMRI data, image volumes are compared to identify differences between them. Then the identified differences in shapes are reduced by stretching, warping and squeezing images of brains mathematically. When the head motion happens, the position of the brain will be inaccurate in some images. Under the motion correction, it will adjust the position of the brain in the images by aligning image volumes spatially using a single volume as a reference, which is known as co-registration. The complete volume of data can be acquired within repetition times which varies from hundreds of milliseconds. This will result in delays between each acquired slice. Thus, time slice correction is used to reduce the time differences between each slice.

Then the features were extracted and selected from the prepared preprocessed dataset. The Seed-based correlation is used as the feature extraction and selection mechanism. In generating the deep learning model, our study has applied CNN as the classifier. We have developed a CNN structure with efficient parameters that leads to improving the learning capacity without using the classical CNN structures such as Lenet or Alexnet. The neural network was created with a convolution layer of 32 filters with 3*3 kernel size and the with the activation function of 'Relu'. The second layer was created by 64 filters and with the same specification as the first layer. Then a max-pooling layer of 2*2 pool size was added. Then a dropout of 0.25 and the network model was flattened. As the fifth layer, a dense layer of 128 units with the activation function of 'Relu' and a dropout of 0.5 was added. Finally, a fully connected layer of 2 units with the activation function of softmax was added to enable the classification.

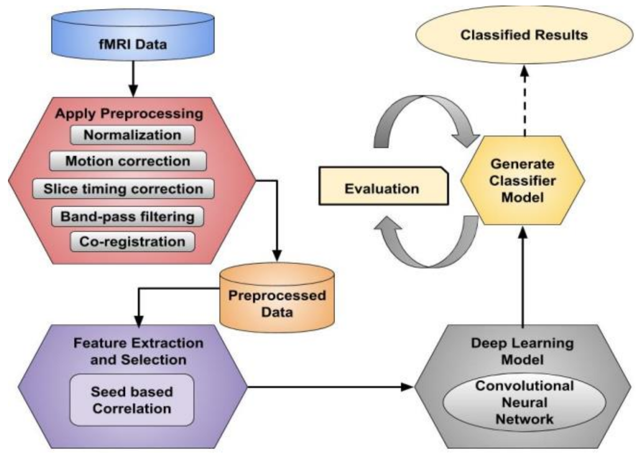

Figure 1. System Overview

Moreover, the model was generated after conducting different evaluation techniques to assess accuracy. The evaluation is designed with a different neural network with several hidden layers and fully connected layers with different activation functions. Hence the evaluation metrics of accuracy will be calculated using these different models generated. Further, since the dataset has high dimensionality, some image preprocessing techniques are yet to be applied to reduce the dimensionality and normalize the images to achieve higher accuracies. Finally, the classifier model was built to identify ADHD accurately using the fMRI data.

4. IMPLEMENTATION

4.1 Dataset

This study is used ADHD 200 - Global Competition data set provided by the Neuro Bureau [22]. This dataset is more diverse as eight different centers were contributed to the data set. This includes both fMRI data and different phenotype information related to each subject with 776 participants. The proposed solution is based on fMRI time series of 40 participants from 3 main data centers as New York University (NYU), Kennedy Krieger Institute (KKI), and Peking University (Peking-1), which represent the entire dataset from ADHD - 200 competition.

All the subjects were categorized into two main groups as subjects who are diagnosed with ADHD and other control groups with 20 ADHD positive subjects between the ages of 08 - 21. Preprocessed resting-state fMRI data were obtained from the open-source software; the Configurable Pipeline for the Analysis of Connectomes (C-PAC) by applying Slice time correction, intensity normalization, temporal filtering, spatial smoothing, motion scrubbing, volume realignment, skull stripping, and functional co-registration. The acquired pre-processed data were visualized using Echo Planar Images for the classification of ADHD. The dataset was split into two main subsets as training and testing datasets with 2:1 ratio as 26 randomly participants for training and the remaining 14 participants for testing.

4.2 Seed-based Correlation Approach

The seed-based approach is used in this study as the feature extraction mechanism from the fMRI dataset. The applied dataset consists of the fMRI data of the resting-state fMRI data and nuisance variables as a confound file. Then the mask for the fMRI data is created with DMN region MNI coordinates for the Posterior Cingulate cortex (PCC), Left Temporoparietal junction (LT), Right Temporoparietal junction (RT), Medial prefrontal cortex (MPC), a region radius of 8, a low pass filter of 0.1 Hz, high pass filter of 0.01 Hz to clean the signal. The aim of using this mask is to extract time series from the fMRI data to generate the correlations.

The similar type of bran mask is created to extract the brain-wide, voxel -wide time series from the fMRI data. Then the correlations are generated from the brain time series and seed time series. Lastly, the correlations plotted in Fig.2 are stored as a new fMRI which then can be used as inputs to the CNN.

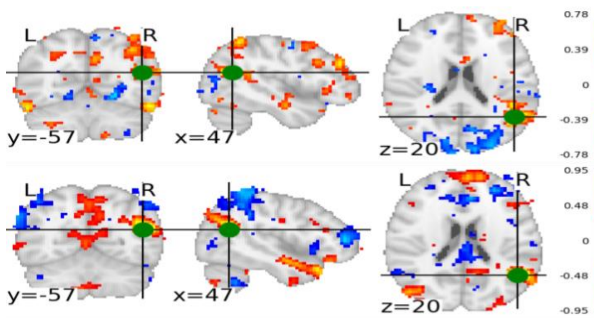

Figure 2. Correlations for ADHD and non-ADHD subjects.

DMN regions are more active during resting state in ADHD subjects compared to normal subjects [10]. Thus, in order to address the effect of main brain regions in DMN for ADHD classification, we have considered the correlations of PCC, LTJ, RTJ, MPC brain regions for the classification process.

4.3 Convolutional Neural Network

The convolutional neural network (CNN) was used as the feature extraction and pattern recognition classifier to classify between ADHD and other control groups. The CNN was used with 7 layers, where the input data for the network was primarily identified as the image data from the correlations of fMRI images. As the initial step, the data were labeled with the use of the phenotypes provided by the dataset. Since the entire collection of images should be collected to create the initial train and test split datasets, the dimension of the entire dataset would be very large. In order to cater to a smaller number of dimensions to address the limited memory, the dimensions were reduced and made the data into 2D data. The classification process is repeated for the brain regions PCC, LTJ, RTJ, MPC by considering their region coordinates (seeds).

5. EVALUATION

This study has evaluated the four main regions in the DMN by their accuracy generated from the CNN model. The train-test split operation included a random state value of 13 to ensure that the model is not biased. The dataset was split into training and testing subsets with 2:1 ratio. We have used another 0.2% of the data for the validation, to further reduce the chances of overfitting. In order to provide robust classification using the CNN model, several measures including (1) design of the number of convolutional layers and activation function for each layer ensuring the model does not maintain a high complexity, (2) data augmentation by dropping out some values randomly to reduce that risk.

Considering the pre-processed data source, Phase 1 of the study used the obtained correlation images for the learning process. The validation accuracy, which is the number of correct predictions out of the total number of predictions, obtained from that analysis of ADHD-Care is shown in Table I. The accuracies obtained are less promising, due to the inherent high dimensionality of the data after the correlations were measured. It has considered due to the less amount of variation within the dataset. In Phase 2, we have used the preprocessed images with more variation and making the data set larger by data augmentation, that enables the improvement of the classification process. ADHD-Care_v1 has obtained higher classification accuracies in Phase 2, as given in Table 1.

Table 1. Accuracies of DMN regions

Region	ADHD-Care_v1		Sensitivity	Specificity
	Phase 1	Phase 2		
PCC	62.5%	84.84%	71.12%	65.22%
LTJ	50.26%	85.05%	72.23%	66.31%
RTJ	50.36%	84.62%	70.85%	64.12%
MPC	51.43%	85.21%	72.80%	66.41%

The classification accuracies indicate that the MPC region has the best accuracy with 85.21% for the CNN model. Thus, it validates the biological theory, where the prefrontal cortex has found as the most effective region [23]. Further, the LTJ and RTJ are also showing a close relationship between each other in the correlations. Also, the PCC has achieved an accuracy of 84.84% which again shows a close relationship between other regions.

When comparing the obtained accuracies with a related study [5], that has analyzed the PCC regional activity in ADHD subjects in NYU, KKI and Perking datasets in the global competition with the accuracies of 37.1%, 71.82% and 54%, respectively. The proposed method has shown high accuracy for the given DMN region. This study shows the promising brain areas that activated in the fMRI resting images. The closely related accuracies from the CNN model suggests that the correlations generated by these areas are important in identifying ADHD using fMRI data. Compared to the study [5] which uses deep belief network approach, the proposed ADHD-Care_v1 shows high accuracy assisted by the usage of CNN. All the DMN regions have shown sensitivity between 70% and 73% along with the specificity values between 64% and 67%. The highest sensitivity and specificity values obtained from MPC region compared to other regions. The major benefits of this study include higher accuracy, sensitivity and specificity values compared to the previous studies [5][9]. Moreover, the effective usage of DMN areas as seeds is found to be highly correlated with ADHD pathology. The ADHD identification process is only supported by a single measure of fMRI, which is a limitation of this study. However, other measures can be combined to assist the classification as future work.

6. CONCLUSION

ADHD is a prevailing psychiatric disorder among children, which also carries a genetic cause and having a high rate of pursuing to adulthood. Therefore, premature detection is important to identify the ADHD for the classification process and start early treatments to prevent severe symptoms. This paper is focused on the effect of the main brain regions in the Default Mode Network (DMN) for the classification of ADHD. The proposed solution based on seed correlation for the classification of ADHD using convolutional neural network was implemented for different DMN by considering the main region coordinates of PCC, LT, RT, and MPC. The accuracies based on the selected regions were 84.84%, 85.5%, 84.62% and 85.21% for PCC, LT, RT, and MPC, respectively. The empirical results prove that the presented method of using correlations in the main DMN areas is superior in performance to the previous studies. Also, the identification of the most correlated brain areas of ADHD subjects is assured with the obtained results.

This work can be extended by considering the connectivity maps within different brain regions in the DMN along with the correlated mapping approach. The proposed solution can also be improved to classify different subtypes of ADHD based on seed correlation approach. Further, a combination of different ADHD classification data such as eye movement, EEG is possible to use along with fMRI data to acquire highly accurate classification process.

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