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Research Paper: Feature Selection Based on Genetic Algorithm in the Diagnosis of Autism Disorder by fMRI

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ABSTRACT

Background: Autism Spectrum Disorder (ASD) occurs based on the continuous deficit in a person's verbal skills, visual, auditory, touch, and social behavior. Over the last two decades, one of the most important approaches in studying brain functions in autistic persons is using functional Magnetic Resonance Imaging (fMRI).

Objectives: It is common to use all brain regions in functional extraction connectivity, which leads to high dimensional space. In this study, a Genetic Algorithm (GA) has been used to select effective regions for the generation of Functional Connectivity Matrix (FCM) to differentiate between healthy and autistic people. The aim is to increase accuracy, reduce processing time, and lower the dimension of the functional connectivity matrix.

Materials & Methods: In this analytical study, the dataset includes 820 fMRI images consisting of 445 healthy samples and 375 people with ASD obtained from the autism brain imaging data exchange database. The K-nearest neighbor classification algorithm and the genetic algorithm were used to optimize the identification of two groups of autism and healthy people.

Results: Regarding the large dimensions of the search space, the use of genetic algorithms after 100 replications estimated the accuracy for test and validation data at 61.08% and 62.59%, respectively. The obtained results show that the genetic algorithm can increase the classification accuracy by 10% on test data and 7% on validation data by selecting 67 regions.

Conclusion: The obtained results prove that the proposed method is a well-designed system and can differentiate between autistic and healthy people effectively.

Keywords: Autism spectrum disorder; Functional magnetic resonance imaging; Classification

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Highlights

- Functional connectivity is a suitable measure for the diagnosis of autism.
- Using all brain regions in FCM generation leads to high dimensional feature space.
- A genetic algorithm is proposed to define effective regions in autism detection.
- The proposed method increases detection accuracy up to 9% by removing 49 regions.

Introduction

Autism Spectrum Disorder (ASD) was introduced in 1943 by Leo Caner, a psychiatrist in the United States. This disorder is a clinical diagnosis based on a spectrum of neurological diseases, including autism, Asperger syndrome, and Rett syndrome leading to a persistent defect in a person's verbal, visual, auditory, touch skills, and social behavior [1, 2]. Due to the progressive increase in ASD in recent years, as well as the lack of its definitive treatment, much research has been done on brain mapping to compare Functional Connectivity (FC) and brain function of autistic and healthy people. Therefore, datasets from the extensive connections regions of the brain are collected [3].

Magnetic Resonance Imaging (MRI), as a non-invasive technique, has been widely used to study brain regional networks. Thus, MRI data can be used to display variations in neural networks, which can help in identifying biomarkers for ASD. MRI scans are further divided into structural MRI (sMRI) and functional MRI (fMRI), according to the type of scanning technique. To understand the basic causes and find treatments, we used functional magnetic resonance imaging leading to potential biomarkers of the disease.

Functional magnetic resonance imaging is an efficient technique for mapping brain activity (task state or rest state) by Blood-Oxygen-Level-Dependent (BOLD) that presented by Seiji Ogawa [4]. Therefore, by studying changes in the brain using fMRI image processing and accurately extracting the pattern of abnormalities in early ages of life, it can be benefited as a reliable method for early diagnosis of autism [5]. For example, functional connectivity computed from resting-state functional MRI (rs-fMRI) has been used to derive features for ASD classification with classical machine learning approaches. With the appearance of fMRI images, the first studies to identify autism disease have been performed by checking the shape and volume of different brain regions. In 1999, Ring et al. using fMRI images in the task state concluded that several brain regions were similarly activated in the two groups. The difference was that the prefrontal cortical regions, were more active in the healthy group [6]. Despite current limitations, the potential of autism biomarker research is enormous. Many studies have been devoted to the role of genetic and biomarkers such as disabilities in speech, behavior, and learning in identifying ASD [7].

In recent years, researchers' investigations in the diagnosis of mental diseases such as autism, epilepsy, schizophrenia, etc., are based on the study of functional connections between different regions of the brain. Recognition of the structure and function of brain networks firstly requires understanding the connection of brain regions with each other. The data analysis based on time-series and functional connectivity matrix, including activity patterns between different regions, is done by determining the correlation between the time signals of the brain image voxels [8]. In this section, various methods addressing the recognition and the structure of brain networks and classification data are discussed.

In 2004, Just et al. found that functional connectivity in brain networks decreased in people with autism [9]. Zanganeh et al. proposed a dimension reduction method using the combination of Artificial Neural Network (ANN) classification algorithm and Genetic Algorithm (GA) for disease (like breast caser, thyroid disease [hypothyroid] diagnosis) [10]. In 2011, Boehm et al. analyzed fMRI image data for identifying cognitive brain functions. In this study, they used the GA and one-class learning method to extract appropriate features and classify visual cognitive tasks [11]. Plitt et al. used the various classification algorithms to detect ASD rs-fMRI, including Random Forest (RF), K-Nearest Neighbor (KNN), Linear Support Vector Machines (L-SVM), Gaussian kernel Support Vector Machines (rbf-SVM), L1-regularized logistic regression, L2-regularized logistic regression, elastic-net-reg-

ularized logistic regression, Gaussian Naive Bayes, and linear discriminant analysis. Specifically, regions identified in this study as most predictive of ASD included the insula, ventromedial prefrontal cortex, anterior, middle, and posterior regions of cingulate cortex, supplementary motor cortex, anterior temporal lobes, posterior aspects of the fusiform gyrus, posterior superior temporal sulcus, temporal-parietal junction, intraparietal sulcus, and inferior and middle frontal gyri bilaterally [12]. Chen et al. investigated atypical connections between the default mode network, frontoparietal network, and cingulo-opercular network that may eventually be used to aid the detection of ASD. They applied an SVM classifier and achieved an accuracy of 79.17%, sensitivity of 77.78%, and specificity of 80.47% [13]. Beheshti et al. diagnosed mild cognitive disorders in the brain of people with Alzheimer using fMRI images. Input data are classified by SVM, and a GA is applied to find the optimal feature subset. The results of the proposed method showed that the proposed method could differentiate between patients with stable Mild Cognitive Impairment (sMCI) and individuals with progressive Mild Cognitive Impairment (pMCI) [14]. Sen et al. derived a novel algorithm for combining MRI and fMRI data features which can then be used to differentiate healthy people and patients. They used the SVM classifier and achieved an accuracy of 64.3% [15]. Eslami et al. presented the Auto-ASD-Network method to combine deep learning methods and support vector machines for diagnosing ASD and reduce the number of features using fMRI data. This study helps in quantifying the current psychiatric diagnosis and can increase the accuracy of diagnosis, prognosis, and treatments to assess mental disorders such as Attention Deficit Hyperactivity Disorder (ADHD) and ASD [16].

One of the main challenges in fMRI analysis is the high-dimension of data. Although Functional Connectivity Matrix (FCM) data provides comprehensive information about communication between different brain regions, the high dimensions of the feature-space impose several challenges in the classification and analysis stage. Therefore, feature selection is considered one of the most critical issues in distinguishing autistic from healthy people. The purposes of feature selection are dimension reduction, increasing the speed of operations, increasing the accuracy of classification algorithms, and better understanding the results.

In studies, various data classifiers and accuracy assessment models have been used to quickly and accurately diagnose the status of ASD and its symptoms. Regarding the recent research in this field, little attention has also been paid to the dimension reduction of FCM. Selecting the appropriate regions to generate FCM leads to increasing classification accuracy. It is an NP-hard problem due to the high dimensions of the search space. In this paper, for the first step, the pre-processing is performed on rs-fMRI images. In the next step, it is divided into 116 regions using automated anatomical labeling of the brain, and the Pearson correlation coefficient is computed for every pair of the 116 brain regions to create a time series of brain activity vectors. Then, the K-Nearest Neighbor (KNN) classifier is used to identify the two groups of autism and healthy. Finally, a genetic algorithm as a meta-heuristic method and a powerful search engine is applied to choose the optimal regions for dimension reduction of the search space. Generally, meta-heuristic search algorithms are inspired by biological processes in nature, and most of them operate as a population. GA is also a branch of evolutionary algorithms whose fundamental principles are adapted from the science of genetics and was introduced in 1975 by John H. Holland [17].

Materials and Methods

Study materials

To evaluate the capability of the proposed method in this analytical study, fMRI images are used in the Autism Brain Imaging Data Exchange (ABIDE) represents data from 17 international sites, including 820 samples where 375 people have ASD, and the rest are healthy, approved by [18]. This research dataset includes sMRI and rs-fMRI, scanned from ASD and healthy groups with information such as age, sex, IQ, etc. (Table 1).

Table 1. Clinical information of healthy and patient groups

Labels	Number of Persons	Age (y)		Sex		FIQ_Test		VIQ_Test		PIQ_Test	
		Range	Average	Female	Male	Range	Average	Range	Average	Range	Average
Healthy Group	445	[6, 56]	16.81	64	381	[73, 146]	110.99	[67, 147]	111.48	[67, 155]	107.92
Autism Group	375	[7, 64]	17.1	32	343	[41, 148]	105.47	[42, 180]	105.25	[37, 149]	104.15

FIQ _Standard Score; VIQ _Standard Score; PIQ _Standard Score.

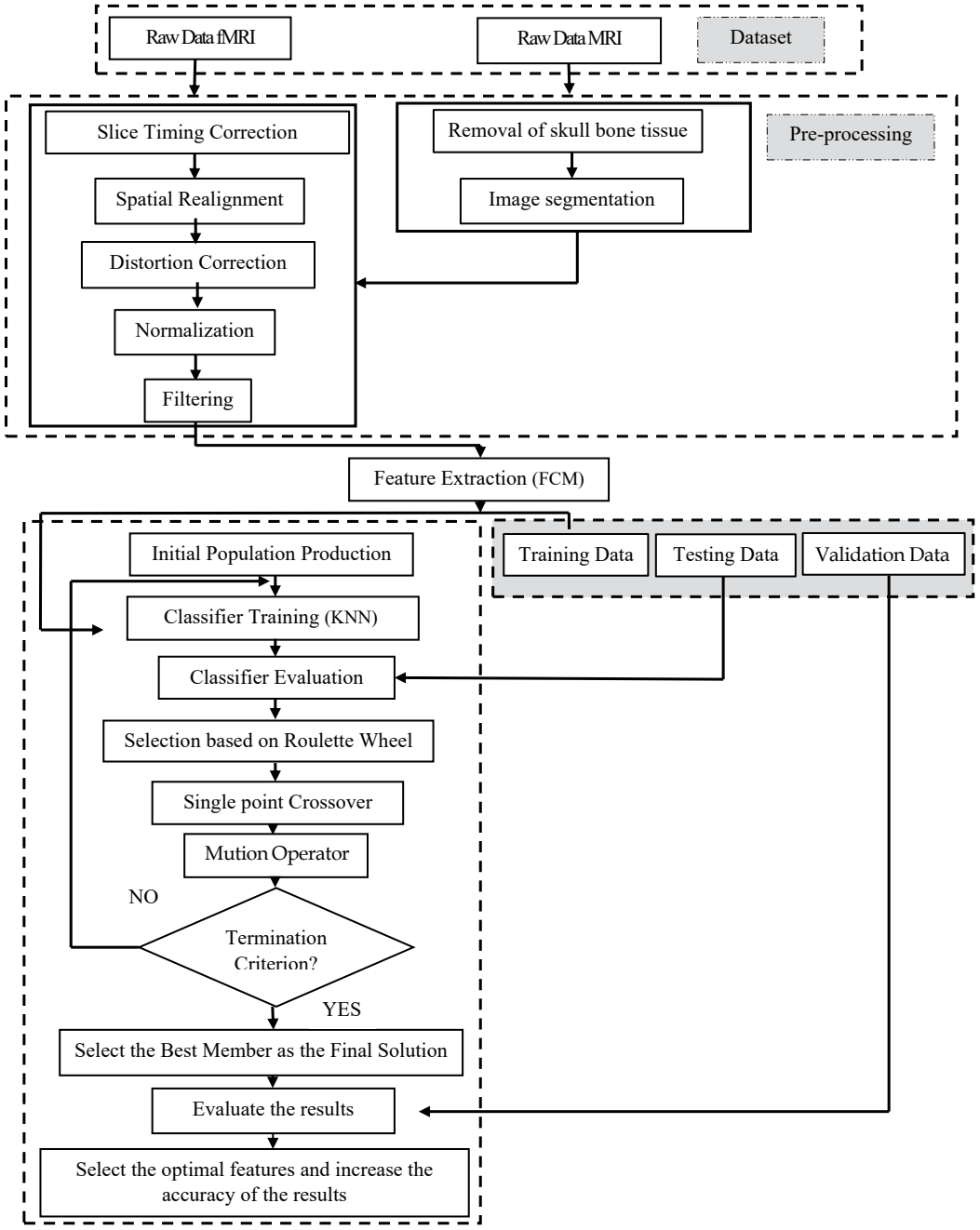

Figure 1. Flowchart of the proposed method

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Methodology

To prepare data for the process, fMRI images are registered, and they are pre-processed using the FMRIB Software Library (FSL) software package. The pre-processing steps are 1) slice timing correction, 2) spatial realignment, 3) distortion correction, 4) normalization, 5) spatial smoothing, and 6) temporal filtering [19].

Then the feature space is generated based on the FCM, and finally, GA is used to find the appropriate features. The flowchart of the proposed method is shown in Figure 1.

Feature extraction based on functional connectivity

By creating a functional connections map of the brain, the function and correlation of time series are determined between different brain regions. Brain FCM is determined based on correlation coefficients between regions [20-22]. In this study, automated anatomical la-

beling, which divides the human brain into 116 regions, has been used [23].

For each region, by averaging the BOLD signal time-series of the voxels of that region in the pre-processed image, a time series is extracted for that region. The FC between 116 brain regions is determined using the Pearson correlation coefficient. It determines the degree of linear correlation between time series of different regions. The value of this coefficient, which is between 1 and -1, determines the power of FC between different brain regions. If there is a high correlation between the two regions, its value will be 1, if two time series are not correlated, it will be 0, and if the time series of the two regions has been completely inverted, it will be -1. The Pearson correlation coefficient is calculated according to Equation 1.

$$1.\ r_{ij} = \frac{\sum^{n}_{t=1}([x_i(t)-\bar{x}_i][x_j(t)-\bar{x}_j])}{\sum^{n}_{t=1}[x_i(t)-\bar{x}_i]^2 \sqrt{(\sum^{n}_{t=1}[x_j(t)-\bar{x}_j]^2}}$$

, where n is the number of images obtained from the whole brain. The values of $x_i(t)$ and $x_j(t)$ are respectively the values of the time-series in the two regions i and j at time t. Also, $\bar{x}_i$ and $\bar{x}_j$ are the averages of the time-series in these two regions.

Dimension reduction based on genetic algorithm

Although FC provides complete information about how different brain regions communicate, its high-dimensional feature space imposes several challenges in the classification and analysis stage. Therefore, feature selection is one of the crucial issues in distinguishing autistic persons from healthy ones. GA, as a meta-heuristic optimization algorithm, considers a set of feature subsets in each iteration and can effectively find an optimal or near-optimal feature subset.

In general, dimension reduction of the data is made using the components of a GA that include chromosome coding, selection, crossover, and mutation. Each chromosome represents an array of numbers 0, 1, that is, the total number of features (length 116×1) in the search space (Figure 2). The values of 0 and 1 present the absence and presence of the corresponding region in the FCM calculation, respectively.

A series of random solutions (initial population) is created, and then the quality of the solutions is evaluated based on the fitness function. The accuracy of the KNN classifier based on selected regions is considered as the fitness function. The roulette wheel selection is applied

Figure 2. Binary coding of chromosome

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to select parents. For this purpose, the probability of selection corresponding to each chromosome is calculated based on Equation 2.

$$2.\ P(h_i) = \frac{F(h_i)}{\sum^{P}_{i=1}F(h_i)}$$

, where, $F(h_i)$ is the fitness value for the solution h_i and p is the size of the population.

The crossover is performed on a pair of parents based on a single-point operator. After generating a member in a new population, some genes are mutated randomly, which provides availability to search all feature space and escape from the local optimal solution. Finally, the GA ends according to the number of iteration repetitions, and the solution with the highest classification accuracy will determine the final feature subset.

To evaluate the solution, the KNN classifier's accuracy is used. Cover et al. introduced this algorithm in 1968 [24]. The KNN classification algorithm is one of the most common supervised classification techniques used for predicting the class of a sample with an unspecified class based on the class of its neighbor samples. The algorithm is made of three steps:

1. Calculating the distance of the unknown sample from all training samples,

2. Arranging training samples based on the distance and selection of K-nearest neighbors,

3. Using the class that is major among the KNN, i.e., this method considers a class of unknown samples observed more than all the other classes among the KNNs.

Generally, for predicting a new class, the algorithm looks for similar samples among a set of the training dataset. Therefore, if the samples have n attributes, they will be considered as a vector in n-dimensional space to predict the class label of a new record based on a distance criterion such as the Euclidean distance in this space as well as the class label of the neighbors. The classifier assumes the distance of samples from each

Table 2. Values of GA parameters

Parameter	Value
Population size	10
Chromosome length	116
Maximum iteration	100
Crossover rate	0.8
Mutation rate	0.01

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other as a criterion for their closeness to select the most similar samples. There are numerous methods to compute the distance, among which the function of Euclidean distance is one of the most common ones defined as Equation 3.

3. $d=\sqrt{\sum_{i=1}^{m}(x_i-y_i)^2}$

, where the parameters x_i and y_i are two samples, and m is the number of features.

Also, when there is a combination of numerical and batch variables in the data set, the issue of standardization of numerical variables between 0 and 1 is raised. It is best to select the optimal value for K by initial inspecting the data. One of the most critical parameters in the KNN algorithm is the K value; in fact, there is no accurate value for K, and its proper amount depends on the data distribution and space of the problem.

After training the classifier with the data, the testing data are used to evaluate the function of the classifier. In this study, classification accuracy has been used as an objective function Equation 4.

(4) Accuracy=(TP+TN)/(TP+TN+FP+FN)

, where TP (true positive) is the number of persons with autism whose classification algorithm correctly diagnose patient. FP (false positive) is the number of healthy persons who misdiagnose with autism. TN (true negative) is the number of healthy persons who correctly diagnose as healthy, and FN (false negative) is the number of autistic persons who misdiagnose as healthy.

To evaluate the results and performance of the classification algorithm, other parameters of the confusion matrix table have been used, which are as Equation 5, 6, 7, 8, 9, 10, and 11:

(5) sensitivity = TP / (TP + FN)

(6) specificity = TN / (FP + TN)

(7) precision = TP / (TP + FP)

(8) Negative Predictive Value (NPV)=TN/(TN+FN)

(9) balanced accuracy=(sensitivity + specificity)/2

(10) Matthews Correlation Coefficient=((TP×TN)-(FP×FN))/sqrt((TP+FP)×(TP+FN)×(TN+FP)×(TN+FN))

(11) Fowlkes–Mallows =sqrt(precision×sensitivity)

Results

To evaluate the proposed method, ABIDE autism database is used, which consists of 820 pre-processed 3D images of the brain. Data are divided into training, testing, and validation randomly: 60% of the samples are selected as training data, 20% as testing data, and 20% as validation data to evaluate the classifier.

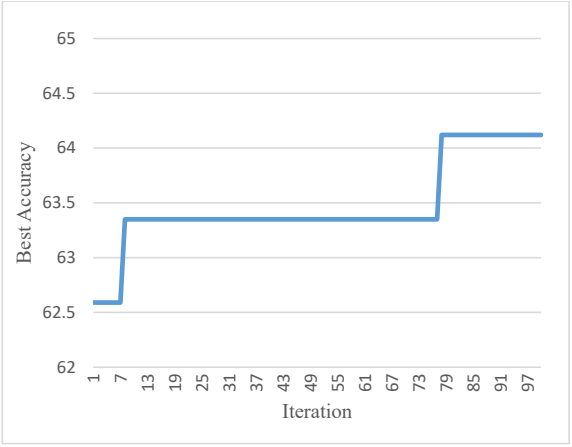

Figure 3. Convergence plot of a GA

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Table 3. Comparison of the proposed method and KNN classifier on test data

Method	Number of Features	Accuracy (%)	Sensitivity	Specificity	Precision	Negative Predictive Value	Balanced Accuracy	Matthews Correlation Coefficient	Fowlkes–Mallows
K-Nearest neighbor	116	51.82	0.72	0.29	0.52	0.48	0.50	0.01	0.61
Proposed Mm	67	61.08	0.78	0.33	0.63	0.51	0.56	0.13	0.70

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By considering 116 regions and 6670 features based on FCM, the accuracy for test and validation data of the KNN classifier are 51.82% and 55.48%, respectively. Then, the GA and KNN classifiers are combined to select a subset of the optimal region subset for ASD identification. The GA parameters are given in Table 2.

Dimension reduction using GA and KNN classifier removed 47 redundant regions, and 67 regions have remained. The convergence diagram of a GA is shown in Figure 3, displaying the best value of the fitness function in each iteration.

Tables 3 and 4 show the classification results of the obtained properties as test and validation data using the KNN classification algorithm and the optimally selected properties with the proposed GA.

Based on the obtained results, the GA algorithm can increase the classification accuracy to 10% on the test data and 7% on the validation data. Using anatomical atlas and genetic algorithm, a significant difference is obtained between the two groups of healthy and autistic people, which leads to the selection of 67 areas out of 116 features. Selected anatomical regions are shown in Table 5.

Comparing functional network criteria between the two healthy and autistic groups showed that 67 areas in the functional network at resting-state have an abnormal pattern, and there is a significant difference in the brain function of patients.

Discussion

In this study, an optimization method for diagnosing autism using fMRI images was presented. In recent years, due to the advance in medical data acquisition technology, improvement in medical image processing methods are required.

High-dimensional feature space with correlated and redundant features encounter diagnosing autism problem with some challenges. To resolve these issues, the use of supervised classification algorithms such as KNN and GA as a meta-heuristic algorithm was proposed for dimension reduction. It increases the accuracy of distinguishing autistic and healthy groups based on fMRI images.

The classification results using selected regions on test and validation data are 61.08% and 62.59%, respectively. In summary, the proposed method results have more quality in terms of accuracy, specificity, and sensitivity, indicating the high capability of the method.

With the progress of medical science, researchers in this field are faced with a large-data from different sources. Regarding the extensive use of meta-heuristic algorithms and their efficiency in dimension reduction of data, it is suggested to use other meta-heuristic algorithms in this field and compare the optimal features extracted from them. Also, they can be used to diagnose other brain disorders such as epilepsy, Alzheimer, Parkinson, etc.

Table 4. Comparison of the proposed method and KNN classifier on validation data

Classifier type	Validation Data								
	Number of Features	Accuracy (%)	Sensitivity	Specificity	Precision	Negative Predictive Value	Balanced Accuracy	Matthews Correlation Coefficient	Fowlkes–Mallows
K-Nearest neighbor	116	55.48	0.67	0.40	0.58	0.50	0.54	0.08	0.62
Proposed method	67	62.59	0.79	0.43	0.64	0.62	0.61	0.25	0.71

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Table 5. Node names in automated anatomical atlas

Number of Nodes	Node Names	Number of Nodes	Node Names
1	Precentral_L	52	Occipital_Mid_R
2	Precentral_R	53	Occipital_Inf_L
3	Frontal_Sup_L	54	Occipital_Inf_R
4	Frontal_Sup_R	56	Fusiform_R
7	Frontal_Mid_L	60	Parietal_Sup_R
8	Frontal_Mid_R	61	Parietal_Inf_L
9	Frontal_Mid_Orb_L	63	SupraMarginal_L
10	Frontal_Mid_Orb_R	65	Angular_L
11	Frontal_Inf_Oper_L	66	Angular_R
12	Frontal_Inf_Oper_R	67	Precuneus_L
13	Frontal_Inf_Tri_L	69	Paracentral_Lobule_L
14	Frontal_Inf_Tri_R	72	Caudate_R
15	Frontal_Inf_Orb_L	75	Pallidum_L
18	Rolandic_Oper_R	76	Pallidum_R
21	Olfactory_L	77	Thalamus_L
22	Olfactory_R	78	Thalamus_R
26	Frontal_Med_Orb_R	80	Heschl_R
27	Rectus_L	81	Temporal_Sup_L
28	Rectus_R	85	Temporal_Mid_L
31	Cingulum_Ant_L	86	Temporal_Mid_R
32	Cingulum_Ant_R	87	Temporal_Pole_Mid_L
33	Cingulum_Mid_L	88	Temporal_Pole_Mid_R
35	Cingulum_Post_L	90	Temporal_Inf_R
36	Cingulum_Post_R	95	Cerebelum_3_L
37	Hippocampus_L	100	Cerebelum_6_R
39	ParaHippocampal_L	101	Cerebelum_7b_L
40	ParaHippocampal_R	102	Cerebelum_7b_R
41	Amygdala_L	103	Cerebelum_8_L
42	Amygdala_R	105	Cerebelum_9_L
43	Calcarine_L	106	Cerebelum_9_R
44	Calcarine_R	109	Vermis_1_2
46	Cuneus_R	112	Vermis_6
49	Occipital_Sup_L	114	Vermis_8
51	Occipital_Mid_L	-	-

Conclusion

In this study, a machine learning algorithm is applied in the Diagnosis of autism disorder. For this purpose, functional connectivity is extracted from fMRI images. Then, effective regions in the brain are selected based on a genetic algorithm as a robust metaheuristic optimization algorithm. For quality determination, a KNN classifier is implemented. The obtained results prove that the proposed method is a well-designed system and can effectively differentiate between autistic and healthy people. It increases the accuracy, specificity, and sensitivity of distinguishing autistic and healthy people based on fMRI images.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were done in compliance with the ethical guidelines of the 2013 Declaration of Helsinki.

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Authors' contributions

Conceptualization: Farzaneh Sadeghian, Hadiseh Hasani; Methodology: Hadiseh Hasani; Investigation, writing the original draft, review, and editing: All authors; Resource: Farzaneh Sadeghian; Supervision: Hadiseh Hasani, Marzieh Jafari.

Conflict of interest

The authors declared no conflict of interest.

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