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An Efficient Autism Detection Using Structural Magnetic Resonance Imaging Based on Selective Binary Coded Genetic Algorithm

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Abstract
In this work, an efficient machine learning technique for autism diagnosis using structural magnetic resonance imaging (MRI) is proposed. The proposed technique employs the voxel-based morphometry (VBM) approach to extract a set of 989 relevant features from MRI. These features are used to train an efficient extreme learning machine (ELM) classifier to identify autism spectrum disorder (ASD) and healthy controls. The proposed selective binary coded genetic algorithm (sBCGA) found a subset of significant VBM features. The selected subset of features was used to build a final ELM classifier with maximum overall accuracy. The proposed sBCGA uses a selective sample-balanced crossover designed to improve the classification of ASD and healthy controls. The proposed sBCGA has been extensively tested, and the experimental results clearly indicated better accuracy than existing methods.

Category: Bioinformatics

Keywords: Autism spectrum disorder; Structural magnetic resonance imaging; Voxel-based morphometry; Genetic algorithm; Extreme learning machine

I. INTRODUCTION

Autism spectrum disorder (ASD) is considered to be one of the most common neurodevelopmental brain disorders. According to a recent review, at least 1 in 54 children is affected by ASD [1]. People with ASD have difficulties with communication, interactions with others, motor functions, and cognitive development. Traditionally, ASD diagnosis is performed based on behavioral testing [2, 3]. The efficiency of such tests depends on the clinician expertise and availability of accurate information provided by patients, and parents/caregivers. Hence, there is a need for a method to automatically detect ASD non-invasively. One of such automatic diagnostic techniques is analyzing brain using magnetic resonance imaging (MRI). MRI based ASD diagnosis is completely non-invasive and subtle changes in the brain regions can be accurately identified.

The use of structural MRI of ASD patients has been intensively studied in the literature. Several studies have

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reported abnormalities in the gray matter of sub-regions of the frontal cortex, such as orbito-frontal cortex [4], middle frontal gyrus [5], temporal sulcus [6], inferior parietal lobule [7], and fusiform gyrus [8]. Whole brain analysis plays a vital role for autism diagnosis in children [9]. MRI has high-dimensional voxels representing gray matter volume in different regions of the brain. The analysis becomes difficult when the number of subjects is much bigger and millions of voxels are involved [9, 10]. Voxel-based morphometry (VBM) is a voxel-wise comparison of gray matter tissue volume within a group of subjects (in this work, ASD vs. healthy controls) [11]. In this study, VBM detected significant regions were used as masks in order to extract the features from MRI scans.

Extensive research of ASD patients has resulted in a few interesting observations [10, 12]. According to recent data, it is observed that 90% of ASD patients are male and only 10% are female. According to a recent study [10], different brain regions in males get affected as compared to females. Hence, several studies have separated male and female subjects and performed independent analysis.

MRI scans used in this study were obtained from the openly available Autism Brain Imaging Data Exchange (ABIDE) database, which consists of data from several institutions and research groups worldwide [13]. The ABIDE database involves both structural and functional MRI of ASD patients and opens many opportunities for researchers to investigate ASD with a fair comparison between methods [14, 15].

Recently, researchers developed various automatic diagnostic techniques to detect ASD by using machine learning and features extracted from MRI. Vigneshwaran et al. [16] used VBM voxels extracted from a limited set of samples from the ABIDE database (both males and females) and reported an overall testing accuracy of about 78%. Authors used a meta-cognitive radial based function method to build a classifier. Later, authors of [11] conducted experiments with a reduced set of samples from ABIDE for males and females separately and achieved higher classification accuracy. Authors in [17] used VBM features extracted from the ABIDE database and metacognitive radial basis function network was used to build an ASD classifier.

In this paper, an efficient machine learning technique called selective binary coded genetic algorithm (sBCGA) was proposed for classifying ASD patients vs. healthy controls. The proposed method used VBM to extract the relevant features from MRI. Extracted VBM features were used in the proposed sBCGA to search for an optimal subset of features, which were then used to build a classifier based on the extreme learning machine (ELM). In this study, experiments were conducted separately for male and female subjects.

The paper is organized as follows: in Section II, detailed information about the ABIDE dataset is presented. The proposed ASD diagnostic technique using sBCGA-ELM is presented in Section III. In Section IV experimental results are presented, and finally, conclusions are drawn in Section V.

II. ABIDE DATABASE

In this work, the openly available ABIDE database was used [13]. The ABIDE database consists of 1,112 MRI scans of ASD patients and healthy controls from several international sites. A set of 1,054 patients is used for experiments and the remaining 58 ASD patients were not included in this study due to incorrect segmentation [17]. Dividing by sex, sets of 154 females and 900 males with ASD form the input database for experiments. The available subjects are divided into six groups for experimental analysis:

Group 1 (All females): Fifty-nine females with ASD and 95 females as healthy controls.

Group 2 (Adolescent females, age $<$ 18): Forty-four adolescent females with ASD and 72 adolescent females as healthy controls.

Group 3 (Adult females, age $\geq$ 18): Fifteen adult females with ASD and 23 adult females as healthy controls.

Group 4 (All males): Four hundred forty-nine males with ASD and 451 males as healthy controls.

Group 5 (Adolescent males, age $<$ 18): Three hundred eight adolescent males with ASD and 292 adolescent males as healthy controls.

Group 6 (Adult males, age $\geq$ 18): One hundred forty-one adult males with ASD and 159 adult males as healthy controls.

The MRI scans from all six groups were processed by the VBM to extract a total of 989 features. A detailed explanation of the Voxel Based Morphometry is given below.

A. Voxel-Based Morphometry

VBM is a voxel-wise comparison of gray matter tissue volume within a group of subjects (in this work, ASD vs. healthy controls) [18]. VBM involves three main steps: spatial normalization, segmentation, smoothing and statistical analysis. The unified segmentation involved tissue segmentation, bias correction, and image registration. Segmented and image registered images were smoothened by applying a 10-mm full-width half-maximum isotopic Gaussian filter. Finally, statistical analysis was used to identify brain regions that showed significant difference in the gray matter between ASD patients and normal persons. VBM-detected significant regions are used as masks in order to extract the features from MRI scans and

a total of 989 voxels/features were extracted. These features were used as input for the proposed sBCGA for further analysis.

III. ASD DIAGNOSTIC APPROACH USING SBCGA-ELM

The proposed ASD diagnostic approach was based on the sBCGA and ELM. The proposed ASD diagnostic approach contained three main steps: "Feature extraction", "Feature selection" and "ASD classifier" as shown in Fig. 1. In the first step, "Feature extraction," a set of 989 features were extracted using VBM detected significant regions. In the second step, "Feature selection," sBCGA was applied to select a subset of significant VBM features. In the third step, "ASD classifier," the reduced feature set from sBCGA was used to build an ELM classifier with high classification accuracy. The final ELM classifier is built with maximum overall training and testing accuracy for ASD diagnosis. A detailed explanation of the sBCGA and ELM is given in the next section.

A. The Selective Binary Coded Genetic Algorithm

The sBCGA is an efficient heuristic optimization tool designed specifically for selecting an optimum subset of VBM features to solve the ASD classification problem (refer to Section III-E). The sBCGA mimics extremely powerful gene exchange mechanisms widely found in nature.

The sBCGA is a variation of the famous genetic algorithm (GA). GA is a heuristic optimization tool for solving various complex optimization problems within reasonable time, which mimics the self-adaptive gene exchange mechanisms from nature. To use GA, an optimization problem from science or engineering must be transformed into a set of chromosomes, which describe the examined problem's characteristics. Each generated combination of chromosomes (or GA solution) must be evaluated using a fitness function, where the fitness value is a numerical estimation of the GA solution's performance. The general purpose of GA is to find advantageous chromosome manipulations, which can enhance fitness. Thus, the efficiency of GA depends on many factors. Firstly, the way the examined problem was transformed into the set of chromosomes must be carefully chosen. Incorrect or incomplete transformation may lead to a poor GA performance. Secondly, chromosome exchange procedures (or GA operators) must be properly selected based on the origin of the examined problem. Thirdly, GA parameters, such as population size, crossover/mutation rates and termination criteria must be properly adjusted.

The framework of the proposed sBCGA is presented in Fig. 2. A set of 989 VBM features was used as the feature set in sBCGA. A sBCGA starts by creating the initial population of n GA solutions. Each GA solution is binary vector with 989 coefficients, where coefficient "1" indicates that the corresponding VBM feature is selected, and coefficient "0" means that it is skipped. In the initial population are all binary vectors, F^0, which are generated randomly by placing 50-200 binary "1" in random locations. The i-th binary vector, F_i^0, thus forms a set of VBM features. This set of VMB features was used to build an ELM classifier. The overall training accuracy of

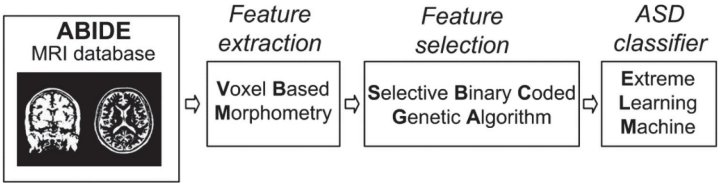

Fig. 1. Framework of the proposed autism spectrum disorder (ASD) diagnostic approach.

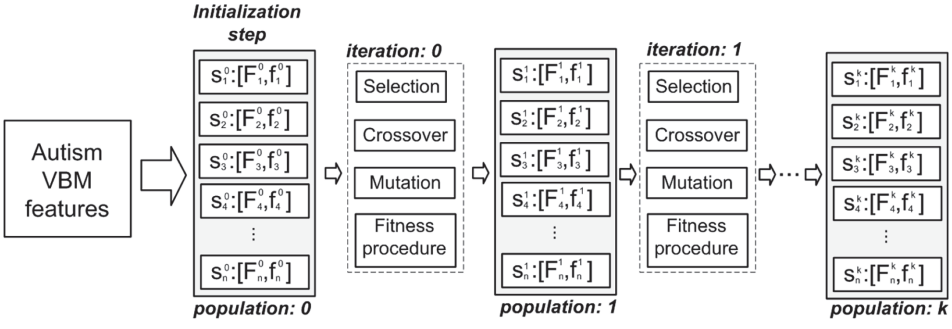

Fig. 2. Framework of the proposed selective binary coded genetic algorithm.

the classifier is used as the fitness value f_i^0 of the binary vector F_i^0. Finally, the i-th GA solution is built as s_i^0:[F_i^0;f_i^0].

The sBCGA processes iterations one by one until the termination criteria is triggered. Each GA iteration (see Fig. 2) involves three main operations: (1) selection, (2) binary operators (crossover and mutation, and (3) fitness procedure (Fp).

The sBCGA used the following settings: population size n = 100, crossover/mutation rate was 0.8, and the termination criteria was to stop sBCGA after the 100th population is generated.

Finally, the best fitness value generated by sBCGA was used in ELM classifier to accurately diagnose ASD.

B. Selection

The selection procedure plays an important role in the GA. Selection determines the probability that a solution from population (i–1) will contribute to next population i. Selection computes the probabilities of solutions based upon their corresponding fitness values: solutions with high fitness value have high probability to be selected, and vice versa. Thus, solutions with better fitness have higher chance to contribute to the next generation, whereas solutions with lower fitness have small but non-zero chance to contribute to the next generation. The selection procedure mimics the natural process when individuals with some particular sets of characteristics are more likely to reproduce. In this paper, the geometric ranking method [19] was used as a selection procedure. In the geometric ranking method solutions are sorted in descending order based on fitness values, and the selection probability of the j-th solution is calculated as follows:

$$P_j = q'(1-q)^{r_j-1}, \quad (1)$$

where

$$q' = \frac{q}{1-(1-q)^n}, \quad (2)$$

q' is a normalization factor, r_j is the rank of j-th solution in the sorted set, n is the population size, and q is 10^{-3}.

C. Binary Operators (Crossover and Mutation)

The Binary operators, crossover and mutation, are a key part of the GA. Crossover is a natural gene exchange procedure, which contributes to the genome of all offspring. Crossover mixes the genes of two individuals to give a child the chance to have better characteristics. Crossover in nature can lead to gradual fitness improvements in the population. Crossover in the GA framework mimics natural crossover behavior. Researchers designed GA crossovers so as to maximize the ability of gene exchange to achieve higher fitness. Each new solution generated by crossover should collect the good characteristics of the parents while neglecting the bad characteristics. Perfectly designed GA crossover guarantees the efficiency of the GA.

In this paper, a selective sample-balanced crossover designed was proposed specifically for sBCGA. The proposed selective sample-balanced crossover significantly accelerates the GA process and helps sBCGA find subsets of features with promising properties, which were used later to build an efficient ASD diagnostic approach. The framework of the selective sample-balanced crossover is presented in Fig. 3.

The proposed selective sample-balanced crossover used two binary vectors, F_1 and F_2, extracted from two solutions selected by the "Selection" procedure and builds two new binary vectors F_1^I and F_2^{II}. The crossover manipulated the positions of the binary "1"s, in a way which balances the number of chosen VBM features in further populations. In the first step, crossover located all coefficients "1" in both binary vectors and builds "F_1 indices" and "F_2 indices"—in Fig. 3, these are (2,3,7,8,9,11) and (1,3,4,6,9,10,11), respectively. In the second step, crossover identifies "Same indices" (3,9,11), and "Different indices" (1,4,6,7,10). In the third step, two random subsets of the set of "Different indices" were chosen. Sets of indices "subset 1" (1,4,7,10), and "subset 2" (1,6,10), were created. In the fourth step, indices from "Same indices" and "subset 1" were unified to build F_{new}^I (1,3,6,9,10,11); and indices from "Same indices" and "subset 2" were unified to build F_{new}^{II} (1,3,4,7,9,10,11).

The selective sample-balanced crossover directly transferred the "Same indices" to both new solution vectors F_{new}^I and F_{new}^{II}, which moved the common features from the old population to the new population. Creating two new solution vectors gives genes from the old population higher chance to contribute to the new population. Finally, in the "Fitness procedure" described below, only the binary vector that resulted in better fitness forms part of the new population; the second binary vector with lower fitness was discarded.

"Mutation" is another important gene manipulation mechanism in nature. Mutation modifies some genes in a random manner. Modified genes produce new characteristics: both good and bad. Mostly mutation fails and mutated genes cause minimum improvement or disadvantage. Sometimes mutations make unacceptable modification in the genome and such individuals fail to survive. In the opposite scenario, mutations may rarely cause a significant improvement which cannot be found through crossover. Crossover only iteratively recombines genes available in past populations, thus, crossover may only increase or decrease the prevalence of existing characteristics, and cannot create completely new characteristics not present in older populations.

In the sBCGA, the mutation operator was implemented

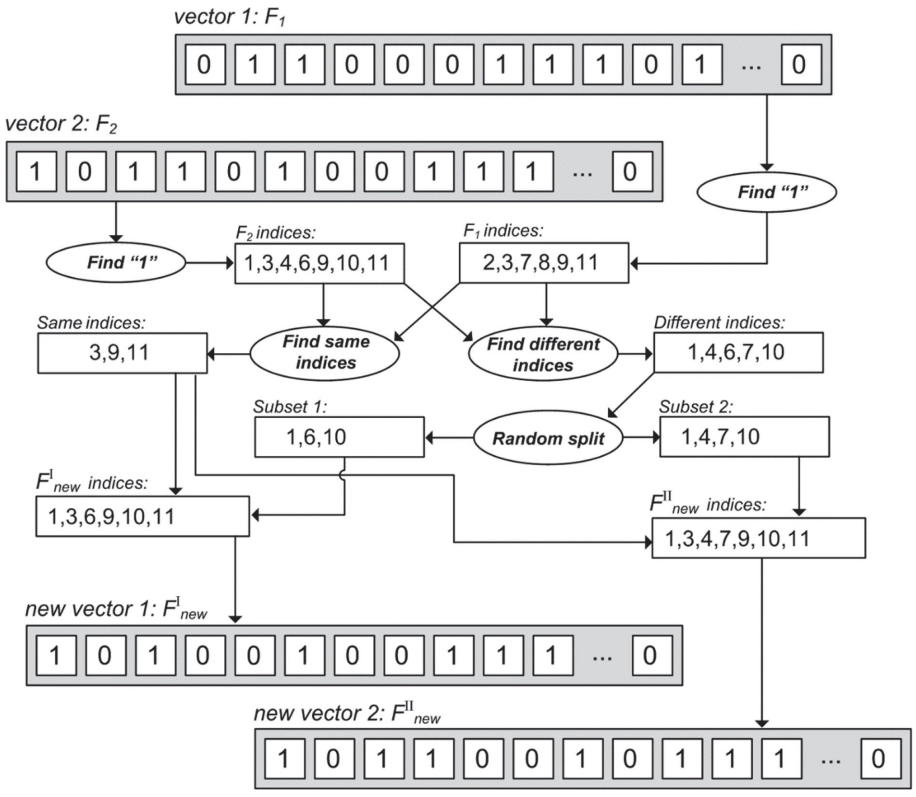

Fig. 3. Proposed selective sample-balanced crossover.

as follows: 50–200 coefficients "1" were randomly allocated in a new binary vector *F*, which was added to the population. The initial set of *n* solutions in the sBCGA framework was also created by using the mutation operator.

D. Fitness Procedure

"Fitness procedure," or Fp, selects a subset of features from "autism VBM features" based upon the vectors F^{I}_{new} and F^{II}_{new} from crossover (see details in Section III-C), to form "Selected set #1" and "Selected set #2". These are used to build two ELM classifiers, and only the one with the best training accuracy (denoted as fitness value, *f*) is added to the new population. The detailed framework of the "Fitness procedure" is presented in Fig. 4.

In the given example (see Fig. 4) the selective sample-balanced crossover created two new vectors, F^{I}_{new} and F^{II}_{new}. Both new vectors were used to build two training sets of VBM features available in the ABIDE database, "Selected set #1" and "Selected set 2", respectively. Both training sets were used then to build two ELM classifiers and the fitness values (training accuracies) were calculated. In the final stage, the vector for which the ELM classifier has higher fitness value was selected for the new sBCGA population.

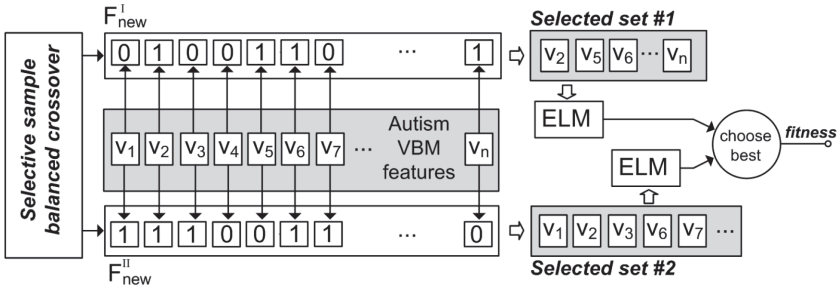

Fig. 4. Fitness procedure.

E. Extreme Learning Machine

The ASD classification involves two classes: the ASD and healthy controls. The sBCGA creates around 20,000 classifiers in total (100 populations × 100 solutions per population × 2 choices by crossover). ELM is employed in this work due to its fast-training phase and relatively high accuracy.

The ELM is a single hidden layer feed-forward neural network with a one-step training process. Compared to other machine learning approaches, ELM does not iteratively update output weights, instead input weights were assigned randomly and output weights were estimated analytically [20]. The ELM may use any type of neuron activation functions including non-linear ones. In this work, a Gaussian activation function was used to activate neurons in ELM. The hidden layer neuron biases were also assigned randomly. Detailed information about the ELM was presented in [20]. Due to the random origin of the ELM, 10-fold experiments were deployed: namely, for each set of selected VBM features the ELM classifier was trained 10 times. The ELM classifier with best training accuracy was then used to determine fitness. Such a med efficiently balanced the performance of the ELM and avoided random failure of the classifier.

IV. EXPERIMENTAL RESULTS

The proposed ASD diagnostic approach has been extensively tested in a few different scenarios. Experiments with ASD were processed separately for males and females; and for adolescents under age 18, and adults over 18. The experiments were divided into six groups:

Group 1 (All females): Fifty-nine ASD, 95 healthy controls, 154 in total.

Group 2 (Adolescent females, age < 18): Forty-four ASD, 72 healthy controls, 116 in total.

Group 3 (Adult females, age ≥ 18): Fifteen ASD, 23 healthy controls, 38 in total.

Group 4 (All males): Four hundred forty-nine ASD, 451 healthy controls, 900 in total.

Group 5 (Adolescent males, age < 18): Three hundred eight ASD, 292 healthy controls, 600 in total

Group 6 (Adult males, age ≥ 18): One hundred forty-one ADS, 159 healthy controls, 300 in total.

Experiments for each group were processed individually using the sBCGA, and results are presented in Table 1. Experiment results were compared with the method presented in the study of Subbaraju et al. [17], where authors used the same set of features for the same groups of ASD patients. Thus, direct comparison with [17] was possible. The proposed method outperforms method [17] in five of the six scenarios. For the group 1, "all females," the proposed method showed 2% less testing accuracy. In other scenarios, group 2 (Adolescent females, age < 18), group 3 (Adult females, age ≥ 18), group 4 (All males), group 5 (Adolescent males, age < 18), and group 6 (Adult males, age ≥ 18), the proposed method shows improvements of 1%, 1%, 4%, 4%, and 1.3% in classification performance, respectively.

In [16], researchers have extracted different VBM sets of voxels for "all females" (66 features), "Adolescent females, age < 18" (104 features) and "Adult females, age ≥ 18" (43 features). The proposed sBCGA is efficient if the feature space is relatively large. In this case the

Table 1. Experimental results

		Accuracy	
		Proposed method	**Vigneshwaran et al. [15]**
Group 1 (All females)	Training	0.99 (72)	0.95
	Test	0.81	0.83
Group 2 (Females, age <18)	Training	0.99 (95)	0.96
	Test	0.86	0.85
Group 3 (Females, age ≥ 18)	Training	0.99 (37)	0.98
	Test	0.99	0.98
Group 4 (All males)	Training	0.67 (62)	0.70
	Test	0.65	0.61
Group 5 (Males, age <18)	Training	0.73 (155)	0.84
	Test	0.65	0.61
Group 6 (Males, age ≥ 18)	Training	0.95 (199)	0.83
	Test	0.718	0.705

Numbers in parentheses denote VBM features selected by sBCGA.

number of possible subsets of features was large and sBCGA has freedom to generate subsets of features with high fitness. However, the reduced set of features for all groups of females significantly limits the efficiency of sBCGA. Hence, original set of 989 VBM features for experiments with groups 1, 2, and 3 was used. The proposed sBCGA performed better for groups 2 and 3 even when using the original set of 989 features.

The sBCGA selects 72 VBM features for group 1 (All females), 95 features for group 2 (Adolescent females, age < 18), 37 features for group 3 (Adult females, age ≥ 18), 62 features for group 4 (All males), 155 features for group 5 (Adolescent males, age < 18), and 199 features for group 6 (Adult males, age ≥ 18).

A. Comparison with Other Existing Methods

Several studies have used the ABIDE database to develop different ASD diagnostic approaches using various machine learning techniques. Authors in [16] build a meta-cognitive radial based function classifier for ASD. Authors used a reduced set of subjects from the ABIDE database and extracted VBM features. Later, in [11], the authors conducted experiments with a reduced set of samples from ABIDE for males and females separately. In their study, VBM features extracted from a reduced number of subjects from the ABIDE database were used to build a support vector machine for the ASD classifier. Due to the reduced set of samples, direct comparison of proposed method was not performed with methods presented in [11, 16].

V. CONCLUSION

In this work an efficient ASD diagnostic approach based on the sBCGA was presented. The sBCGA was designed to select an optimal subset of VBM features extracted from the ABIDE database. A selective sample-balanced crossover, designed specifically for sBCGA was used to improve the optimization process. The final ELM classifier created from the subset of VBM features selected by sBCGA produced better classification performance for ASD diagnosis.

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Conflict of Interest(COI)

The authors have declared that no competing interests exist.

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