Can Evolutionary-based Brain Map Be Used as a Complementary Diagnostic Tool with fMRI, CT and PET for Schizophrenic Patients?

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ABSTRACT

Objective: In this research, a new approach termed as "evolutionary-based brain map" is presented as a diagnostic tool to classify schizophrenic and control subjects by distinguishing their electroencephalogram (EEG) features.

Methods: Particle swarm optimization (PSO) is employed to find discriminative frequency bands from different EEG channels. By deploying the energy of those selected frequency bands from different channels within each time frame (window) on the scalp geometry, a sort of two dimensional points along with their values are created; by applying Lagrange interpolation, an image can be constructed. Finally, by averaging the images belonging to successive time frames, an evolutionary-based brain map is created.

Results: In this study, twenty subjects from each group voluntarily participated and their EEG signals were caught from 20 channels. The energy of selected bands for different channels are arranged in a feature vector for each time frame and applied to Fisher linear discriminant analysis (FLDA) resulting in 83.74% diagnostic accuracy between the two groups. The achieved result by the proposed method was much higher than applying the energy of standard EEG bands (delta, theta, alpha, beta and gamma) to the same classifier which just provided 77.04% accuracy. Applying T-test to the achieved results supports the supremacy of the proposed method as an automatic powerful diagnostic tool.

Conclusion: The proposed brain map is capable of highlighting the same physiological and anatomical changes which are observed in fMRI, PET and CT as differentiable indicators between controls and schizophrenic patients.

Keywords

EEG Classification, Schizophrenia Disorder, Band Power, PSO

Introduction

Accurate diagnosis of schizophrenic patients is still a hot topic among psychiatrists. There is no quantitative measurement for the exact diagnosis of this disease; in other words, no physiologically based measurement is performed for this diagnosis, and psychiatrists have to rely on some qualitative criteria such as DSM-V-TR [1] or ICD-10 [2]. Since some psychiatric diseases share a lot of common qualitative clinical symptoms, it is hard to distinguish them precisely, especially in the first interview session. In this regard, some diagnostic apparatuses include functional magnetic resonance image

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(fMRI) [3-4], positron emission tomography (PET) [3], computed tomography (CT) scan [5] and electroencephalography (EEG) [6] are developed to observe differences between patients and healthy subjects. Lots of changes are observed between the brain images of schizophrenic and normal subjects by different imaging equipment. From the physiological and functional viewpoints, positron emission tomography (PET) images show a lower activity in the frontal lobe of schizophrenic patients compared to normal subjects [7]. In contrast, in fMRI images decreasing in the volume of Hypocampus-Amigdala and Para-Hypocampus, especially in the left sphere and also decreasing of blood flow in the occipital lobe of the schizophrenic brain, compared to control subjects, are investigated [8]. Moreover, from the anatomical point of view, CT images of schizophrenic patients show a bigger volume of lateral and third ventricular in their brain compared to normal people [7]. Nevertheless, research findings on PET, SPECT and fMRI images are much more than that of CT images to diagnose schizophrenia, because they reflect the functional information while CT can just provide anatomical information. Nevertheless, catching an image by each of these imaging apparatuses is very expensive for people. fMRI images cannot reveal the similar discrimination observations as CT images demonstrate between the two groups; therefore, each imaging apparatus, depending on the method of image catching, is capable of showing specific sorts of changes between the two groups.

Although there are different imaging methods for brain function analysis, EEG is still a suitable tool for brain activity monitoring. Electroencephalogram (EEG) monitoring offers a unique tool in the early diagnosis and management of several brain functions. Clinical experts in this field are familiar with the manifestation of standard EEG brain rhythms including delta (δ), theta (θ), alpha (α), beta (β) and gamma (γ) bands [6], but the efficient changes of EEG in these standard frequency bands are not the same for all people, and it changes from a person to another one. Even in other applications like brain computer interface (BCI), the energy of EEG signals in these standard frequency bands, within each frame, considered as state-of-the-art features to classify the imagery movements [9] but in several studies, BCI researchers tried to optimize the standard frequency bands for each participant, separately [10]. Hoyer et al. [11] attempted to find individually relevant EEG power spectral parameters with a hybrid analysis system. They used a hybrid analysis system containing variable frequency band power estimators and a neural network. This network was trained with regard to brain function during well-defined states of hemorrhagic hypotension. Their results showed better detection and classification of moderately reduced brain supply than the EEG standard frequency bands. Jaffe et al. [12] optimized the frequency intervals to extract spectral characteristics of parasympathetic and sympathetic control of heart rate. Sabeti et al. [13] performed a comprehensive study in which L-plus R-Minus search is employed for channel selection, and in the second phase dimension reduction by genetic algorithm is carried out along with different classifiers to reduce the computational complexity. In another attempt [14], frequency band selection of EEG signals by genetic algorithm is performed in order to find the discriminative frequency bands for each channel to classify the two groups. In particular, many EEG-based attempts have been made to classify schizophrenic patients from healthy subjects by discriminating elicited chaotic dimensions from their EEG channels [15-17].

In this research, we present a new brain map technique for better demonstration of physiological and anatomical changes between the two groups. Further development of this low price technique could be a suitable complementary tool for other expensive imaging techniques. In this study, particle swarm optimization (PSO) is selected as a fast and robust method to optimize the discriminative frequency intervals to develop a more informative brain map based on these optimized frequency intervals. To show the performance of PSO in optimizing the frequency bands, classification results of the two groups using their optimized bands are compared to that of standard brain rhythms including delta (δ), theta (θ), alpha (α), beta (β) and gamma (γ) bands. The rest of the paper is organized as follows: Section 2 describes the data acquisition and in Section 3, PSO algorithme is explained. Section 4 introduces the proposed evolutionary-based brain map with the optimized frequency band selection. Finally, in Sections 5 and 6, experimental results and conclusion are presented, respectively.

Material and Methods

Twenty patients with schizophrenia and twenty age-matched control subjects (all male) ranged within age from 18 to 55 years participated in this study. They were recruited from the Center for Clinical Research in Neuropsychiatry, Perth, Western Australia. The patients were diagnosed according to DSM-IV [1] for a lifetime diagnosis of schizophrenia or schizophrenia spectrum disorder was recruited from consecutive admissions to a psychiatric hospital. Each participant was seated upright with eyes open, and the experiment took around two minutes. EEG signals were recorded using a Neuroscan 24-Channel Synamps system, with a signal gain equal to 75K (150x at the headbox). In the recording paradigm, EEG signals from 20 electrodes (Electrocap 10-20 standard system with reference to linked earlobes) were recorded plus left and right mastoids, VEOG and HEOG. The eye-blink artifacts were corrected using the techniques proposed in [18], and elimination of artifacts due to muscle activities was visually performed by an expert. In addition, EEG signals were filtered with a Butterworth band pass filter (order 5) at 0.5-50Hz. According to the international 10-20 recording system, EEG data were continuously recorded from 20 electrodes with sampling frequency of 200 Hz.

Evolutionary Methods

In this research, PSO [19-20] is used to find discriminative frequency bands to increase the classification rate of schizophrenic and control subjects. Evolutionary algorithms such as PSO, genetic algorithm (GA) [21] and Ant colony optimization (ACO) [22-23] are usually called meta-heuristic methods which widely explore and exploit the search space rather greedy search. Among the mentioned evolutionary algorithms, here, PSO is selected due to its fast convergence and also considering both local and global fitness of each particle. First, a population of candidate solution called particles, is randomly generated and this population has a potential of being a suitable solution after some PSO epochs under a suitable criterion. At each iteration, particles are optimized under two different criteria; *gbest* and *pbest* which assess the global and local fitness of a particle. Velocity of each particle (the *i*th particle $X_i=(x_{i1}, x_{i2}, ..., x_{iS})$ where S is the dimension) is updated according to the following relations:

$$v_{id} = w * v_{id} + c_1 * rand() * (p_{id} - x_{id}) + c_2 * Rand() * (p_{gd} - x_{id}) \qquad (1)$$

$$x_{id} = x_{id} + v_{id} \qquad (2)$$

where d=1, 2, ..., S , w is the inertia weight, and c_1 and c_2 are the acceleration representing the weighting of the stochastic acceleration terms pulling each particle toward *pbest* and *gbest* positions. *Rand*(.) and *rand*(.) are two random functions in the range of [0, 1]. Velocity of each particle (v) is limited between V_{min} to V_{max} defined by the user as input parameters that determine the step size through the solution space that each particle is allowed to take. Figure 1 shows the pseudo-code of PSO.

Proposed Evolutionary-based Brain Map

The standard brain rhythms include delta (δ), theta (θ), alpha (α), beta (β) and gamma (γ) bands, but these standard frequency bands are not optimized for all people, and it changes

```
PSO Procedure
Input:
    m: the swarm size
    c1 , c2 : positive acceleration constants
    w: inertia weight
    MaxV: maximum velocity of particles
    MaxGen: maximum generation
    MaxFit: maximum fitness value
Output:
    Pgbest: Global best position
Begin
    Swarms { x_id , v_id } = Generate(m); /* Initialize a population of particles*/
    Pbest(i) = 0; i = 1,. . . ,m, d = 1,. . . ,S
    Gbest = 0; Iter = 0;
    While(Iter < MaxGen and Gbest < MaxFit)
      {
         For(every particle i)
         {
            Fitness(i) = Statistical_Evaluation (i);
            IF(Fitness(i) > Pbest(i))
               {Pbest(i) = Fitness(i);  p_id = x_id ; d = 1,...,S }
            IF(Fitness(i) > Gbest)
               {Gbest = Fitness(i); gbest = i;}
         }
         For(every particle i)
         {
            For(every d){
            v_id = w * v_id + c1 * rand() * (p_id - x_id) + c2 * Rand() * (p_gd - x_id)
            IF( v_id > MaxV ) { v_id = MaxV; }
            IF( v_id > -MaxV ) { v_id = -MaxV; }
            x_id = x_id + v_id
            }
         }
         Iter=Iter+1;
      }/*rand() and Rand() are two random functions in the range [0,1]*/
      Return P(gbest)
End
```

Figure 1: Pseudo-code of PSO Algorithm

with age and medication. In this part, continuous version of PSO is employed to find the lower and upper cut-off frequencies of each frequency band for each channel, separately. The average power of each band at each electrode position is estimated as band power. This is accomplished by filtering the signal in *n* frequency ranges (each with a lower and upper cut-off frequency fl and fh) using a digital band pass filter (Butterworth of order five).

The EEG signal is practically a non-stationary time series [24] and to deal with this problem, the time series are divided into successive one-second windows and its dynamics is assumed to be approximately stationary within each window such that band power estimation can be appropriately applied. Then, band power at each windowed signal (200 samples) is determined. Output of this estimator is *n* band power parameters *Pn* representing the power within each frequency band. The resulting parameter vector *Pn* is evaluated by a Fisher linear discriminant analysis (FLDA) [25], in which feature vectors are projected to a direction that maximizes the ratio of between- to within-class scatter matrices. Afterwards, each test vector is projected to that direction and the class label is assigned. Block diagram of evaluation system to find the best frequency bands is shown in Figure 2.

The brain map according to the standard frequency bands and the PSO-based optimized frequency bands are depicted in Figure 3. To sketch the brain map, EEGLAB toolbox is employed [26]. The brain maps in the left and right columns (Figure 3) illustrate the average distribution of band power on all control and schizophrenic subjects. Incidentally, brain map of each subject is drawn based on the average of standard and optimized band powers in all windowed signals through a two-minute paradigm. It can be clearly seen that the achieved average brain map by the optimized bands shows a much higher discrimination between the schizophrenic and control subjects compared to the constructed brain map based on the standard EEG bands. Moreover, the proposed PSO-based brain map definitely can reflect the anatomical and physiological changes between the two groups with the same accuracy in comparison with differentiable indicators observed in fMRI, PET and CT images.

Results and Discussion

In this study, as we mentioned, the data set contains EEG signals of 20 subjects, ten schizophrenic and 10 healthy subjects, were acquired via 20 silver channels. Ten-time tenfold cross validation was applied to find the optimal value for the parameters. At each fold, PSO was applied to the train set in order to optimize the frequency bands of different channels and then, FLDA classifier was applied to the optimized bands of test subjects. The results of applying the optimized and standard

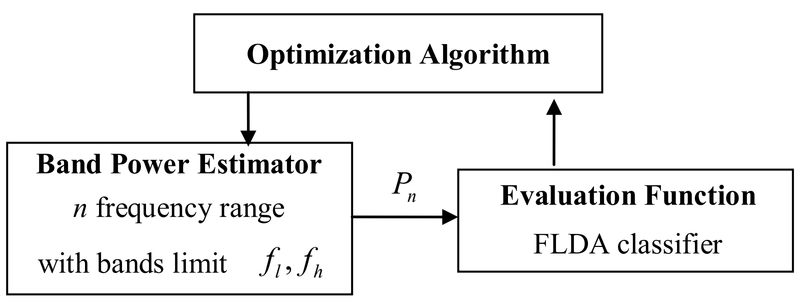

Figure 2: Scheme of the hybrid analysis system (HAS)

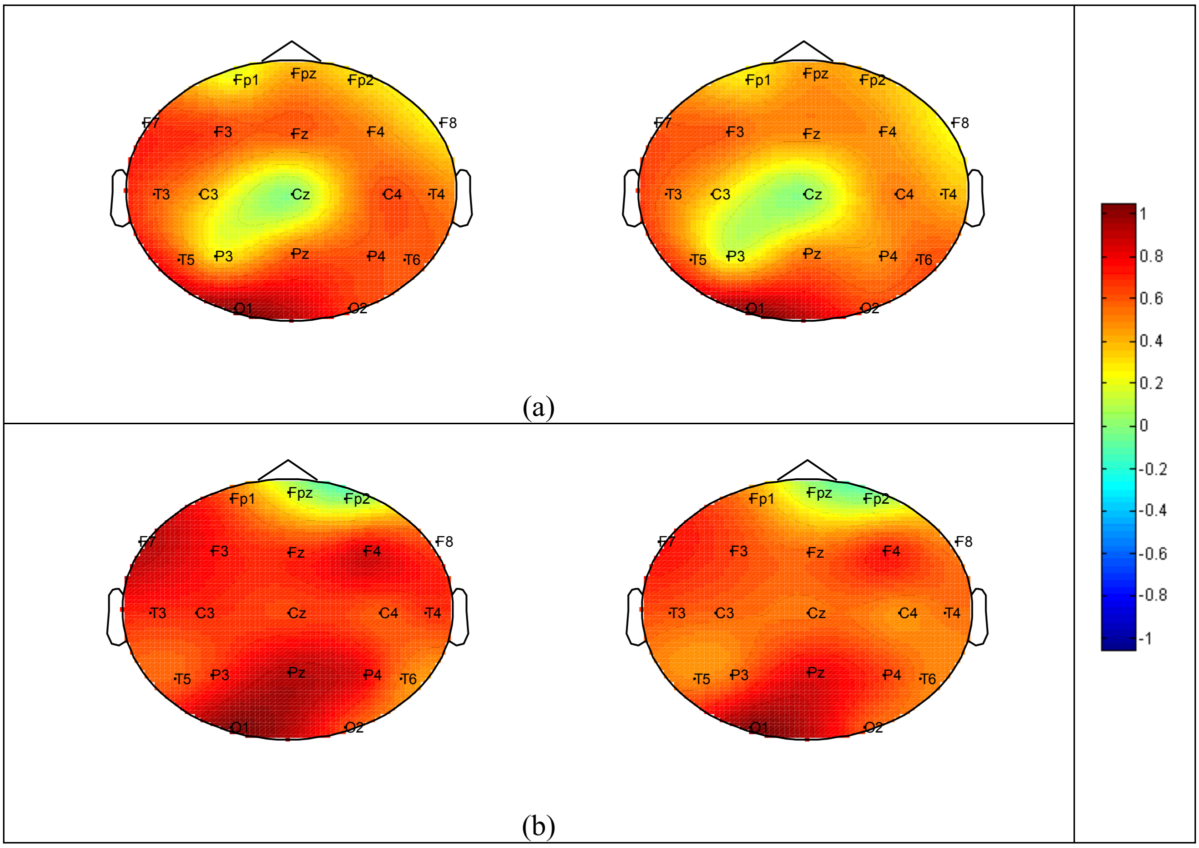

Figure 3: The average distribution of band power on the all control and schizophrenic subjects. Distribution of band power in the form of brain map is shown for the standard band in (a) and the optimized bands by PSO in (b). Left figures shows the control group, and right figures shows the schizophrenic group.

band powers for classifying the two groups are shown in Table 1 for each subject. Table 2 illustrates the classification average over the individuals for the optimized and standard bands. The average band power of standard and optimized frequency bands on the subjects are depicted in Figure 3 in the form of brain mapping images. Table 3 shows the selected values for the parameters of evolutionary algorithms in the cross validation phase. It can be seen from the results that the PSO algorithm is found more discriminative frequency bands leading to a much higher classification accuracy in comparison with using the standard band powers (delta (δ), theta (θ), alpha (α), beta (β) and gamma (γ)). In Figure 4, the mean classification rates along with their standard deviation are illustrated which implies on the supremacy of PSO in comparison with other utilized methods. The differences between the results of PSO and other employed methods (standard bands, GA and ACO) are statistically analyzed by the T-test. Our results show that the differences between classification accuracy of PSO and standard bands is statistically significant ($p < 0.05$).

These results point to this physiological fact that each certain brain disease changes the balance of band power over different EEG channels. The most important difference between the brain of schizophrenic and control subjects is located on the frontal, temporal and occipital

Table 1: Comparison of the classification rate of standard and optimized frequency bands by PSO on the schizophrenic and control subjects in the test set (N is the abbreviation for normal subject while S is for schizophrenic patients)

	N1	N2	N3	N4	N5	N6	N7	N8	N9	N10
Standard bands	62.57	79.10	85.14	56.92	45.56	89.60	79.78	64.44	86.79	83.54
GA	65.36	88.06	89.86	64.62	90.75	75.28	68.89	84.91	84.81	77.58
ACO	69.27	86.57	91.89	63.85	89.60	74.16	65.56	86.79	82.91	82.51
PSO	68.16	88.06	85.81	91.91	74.16	71.11	84.91	85.44	78.03	85.90
	S1	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**
Standard bands	82.96	73.13	83.33	75.95	71.98	77.69	89.57	82.81	82.61	87.32
GA	83.26	83.33	72.78	78.02	92.35	83.21	86.26	85.26	83.85	89.71
ACO	78.41	85.59	73.42	74.73	90.82	80.95	87.20	84.91	83.85	88.28
PSO	83.33	82.79	75.95	84.07	93.37	87.47	88.15	86.32	86.96	92.82

Table 2: The average of classification accuracy over all participants using the standard and optimized frequency bands by PSO

	Mean ± Std
Standard bands	77.04 ± 11.65
GA	81.41 ± 8.29
ACO	81.06 ± 8.32
PSO	83.74 ± 6.93

Table 3: Values of the PSO parameters

PSO	
Parameter	Value
Particles	50
Maximum number of iterations	100
w	0.7
c_1	0.6
c_2	0.6

lobes, as demonstrated in Figure 3. We did not have PET, fMRI and CT images of our participants; therefore, to verify our method, results of the most valid comprehensive textbooks of psychiatry about the research findings of fMRI, PET and CT images on the healthy and schizophrenic subjects are referred and shown in this part. In PET images, low activity of schizophrenic patients in the left pre-frontal lobe and superior temporal regions is shown [7, 27, 28] which confirms a part of our representation. Ragland et al. [29] showed the differences of PET images of 23 control subjects and 23 patients during word encoding (Penn word retrieval test). PET images of 23 normal subjects minus 23 schizophrenic patients are shown in Figure 5 in which colored area has a more active region which remained in the image difference that is completely similar to our results; area around electrodes F7 (left pre-frontal), F3 and Cz (superior temporal regions) show more activity in the control subjects compared to the patient group.

In fMRI images, decreasing of the volume of Hippocampus-Amygdala and Para-Hippocampus, especially in the left sphere of the brain for schizophrenic patients are investigated [7]. Decreasing the volume on those areas leads to diminishing of EEG power above that region (limbic system) [27] which confirms

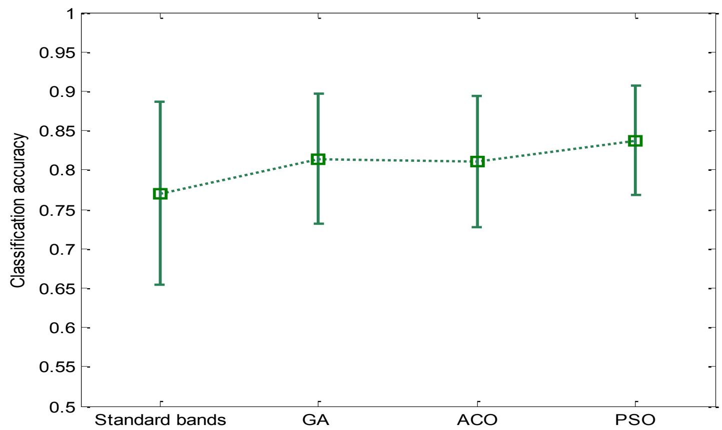

Figure 4: Average classification accuracies between the two groups along with their standard deviation by applying the standard and optimized frequency bands to FLDA.

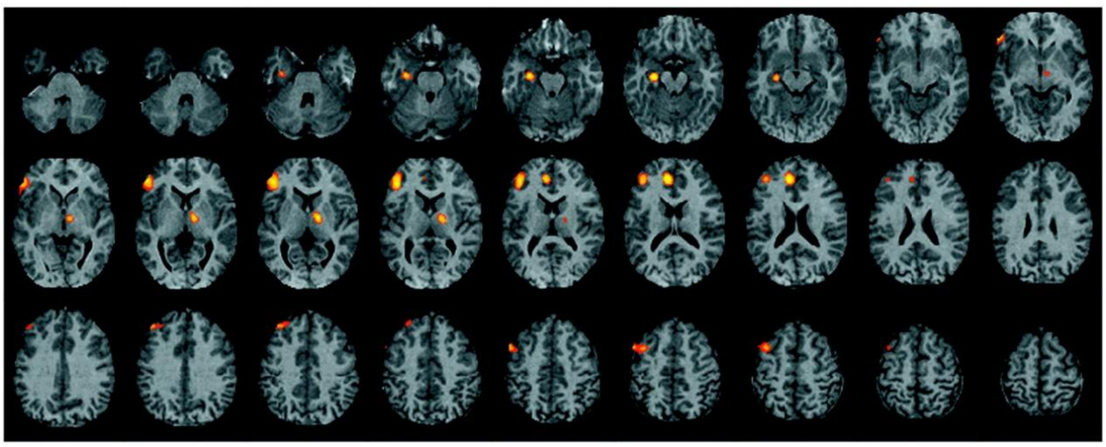

Figure 5: PET images of 23 normal subjects minus 23 schizophrenic patients are shown during the Penn word retrieval test [7,27,28].

the same observation by EEG in our research (illustrated in Figure 3). To show a better visual difference between fMRI images of the two groups, Shenton et al. [8] and Gur et al. [30] performed two comprehensive researches about MRI results in schizophrenic patients. A sample of their results [30] is depicted in Figure 6 in which 14 healthy and 14 schizophrenic subjects were stimulated by two different emotional valence tasks. Reflex of their emotions in their fMRI images shows more activation (colored regions) of Amygdala, Hippocampus and Para-Hippocampus regions in healthy subjects compared to schizophrenic patients (Figure 6).

Moreover, fMRI images of schizophrenic patients at the rest state show the decrease of blood flow in the occipital part compared to normal subjects [7] which confirms the increase of EEG optimized band powers around electrodes O1, O2 and Pz on the healthy subjects which are exactly located on the brain occipital lube.

In addition, increasing the volume of lat-

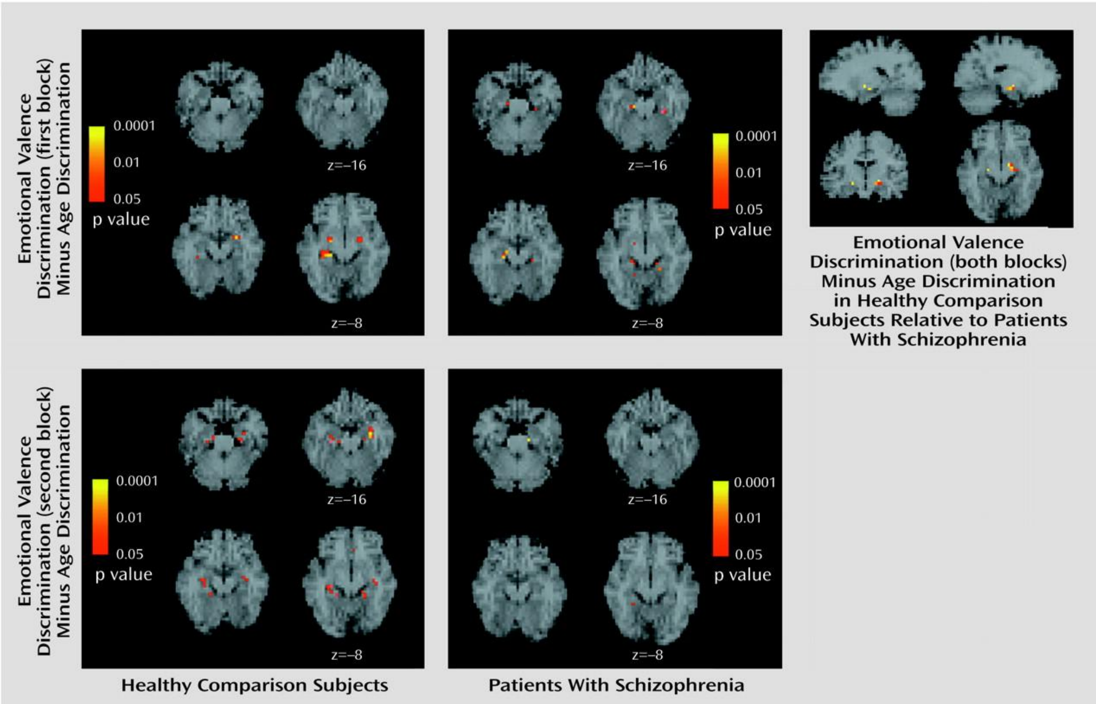

Figure 6: Some fMRI slices from 14 healthy and 14 schizophrenic subjects are shown. These images are caught in two different emotional valence discrimination tasks (first and second blocks) [30].

eral and third ventricular in the CT images is shown. Illowsky et al. [31] in a long time research showed the increasing volume of two patients from their primary stages of schizophrenia till the following 9 years. The CT images of these two patients are shown in Figure 7 during the 9 years. Increasing the volumes of the mentioned ventricular leads to a decrease of neuron population on that area; consequently, it is completely obvious that the power of EEG above that area has decreased [28] that can be similarly seen in Figure 3. Moreover, structural brain abnormalities in patients with schizophrenia and their healthy siblings [32] and volume changes in gray matter in patients with schizophrenia compared to healthy subjects [33] are investigated.

In order to show this difference, CT images of a schizophrenic patient with a normal subject are depicted in Figure 8. Nevertheless, this difference does not convince everyone

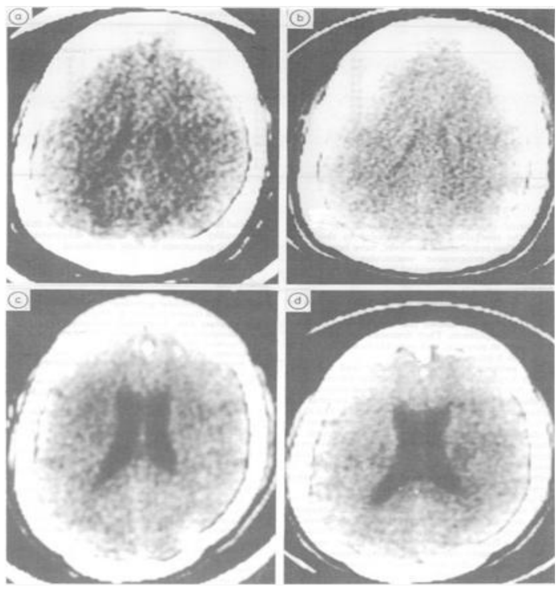

Figure 7: Initial and follow up CT scans of obtained in two patients. Images (a) and (b) show the CAT scan of two different males in 1977 and (c) and (d) show the CAT scan of the same patients in 1986 respectively [31].

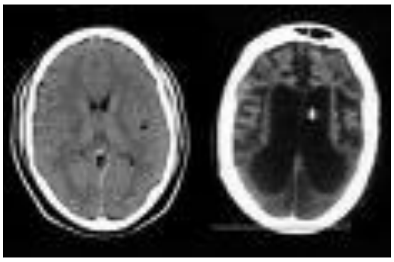

Figure 8: CT images of a schizophrenic (right) and a normal subject (left) are shown. Lateral ventricular of the patient with schizophrenic is much bigger than lateral brain ventricular of the normal subject [7].

because some experts found no significant difference in the ventricle size between the two groups [7].

Conclusion

Specialists use PET, fMRI and also registration of these two modalities to achieve a more accurate diagnosis of schizophrenic patients from the controls. This research presents a PSO-based brain map that is capable of demonstrating the key discriminative information between the two groups as PET, fMRI and CT images present. Since, EEG recording is much cheaper, and has no side-effects, it is preferable to take EEG signals and detect abnormalities between the patient and control groups. The proposed method heuristically searches through different bands among all channels to select discriminative frequency bands for each channel, separately. Among the employed optimization methods, PSO results showed the most discriminant one among the two groups. Our results imply the supremacy of PSO in comparison with other meta-heuristic search methods. Moreover, PSO-based brain map has a better compatibility with the results of CT, fMRI and PET images which demonstrates most of their discriminative information. Thus, the proposed method can be introduced as an automatic diagnostic tool which is informative, efficient, fast and robust. As a future work, registration of the proposed method to the imaging methods is of interest in order to provide more accurate diagnostic information.

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Conflict of Interest

None

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