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High-Precise Bipolar Disorder Detection by Using Radial Basis Functions Based Neural Network

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Abstract: Presently, several million people suffer from major depressive and bipolar disorders. Thus, the modelling, characterization, classification, diagnosis, and analysis of such mental disorders bears great significance in medical research. Electroencephalogram records provide important information to improve clinical diagnosis and are very useful in the scientific community. In this work, electroencephalogram records and patient data from the Hospital Virgen de la Luz in Cuenca (Spain) were processed for a correct classification of bipolar disorders. This work implemented an innovative radial basis function-based neural network employing a fuzzy means algorithm. The results show that the proposed method is an effective approach for discrimination of two kinds of classes, i.e., bipolar disorder patients and healthy persons. The proposed algorithm achieved the best performance compared with other machine learning techniques such as Bayesian linear discriminant analysis, Gaussian naive Bayes, decision trees, K-nearest neighbour, or support vector machine, showing a very high accuracy close to 97%. Therefore, the neural network technique presented could be used as a new tool for the diagnosis of bipolar disorder, considering the possibility of integrating this method into medical software.

Keywords: electroencephalography (EEG); machine learning; deep learning; neural network; bipolar disorder

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1. Introduction

Electroencephalogram (EEG) signals can reveal a great variety of brain pathologic, behavioural, and medication patterns, thus providing a valuable aid in clinical applications, for instance in early diagnosis, treatment, rehabilitation, and classification [1–4]. Visual inspection of the EEG for seizure detection varies with human expertise. Thus, an automatic diagnosis of bipolar disorders (BD) can be crucial in clinical environments. BD is a grave mental illness characterized by episodes of depression, psychosis, changes in mood state, and manias. The main consequences of late diagnosis/treatment involves high rates of suicide, lower productivity, and poorer quality of life. The causes of bipolar disorder are unidentified, but present research indicates a combination of genetic components (about 70–90%) and environmental factors [5]. As a consequence, early diagnosis of BD may significantly reduce health care costs [6]. The prevalence of bipolar disorder is between 2.6% and 5% of the population [7]. According to diverse authors, misdiagnosed patients received inappropriate and costly treatment regimens involving suboptimal medication treatment [8,9]. When untreated, the illness poses a high risk of morbidity and mortality [10]. There is also an increased risk of suicide compared with unipolar depression [11]. BD is a leading cause of global disability. Therefore, correctly diagnosing bipolar disorder should be a priority for the health care systems for clinical, administrative, and research purposes.

For sixty years, psychiatric case records have been considered important epidemiological research tools for estimating the incidence and prevalence of treatment and care patterns [12]. Classification is considered as a useful instrument for medical problems, which has a common application area focusing on medical diagnosis. Recent studies contributed to the classification of diseases using techniques such as expert systems, artificial neural networks, linear programming, database systems, evolutionary algorithms, and swarm intelligence [13–15]. As for classification algorithms of EEG signals, conventional classifiers such as neural networks (NN) [16–18], singular value decomposition (SVD) [19] and Bayesian linear discriminant analysis (BLDA) [20] are widely used. In addition, researchers have also attempted various classifiers such as support vector machines (SVM) [21–24], K-nearest neighbour (KNN) [25,26], logistic regression (LR) [27,28], Bayes classification (BC) [29,30], Gaussian naive Bayes (GNB) [31], decision tree (DT) [32,33], or adaptive neuro-fuzzy inference systems [34,35] to classify data.

This study was based on the use of deep learning techniques. These techniques have been implemented for years in different topics, for example, classification networks, medical research, or pattern recognition [36–39]. Deep learning has been used as a precise tool for the classification of medical records, e.g., EEG, ECG. For our study, we focused on radial basis function (RBF) neural networks [40–42]. Not many uses of the RBF architecture have been reported in the literature in bipolar diseases classification. It employs radial basis functions as activation functions where the output is a linear combination of RBFs of the inputs and neuron weights. This type of network has some characteristics that make it ideal for this work. On the one hand, good performance with different patterns used in the training phase, fast training procedures, and simple network configurations [43,44] can be achieved. On the other hand, its network structure can grow to the desired degree of accuracy [43,44]. Finally, the designed application can be integrated into medical devices due to its rapid response and reduced complexity, which would allow the creation of a diagnostic aid tool that can be used effectively by healthcare personnel.

In order to develop the neural network classifiers, an innovative method based on the fuzzy means (FM) algorithm was employed. The method starts with an initial fuzzy partition (FP) of the multidimensional input space. Then, it uses the FM algorithm to select the size of the network and the hidden nodes. The rest of the network parameters are calculated using standard techniques. It must be emphasized that as opposed to both the K-means and the C-means clustering algorithms, the FM technique does not need a fixed number of clusters prior to the execution of the method. Moreover, since it is a one-phase algorithm, it is extremely fast, even in the case of a large database. The proposed method was compared with different machine learning (ML) techniques for classification. EEG records from two types of subjects (bipolar disorder and healthy control) were utilized to check the accuracy of the proposed system.

The paper is organized as follows: Section 2 introduces the materials used in this study. Section 3 presents our proposed approach. The description of the experiments and the discussion of the results are given in Sections 4 and 5, respectively. Finally, the conclusions of this paper are summarized in Section 6.

2. Materials

In this study, real EEG recordings were used to review the operation of the NN system. One hundred and five bipolar disorder and two hundred and five comparison subjects were tested for brain disorder diagnosis measured by EEG recording. In this regard, Table 1 details both the patients and healthy volunteers by gender grouping, age average, and standard deviation. The Structured Clinical Interview for *DSM-IV* (SCID) was administered to all subjects to obtain *DSM-IV* diagnoses. All patients and controls resided in the health area of Cuenca, Spain, and were enrolled in the Severe Mental Disorder Program of the Psychiatric Service of Virgen de la Luz Hospital, Cuenca, Spain. All participants provided written informed consent after being given an explanation of the study and the procedures involved. The study was approved by the Clinical Research Ethics Committee of the Cuenca

Health Area. Selected patients met a series of criteria for inclusion in the database, such as being between 18 and 55 years of age, having an IQ > 70, fulfilling the *DSM-IV* criteria for bipolar disorder, and understanding/speaking Spanish correctly. On the other hand, exclusion criteria comprised mental retardation, some type of traumatic brain injury with loss of consciousness, severe neurological disease, and abuse or dependence on alcohol or other substances during the 12 months prior to the study.

Table 1. Patients and healthy controls included in the study grouped by gender and age.

	Adults		**Children**
	(31 ± 5 Years)	**(22 ± 3 Years)**	**(14 ± 3 Years)**
Male	71	63	32
Female	54	56	34

The EEG records were obtained at the Psychiatric Service of the Virgen de la Luz Hospital. The equipment available at the Hospital was used to perform the EEGs, specifically a BrainAmp DC-32 channel Brain Vision system with a sampling frequency of 500 Hz. The International System 10–20 was used to place the electrodes, and the EEG recording standard was maintained with that format according to the clinical practice manual. Silver chloride electrodes and gel were used for measurements [45]. The impedance value between the electrode and the scalp remained less than 10 KΩ during the recording. For this, the measuring BrainAmp DC-Brain Vision System had an impedance warning system, indicating values above this limit (in this case, the electrodes were placed again or filled with more gel). The entire measuring process was standardized and strictly followed a medical protocol. It should be noted that the placement, impedance adjustment, and EEG recording were carried out by medically trained staff. The EEG records of different patients presented various noise samples, such as muscle noise, artefacts, baseline, etc. To obtain a more accurate result of the neural network, the raw brain signal measured by the electrodes was pre-processed [46,47] prior to classification. By this means, this noise and artefacts were removed. In this study, the signal was filtered between 0.5 Hz and 40 Hz, and a notch filter at 50 Hz was applied.

Figure 1 shows a sample of the raw EEG recording and scalp maps. More specifically, the results obtained for all electrodes are presented at different times i.e., from 1028 ms to 9976 ms, to check which part of the brain was activated. Scalp maps display the distribution of voltage in the time or frequency domain. Information about the position of the electrodes was used to create the maps. The algorithm used to create the scalp map was based on spherical spline interpolation [48]. To calculate the spherical splines, different parameters were used: the order of the splines and the maximum degree of the Legendre polynomial. The values of the parameters used the interpolation to provide different ripple, whereas high-order splines provide flat responses.

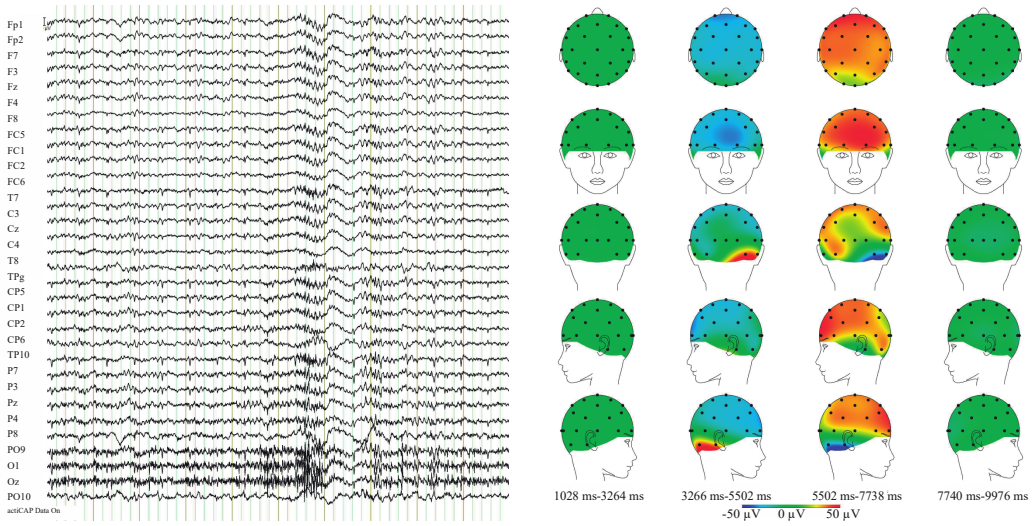

Figure 1. Raw EEG and scalp maps recorded.

3. Method

An artificial neuronal network (ANN) is a computational model based on the structure and functions of biological neural networks, inspired by the known behaviour of the human brain. ANN systems have a non-linear behaviour and allow adjustment to various objectives. The inputs are the stimuli that the artificial neuron receives, and the outputs are the responses to those stimuli. The neuron can adapt and learn by modifying the value of its synaptic weights since they can be modified and adapted to perform a given target [37,43,44].

The training method and RBF network architecture developed for the classification of bipolar disorder are shown below. In our proposed system, we created two classes: class BD corresponds to bipolar disorders, and class CN corresponds to control subjects. The characteristics of the proposed neuronal network system can be seen in Figure 2. It has three layers: an input layer, a hidden layer with a non-linear RBF activation function, and a linear output layer.

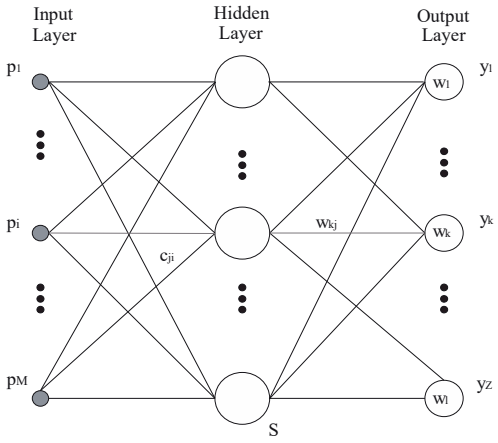

Figure 2. Structure of the proposed RBF network.

Equation (1) shows the activity $a_s(p)$ of the s_{th} node, which represents the Euclidean norm.

$$a_s(p) = \| p - \hat{p}_s \| = \sqrt{\sum_{m=1}^{M} (p_m - \hat{p}_{s,m})^2} \quad (1)$$

where $p_T = [p_1, p_2, \ldots, p_M]$ denotes the input vector, and $\hat{p}_s^T = \left[\hat{p}_{s,1}^T, \hat{p}_{s,2}^T, \ldots, \hat{p}_{s,M}^T\right]$ represents the center of the s_{th} node. For node output, a radial symmetric function was used. A Gaussian function can also be applied:

$$y(v) = e^{\left(a_s^2/w_s^2\right)} \tag{2}$$

with w_s^2 being the width of the node.

3.1. Training of the Proposed Neural Network

In order to train the neural network, a group of known inputs and outputs $(p_k; f_k)(k = 1, 2, \ldots, K)$ training pairs was used. In the proposed system, the training of the neural network consisted of two steps:

1. First, the parameters of the hidden layer $c_s(p)$ were calculated;
2. They are determined from the junction weights between the output and the hidden layer.

In addition, the FM algorithm was applied to choose the network structure and the centres of the hidden nodes [37,43,44]. The proposed algorithm used the FP of the input space, where a number of fuzzy sets were defined for each input variable. The innovative RBF method applied a uniform division of the discourse universe for its input p_j $(j = 1, 2, \ldots, M)$ into c_j fuzzy sets $F_j^1, F_j^1, \ldots, F_j^{c_j}$ with functions of form as follows:

$$F_j^s(p_j) = \begin{cases} 1 - \frac{\left|a_j - v_j^s\right|}{l_j^s} & if\ p \in \left[v_j^s - l_j^s, v_j^s + l_j^s\right]\ (s = 1, \ldots, c_j) \\ 0 & otherwise \end{cases} \tag{3}$$

where v_j^s represents the central element to which the unit's membership value is set, and l_j^s is half of the respective width. The sum of the degrees of correspondence at any point in the discourse universe is close to 1 for each input variable. Defining a FP into the M dimensional input space results in the initial FP of every input. From this, the following algorithm is proposed to find, from the input data vector, the nearest fuzzy subspace [37,43,44].

- Algorithm A: The closest diffuse subspace to a determined input vector is created.
  - Phase 1: From an input data vector $p = [p_1, p_2, \ldots, p_M]^T$ and for $j = 1, 2, \ldots, M$, the fuzzy set that fixes the maximum degree of membership to p_j is elected.
  - Phase 2: As for p, a fuzzy subspace F is created, obtained as the sum of the fuzzy sets chosen in phase 1.
- Through the FM algorithm, the size and centres of the hidden layer are decided. The phases in the algorithm used to select the centres and size of the hidden layer are explained below [37,43,44].
  - Phase 1: From input and output data $(p_k; f_k)(k = 1, 2, \ldots, K)$, the rules number S is established to 0.
  - Phase 2: The initial input data $p(1)$ is selected, and we applied Algorithm A to create the initial diffuse subspace $F^1 = \left\{v^1, 1^1\right\}$. In addition, S is fixed to 1.
  - Phase 3: The $k-1$ input vectors are exanimated, and S diffuse subspaces are generated, with $1 \le S \le k-1$. The kth input vector $p(k)$ is inserted, and the Euclidean relative distances $zl^s(p(k))(s = 1, \ldots, S)$ are calculated between $p(k)$ and all fuzzy subspaces S created using Equation (4).

$$zl_j^s r(p(k)) = \begin{cases} \frac{\left[\sum_{j=1}^M \left(v_j^s - p_j(k)\right)^2\right]^{1/2}}{\left[\sum_{j=1}^M \left(l_j^s\right)^2\right]^{1/2}} & if\ \left[\sum_{j=1}^M \left(v_j^s - p_j(k)\right)^2\right]^{1/2} \le \left[\sum_{j=1}^M \left(l_j^s\right)^2\right]^{1/2} \\ 1 & otherwise \end{cases} \tag{4}$$

The minimum distance $zl^{s0}(p(k))$ is assumed to belong to the fuzzy subspace $F^{S0} = \{v^{S0}, 1^{S0}\}$. Then, whether the next comparison is true is checked:

$$zl^{s0}(p(k)) < 1 \tag{5}$$

If the condition is met, phase 4 can be skipped. Otherwise, the algorithm continues its normal order in phase 4.

- Phase 4: Algorithm A is applied and a novel fuzzy subspace is created for $p(k)$. In addition, the S value is updated to $S = S + 1$.
- Phase 5: It stops if $k = K$. Otherwise, the successive input vector is included and returns to phase 3. The final step of the initial phase aims to define the width w of the Gaussian activation function. For each i node, the width w_i is estimated using the g heuristic of the nearest neighbour:

$$w_i(p) = \left(\frac{1}{g} \sum_{j=1}^{g} \|c_{i-} c_j\|^2 \right)^{1/2} \tag{6}$$

where $c_1, c_2, \ldots, c_g$ represents the node centres closest to the hidden i node. The g value was chosen so that entering an input vector into the system activates a large number of nodes.

3.2. Performance Metrics

For this study, the techniques used to check performance are described below:

$$Recall\ (\%) = \frac{TP}{TP + FN} \times 100 \tag{7}$$

$$Specificity\ (\%) = \frac{TN}{TN + FP} \times 100 \tag{8}$$

$$Precision\ (\%) = \frac{TP}{FP + FP} \times 100 \tag{9}$$

$$Balanced\ accuracy\ (\%) = \frac{Recall + Specificity}{2} \times 100 \tag{10}$$

In these equations, TP represents the number of true positive cases, TN the true negatives, FN the false negatives, and FP corresponds to the false positive cases.

The F_1 score can be defined as

$$F_1\ score\ (\%) = \frac{Precision \cdot Recall}{Precision + Recall} \times 100 \tag{11}$$

Another measure of overall model classification performance is the Matthew's correlation coefficient (*MCC*) [49], which is defined as

$$MCC\ (\%) = \frac{TP \cdot TN - FP \cdot FN}{\sqrt{(TP + FP)(TP + FN)(TN + FP)(TN + FN)}} \times 100 \tag{12}$$

Finally, degenerated Younden's index (*DYI*) [49] and Cohen's Kappa (*CK*) parameters are also employed to analyse the performance of the proposed method [49].

3.3. Proposed Methodology

In the cross validation, the train sample was divided into several box folds that were retained from the training process, with training carried out iteratively with the remaining cases. The diagnostic performance of classification methods was evaluated by repeated ten-fold cross-validation and percentage split strategies. The dataset was divided into 70% for training and 30% for testing. Recorded brain signals employed during the training

phase were pre-processed as described in Section 2. These pre-processed EEG data were not shared during the training and testing subsets in order to avoid the use of the same data for classification and training. The methodology applied in this study can be observed in Figure 3. To check the performance of the proposed method, its operation was compared with different machine learning algorithms. From all of them we selected the following algorithms: BLDA, GNB, KNN, DT, and SVM. All of these ML methods were implemented using the statistics and machine/deep learning MATLAB toolbox [50].

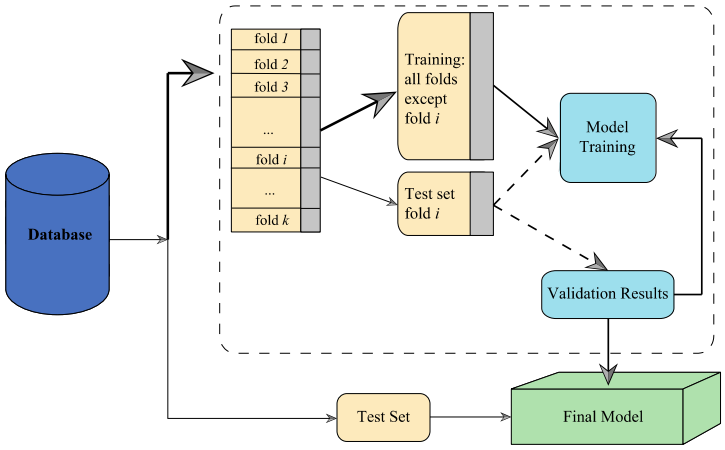

Figure 3. Methodology used for the development of the study.

Machine learning techniques usually have one or more hyperparameters that allow a different adjustment of the algorithm during the training process. The values of these hyperparameters (number of splits, learners, neighbours, distance metric, distant weight, kernel, box constraint level, multiclass method, etc.) for each method lead to algorithms with different prediction performances to obtain the best possible accuracy. In order to optimize these hyperparameters for each ML technique used in this study, each model was trained with a Bayesian optimization approach. Bayesian optimization aims to estimate which configuration of hyperparameters is the one that would maximize the performance of the algorithm from the previous attempts, based on the assumption that there is a relationship between the various hyperparameters and the performance achieved by the algorithm. In this regard, the area under the curve (AUC) and the balanced accuracy were used as performance measures to be maximized.

4. Results

This section describes the results obtained during the training and classification of bipolar disorder patients. The performance of the proposed system was compared with different classification machine learning methods accepted in the scientific community. Table 2 shows the values of balanced accuracy, recall, precision, and F_1 score of the classification methods for bipolar disorder and healthy patients. Systems based on BLDA and GNB obtained lower classification values than other methods, with accuracy values close to 86%; this value is improved with SVM and KNN methods that reached values around 89%. On the other hand, the proposed system, based on a NN, obtained the best performance, achieving accuracy values close to 96.78% for real EEG records. As for the precision and recall values, the KNN and SVM methods were the closest to the proposed NN-based system. In the case of the F_1 score value, the BLDA and GNB methods obtained values close to 86%. KNN and SVM also provided lower performance compared with the proposed method.

Table 2. Values of balanced accuracy, recall, precision, and F_1 score of the machine learning models and the proposed method implemented.

Method	Balanced Accuracy (%)	Recall (%)	Precision (%)	F_1 Score (%)
BLDA	86.93	87.03	86.31	86.67
DT	87.42	87.52	86.80	87.16
GNB	86.30	86.40	85.69	86.04
SVM	88.17	88.28	87.54	87.91
KNN	89.63	89.74	88.99	89.36
RBF	96.78	96.89	96.09	96.49

Other parameters used in performance studies, such as the AUC, MCC, DYI, and Kappa index, were also analysed to check the operation of the proposed system. These parameters helped us to check the correct implementation of the methods when classifying the classes investigated in the study, i.e., bipolar patients and controls. The Matthews correlation coefficient is a more reliable statistical rate which produces a high score only if the prediction gives good results in all the confusion matrix categories (true positives, false negatives, true negatives, and false positives). As it can be seen in Table 3, the NN-based method achieved the highest MCC value. KNN and SVM were the systems that presented a MCC value close to the proposed method. The rest of the methods obtained a smaller value. Another parameter used was the Kappa index; in this case, the NN-based system again obtained the highest value. The other systems used in the comparison reached lower parameter values.

Table 3. Values of AUC, MCC, DYI, and Kappa of all the tested machine learning models and the proposed method implemented.

Method	AUC (%)	MCC (%)	DYI (%)	Kappa (%)
BLDA	86	80.73	86.93	77.39
DT	87	81.18	87.42	77.83
GNB	86	80.14	86.30	76.83
SVM	88	81.28	88.17	78.50
KNN	89	81.71	89.63	79.80
RBF	96	92.45	96.78	92.76

Table 4 displays the result of the classification for the different types of patients and healthy people. As can be observed, the results of the different methods were not modified by these variables. The values of balanced accuracy were very similar between females, males, adults, and children. It should be noted that the proposed method maintained the highest precision in the classification.

Table 4. Values of balanced accuracy of the machine learning models and the proposed method implemented for different types of patients and healthy controls.

	Balanced Accuracy (%)			
Method	Male	Female	Adult	Children
BLDA	86.95	86.93	86.96	86.91
DT	87.44	87.42	87.45	87.40
GNB	86.32	86.30	86.33	86.28
SVM	88.19	88.17	88.20	88.15
KNN	89.65	89.62	89.63	89.61
RBF	96.80	96.78	96.81	96.75

In order to evaluate the classification capacity of the systems presented, the receiver operating characteristic (ROC) were also considered. The curve is the result of representing,

for each threshold value, the sensitivity and specificity measurements [51]. Figure 4 shows the results obtained for the different classification algorithms. According to Table 3, the RBF-based system had the best AUC (0.96), and the KNN method possessed the second highest value (0.89). Specifically, the NN-based system achieved an improvement of 7%, 9%, and 10% with respect to KNN, SVM, and BLDA methods, respectively. As it can be seen, the proposed system can achieve high classification of bipolar disorder disease automatically, resulting in a tool that could help the healthcare personnel for clinical diagnosis.

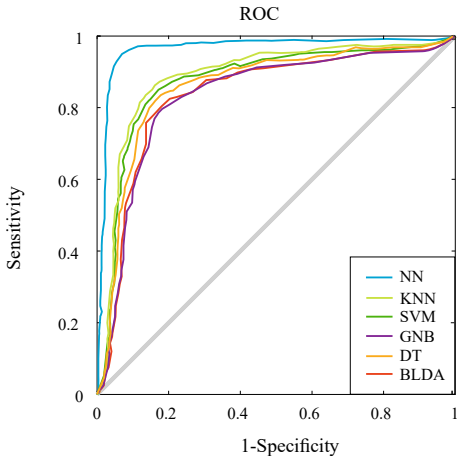

Figure 4. ROC curves for the 9 classification systems compared.

For clarity, all metrics are presented as radar charts, grouped by each training and test dataset. The shape of the plots may be indicative of the quality of the models, where a perfect score would be represented by a circle. The NN-based system (Figure 5) has the best-balanced model. The training and test sets are both virtually represented by similar circular plots. As it can be observed, BLDA and GNB methods have the worst performance in different metrics.

Additionally, Big-O notation (used in computer science to describe the complexity of an algorithm) was applied to the proposed and the classic machine learning methods studied in this paper. Big-O representation specifically defines the worst case and can be used to describe the execution time required or the space used (e.g., in memory or on disk) [52,53]. Table 5 shows the complexity in seconds for the proposed systems, where N is the number of samples used in the input vector. As can be seen, the proposed RBF method presents the lowest complexity as it is a very simple neuronal network with just one hidden layer. It shows a logarithmic growth O(log(N)) (as in the case of the DT algorithm). Conversely, the SVM system takes the longest processing time, of the order of $O(N^2)$, for a high number of samples. The rest of the classifiers have a linear processing time O(N).

Table 5. Complexity of the classification algorithms obtained for the Big-O notation.

Method	**Number of Samples N**				**Big-O**
	10^4	2×10^5	5×10^6	10^7	
BLDA	3145	6158	12,325	24,235	O(N)
DT	3426	6325	8325	10,325	O(log(N))
GNB	2789	5698	11,256	23,246	O(N)
SVM	2324	4896	18,324	310,261	$O(N^2)$
KNN	2035	4256	9245	21,125	O(N)
RBF	1235	2648	3845	3893	O(log(N))

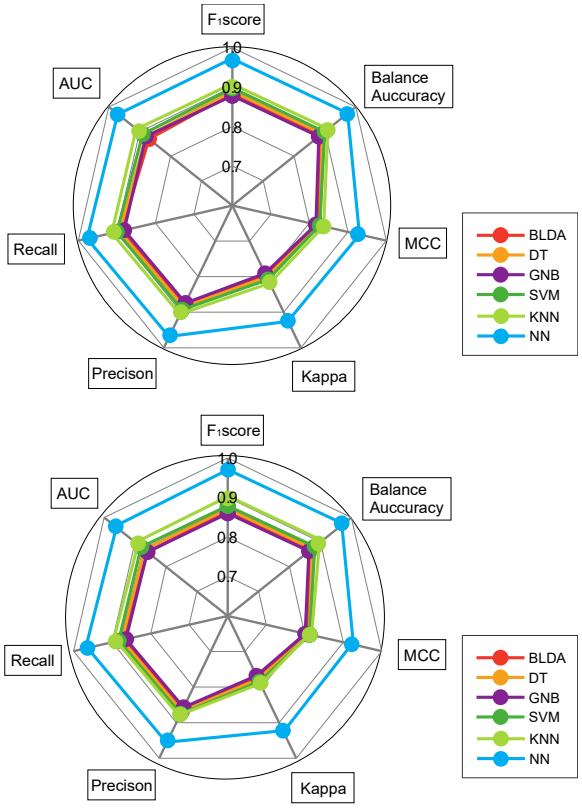

Figure 5. Radar plot of the training phase (**above**) and test (**below**) for the classification of bipolar disorder patients.

5. Discussion

The discrimination of bipolar disorders is a hard classification problem which requires the use of a strong optimizing algorithm and an effective feature set selection procedure. Automated detection can guide treatment decisions, help prognostication, and study the pathophysiology of bipolar disorders [47]. In this study, a radial basis function neural network was successfully used for this pattern recognition task. The results show that discriminating between BD patients and healthy controls with high accuracy can be possible by using our proposed NN classification framework. A maximum classification accuracy of 96.7% was obtained, demonstrating the potential clinical use to classify BD patients by means of EEG datasets.

The proposed algorithm was analysed with different classification methods described in the literature. In the comparison of the systems, it was possible to appreciate the considerable improvement achieved by the proposed NN. This resulted in a tool that facilitates the automatic analysis of EEG signals to aid in the diagnosis of bipolar disorder. One of the limitations of the NN systems is the initialization of the centres and the choice of the base function [43,44]. In our study, the fuzzy initialization of the RBF neural network was used to improve performance. Different techniques have been developed that allow an optimal combination of the results of simple classifiers through alpha integration to exploit the complementarities of simple classifiers under an optimization criterion [54]. The use of NN method brings many advantages. For example, they simplify the configuration of the network, the training method is faster, and the approach capabilities are improved. In addition, the NN proposed introduces an innovative contribution, such as the fuzzy initialization of the network.

Finally, Table 6 provides a comparison of the performance for the proposed method and different relevant related research works presented in the literature. The references were selected because they report novel algorithms classifying BD. Each column in the table specifies the reference and year of publication, acquisition data employed, classification

system, and accuracy obtained. In this regard, it is important to remark that different data or training processes may lead to distinct performance results. Hence, the methods compared can present unlike accuracy depending on the input information/training employed. However, this sort of comparison analysis helps to understand the advantages of the proposed classification method.

Table 6. Performance comparison of different classification methods presented in similar research.

Reference/Year	Acquisition Data	Classification Method	Accuracy (%)
[55]/2010	Electroencephalogram	Mixture Factor Analysis	92.7
[56]/2013	Neurophysiological Endophenotypes	Multivariate Logistic Regressions	72.0
[57]/2015	Electroencephalogram	Support Vector Machine	80.2
[58]/2015	Electroencephalogram	Multilayer Perceptron Neural Network	91.8
[59]/2016	Electroencephalogram	Artificial Neural Network	83.9
[60]/2017	Electroencephalogram	Support Vector Machine	81.2
[61]/2019	Electroencephalogram	Convolutional Neural Network	85.6
Our work	Electroencephalogram	RBF Network Fuzzy Means	96.8

The proposed RBF system has advantages in comparison with the other classification algorithms. Those advantages include: (i) high accuracy close to 97%; (ii) simple network configuration; (iii) fast training procedures; and (iv) potential to be integrated into real-time commercial tools due to its low computational complexity.

6. Conclusions

In this paper, a novel neuronal network model based on radial basis functions employing a fuzzy means algorithm for the classification of bipolar disorder patients is presented. The method proposed in this work achieved the highest values of balanced accuracy, recall, precision, and F_1 score—higher than those achieved with other classical methods, i.e., Bayesian linear discriminant analysis, support vector machines, Gaussian naive Bayes, K-nearest neighbours, or decision trees. This guarantees its reliability for the automatic classification of the pathology treated in this study. Experimental results obtained from real EEG records illustrate the high accuracy of the proposed approach. Therefore, the proposed radial basis function-based neural network can be a complementary tool to help healthcare personnel diagnose brain impairments such as bipolar disorder.

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References

1. Luján, M.Á.; Jimeno, M.V.; Mateo Sotos, J.; Ricarte, J.J.; Borja, A.L. A Survey on EEG Signal Processing Techniques and Machine Learning: Applications to the Neurofeedback of Autobiographical Memory Deficits in Schizophrenia. *Electronics* **2021**, *10*, 3037. [CrossRef]
2. Thompson, P.M.; Jahanshad, N.; Ching, C.; Salminen, L.E.; Thomopoulos, S.I.; Bright, J.; Baune, B.T.; Bertolín, S.; Bralten, J.; Bruin, W.B.; et al. ENIGMA and global neuroscience: A decade of large-scale studies of the brain in health and disease across more than 40 countries. *Transl. Psychiatry* **2020**, *10*, 100. [CrossRef] [PubMed]
3. Hallett, M.; de Haan, W.; Deco, G.; Dengler, R.; Di Iorio, R.; Gallea, C.; Gerloff, C.; Grefkes, C.; Helmich, R.C.; Kringelbach, M.L.; et al. Human brain connectivity: Clinical applications for clinical neurophysiology. *Clin. Neurophysiol.* **2020**, *131*, 1621–1651. [CrossRef]
4. Kruse, A.; Suica, Z.; Taeymans, J.; Schuster-Amft, C. Effect of brain-computer interface training based on non-invasive electroencephalography using motor imagery on functional recovery after stroke-A systematic review and meta-analysis. *BMC Neurol.* **2020**, *20*, 385. [CrossRef]
5. Anderson, I.M.; Haddad, P.M.; Scott, J. Bipolar disorder. *BMJ* **2012**, *345*, e8508. [CrossRef]
6. McCombs, J.S.; Ahn, J.; Tencer, T.; Shi, L. The impact of unrecognized bipolar disorders among patients treated for depression with antidepressants in the fee-for-services California medicaid (medical) program: A 6-year retrospective analysis. *J. Affect. Disord.* **2007**, *97*, 171–179. [CrossRef]
7. Angst, J. The emerging epidemiology of hypomania and bipolar II disorder. *J. Affect. Disord.* **1998**, *50*, 143–151. [CrossRef]
8. Birnbaum, H.; Shi, L.; Dial, E.; Oster, E.; Greenberg, P.; Mallett, D. Economic consequences of not recognizing bipolar disorder patients: A cross-sectional descriptive analysis. *J. Clin. Psychiatry* **2003**, *64*, 1201–1209. [CrossRef]
9. Matza, L.; Rajagopalan, K.; Thompson, C.; de Lissovoy, G. Misdiagnosed patients with bipolar disorder: Comorbidities, treatment patterns, and direct treatment costs. *J. Clin. Psychiatry* **2005**, *66*, 1432–1440. [CrossRef]
10. Angst, F.; Stassen, H.; Clayton, P.; Angst, J. Mortality of patients with mood disorders: Follow-up over 34–38 years. *J. Affect. Disord.* **2002**, *68*, 167–181. [CrossRef]
11. Rihmer, Z.; Kiss, K. Bipolar disorders and suicide risk. *Clin. Appr. Bipol. Disord.* **2002**, *1*, 1–21.
12. Wierdsma, A.; Sytema, S.; van Os, J.; Mulder, C. Case registers in psychiatry: Do they still have a role for research and service monitoring? *Curr. Opin. Psychiatry* **2008**, *21*, 379–384. [CrossRef] [PubMed]
13. Belizario, G.; Junior, R.; Salvini, R.; Lafer, B.; Dias, R. Predominant polarity classification and associated clinical variables in bipolar disorder: A machine learning approach. *J. Affect. Disord.* **2019**, *245*, 279–282. [CrossRef] [PubMed]
14. Alimardani, F.; Cho, J.; Boostani, R.; Hwang, H. Classification of bipolar disorder and schizophrenia using steady-state visual evoked potential based features. *IEEE Access* **2018**, *6*, 40379–40388. [CrossRef]
15. Varone, G.; Boulila, W.; Lo Giudice, M.; Benjdira, B.; Mammone, N.; Ieracitano, C.; Dashtipour, K.; Neri, S.; Gasparini, S.; Morabito, F.C.; et al. A Machine Learning Approach Involving Functional Connectivity Features to Classify Rest-EEG Psychogenic Non-Epileptic Seizures from Healthy Controls. *Sensors* **2022**, *22*, 129. [CrossRef]
16. Ghayab, H.A.; Li, Y.; Siuly, S.; Abdulla, S. Epileptic EEG signal classification using optimum allocation based power spectral density estimation. *IET Signal Process.* **2018**, *12*, 738–747. [CrossRef]
17. Ghasemzadeh, P.; Kalbkhani, H.; Shayesteh, M.G. Sleep stages classification from EEG signal based on stockwell transform. *IET Signal Process.* **2018**, *13*, 242–252. [CrossRef]
18. Bajaj, V.; Rai, K.; Kumar, A.; Sharma, D.; Singh, G.K. Rhythm-based features for classification of focal and non-focal EEG signals. *IET Signal Process.* **2017**, *11*, 743–748. [CrossRef]
19. Yücelbaş, C.; Yücelbaş, S.; Özşen, S.; Tezel, G.; Küçüktürk, S.; Yosunkaya, Ş. A novel system for automatic detection of K-complexes in sleep EEG. *Neural Comput. Appl.* **2018**, *29*, 137–157. [CrossRef]
20. Zhang, Y.; Zhou, G.; Jin, J.; Zhao, Q.; Wang, X.; Cichocki, A. Sparse Bayesian classification of EEG for brain–computer interface. *IEEE Trans. Neural Netw. Learn. Syst.* **2016**, *27*, 2256–2267. [CrossRef]
21. Jie, N.; Zhu, M.; Ma, X.; Osuch, E.; Wammes, M.; Théberg, J.; Li, H.; Li, H.; Zhang, Y.; Jiang, T.; et al. Discriminating bipolar disorder from major depression based on SVM-FoBa: Efficient feature selection with multimodal brain imaging data. *IEEE Trans. Auton. Ment. Dev.* **2015**, *7*, 320–331. [CrossRef]
22. Mwangi, B.; Wu, M.; Bauer, I.; Modi, H.; Zeni, C.; Zunta-Soares, G.; Hasan, K.; Soares, J. Predictive classification of pediatric bipolar disorder using atlas-based diffusion weighted imaging and support vector machines. *Psychiatry Res.* **2015**, *234*, 265–271. [CrossRef] [PubMed]
23. Pan, Z.; Gui, C.; Zhang, J.; Zhu, J.; Cui, D. Detecting manic state of bipolar disorder based on support vector machine and gaussian mixture model using spontaneous speech. *Psychiatry Investig.* **2018**, *15*, 695–700. [CrossRef] [PubMed]
24. Manohar, L.; Ganesan, K. Diagnosis of schizophrenia disorder in MR brain images using multi-objective BPSO based feature selection with fuzzy SVM. *J. Med Biol. Eng.* **2018**, *38*, 917–932. [CrossRef]
25. Lahmiri, S.; Shmuel, A. Accurate classification of seizure and seizure-free intervals of intracranial EEG signals from epileptic patients. *IEEE Trans. Instrum. Meas.* **2019**, *68*, 791–796. [CrossRef]
26. Hu, B.; Li, X.; Sun, S.; Ratcliffe, M. Attention recognition in EEG-based affective learning research using CFS+ KNN algorithm. *IEEE ACM Trans. Comput. Biol. Bioinform.* **2018**, *15*, 38–45. [CrossRef]

27. Prasad, P.D.; Halahalli, H.N.; John, J.P.; Majumdar, K.K. Single-trial EEG classification using logistic regression based on ensemble synchronization. *IEEE J. Biomed. Health Inform.* **2014**, *18*, 1074–1080. [CrossRef]
28. Zeng, H.; Song, A. Optimizing single-trial EEG classification by stationary matrix logistic regression in brain–computer interface. *IEEE Trans. Neural Netw. Learn. Syst.* **2016**, *27*, 2301–2313. [CrossRef] [PubMed]
29. Arribas, J.; Calhoun, V.; Adali, T. Automatic Bayesian classification of healthy controls, bipolar disorder, and schizophrenia using intrinsic connectivity maps from FMRI data. *IEEE Trans. Bio-Med. Eng.* **2010**, *57*, 2850–2860. [CrossRef]
30. Esfahani, M.S.; Dougherty, E.R. Incorporation of biological pathway knowledge in the construction of priors for optimal Bayesian classification. *IEEE/ACM Trans. Comput. Biol. Bioinform.* **2014**, *11*, 202–218. [CrossRef]
31. Geethanjali, A.S.P. DWT based detection of epileptic seizure from EEG signals using Naive Bayes and k-NN classifiers. *IEEE Access* **2016**, *4*, 7716–7727.
32. Rabcan, J.; Levashenko, V.; Zaitseva, E.; Kvassay, M.; Subbotin, S. Application of fuzzy decision tree for signal classification. *IEEE Trans. Ind. Inform.* **2019**, *15*, 5425–5434. [CrossRef]
33. Zhang, Z.; Song, Y.; Cui, H.; Wu, J.; Schwartz, F.; Qi, H. Topological analysis and gaussian decision tree: Effective representation and classification of biosignals of small sample size. *IEEE Trans. Biomed. Eng.* **2017**, *64*, 2288–2299. [CrossRef] [PubMed]
34. Saucedo, J.A.M.; Hemanth, J.D.; Kose, U. Prediction of electroencephalogram time series with electro-search optimization algorithm trained adaptive neuro-fuzzy inference system. *IEEE Access* **2019**, *7*, 15832–15844. [CrossRef]
35. Ubeyli, E.D. Adaptive neuro-fuzzy inference systems for automatic detection of breast cancer. *J. Med. Syst.* **2009**, *33*, 353–358. [CrossRef] [PubMed]
36. Muñoz, L.; Villarreal, V.; Nielsen, M.; Caballero, Y.; Sittón-Candanedo, I.; Corchado, J.M. Artificial Intelligence Models and Techniques Applied to COVID-19: A Review. *Electronics* **2021**, *10*, 2901. [CrossRef]
37. Maglogiannis, I.; Sarimveis, H.; Kiranoudis, C.T.; Chatziioannou, A.A.; Oikonomou, N.; Aidinis, V. Radial basis function neural networks classification for the recognition of idiopathic pulmonary fibrosis in microscopic images. *IEEE Trans. Inf. Technol. Biomed.* **2008**, *12*, 42–54. [CrossRef]
38. Andreou, A.; Mavromoustakis, C.X.; Mastorakis, G.; Batalla, J.M.; Pallis, E. Evaluation of the COVID-19 Era by Using Machine Learning and Interpretation of Confidential Dataset. *Electronics* **2021**, *10*, 2910. [CrossRef]
39. Alsharif, R.; Al-Issa, Y.; Alqudah, A.M.; Qasmieh, I.A.; Mustafa, W.A.; Alquran, H. PneumoniaNet: Automated Detection and Classification of Pediatric Pneumonia Using Chest X-ray Images and CNN Approach. *Electronics* **2021**, *10*, 2949. [CrossRef]
40. Jiang, C.; Li, Y. Health big data classification using improved radial basis function neural network and nearest neighbor propagation algorithm. *IEEE Access* **2019**, *7*, 176782–176789. [CrossRef]
41. Rizaner, F.B.; Rizaner, A. Approximate solutions of initial value problems for ordinary differential equations using radial basis function networks. *Neural Process. Lett.* **2018**, *48*, 1063–1071. [CrossRef]
42. Lee, H.; Choi, J.; Kim, S.; Jun, S.C.; Lee, B. A Compressive Sensing-Based Automatic Sleep-Stage Classification System with Radial Basis Function Neural Network. *IEEE Access* **2019**, *7*, 186499–186509. [CrossRef]
43. Han, J.; Pei, J.; Kamber, M. *Data Mining: Concepts and Techniques*; Elsevier: Amsterdam, The Netherlands, 2011.
44. Khosrow-Pour, D.B.A. *Advanced Methodologies and Technologies in Network Architecture, Mobile Computing, and Data Analytics*; IGI Global: Hershey, PA, USA, 2018.
45. Nunez, P.L.; Srinivasan, R. *Electric Fields of the Brain: The Neurophysics of EEG*; Oxford University Press: New York, NY, USA, 2006.
46. Mateo, J.; Torres, A.M.; García, M.A.; Santos, J.L. Noise removal in electroencephalogram signals using an artificial neural network based on the simultaneous perturbation method. *Neural Comput. Appl.* **2016**, *27*, 1941–1957. [CrossRef]
47. Sörnmo, L.; Laguna, P. *Bioelectrical Signal Processing in Cardiac and Neurological Applications*; Elsevier Academic Press: Cambridge, MA, USA, 2005.
48. Perrin, F.; Pernier, J.; Bertrand, O.; Echallier, J. Spherical splines for scalp potential and current density mapping. *Electroencephalogr. Clin. Neurophysiol.* **1989**, *72*, 184–187. [CrossRef]
49. Zhou, X.; Obuchowski, N.A.; McClish, D.K. *Statistical Methods in Diagnostic Medicine*, 2nd ed.; John Wiley and Sons: Hoboken, NJ, USA, 2011.
50. *MATLAB Toolbox (MATLAB 2021a)*; The Mathworks Inc.: Natick, MA, USA, 2021.
51. Fawcett, T. An introduction to ROC analysis. *Pattern Recognit. Lett.* **2006**, *27*, 861–874. [CrossRef]
52. Kosmala, W.A.J. *A Friendly Introduction to Analysis*; Pearson Prentice Hall: Hoboken, NJ, USA, 2004.
53. Nielsen, M.; Chuang, I. *Quantum Computation and Quantum Information*, 10th ed.; Cambridge University Press: Cambridge, UK, 2011.
54. Safont, G.; Salazar, A.; Vergara, L. Multiclass alpha integration of scores from multiple classifiers. *Neural Comput.* **2019**, *31*, 806–825. [CrossRef]
55. Khodayari-Rostamabad, A.; Reilly, J.P.; Hasey, G.; de Bruin, H.; MacCrimmon, D. Diagnosis of Psychiatric Disorders Using EEG Data and Employing a Statistical Decision Model. In Proceedings of the 2010 Annual International Conference of the IEEE Engineering in Medicine and Biology, Buenos Aires, Argentina, 31 August–4 September 2010; pp. 4006–4009.
56. Johannesen, J.K.; O'Donnell, B.F.; Shekhar, A.; McGrew, J.H.; Hetrick, W.P. Diagnostic specificity of neurophysiological endophenotypes in schizophrenia and bipolar disorder. *Schizophr. Bull.* **2013**, *39*, 1219–1229. [CrossRef]
57. Erguzel, T.T.; Tas, C.; Cebi, M. A wrapper-based approach for feature selection and classification of major depressive disorder–bipolar disorders. *Comput. Biol. Med.* **2015**, *64*, 127–137. [CrossRef]

58. Khaleghi, A.; Sheikhani, A.; Mohammadi, M.R.; Nasrabadi, A.M.; Vand, S.R.; Zarafshan, H.; Moeini, M. EEG classification of adolescents with type i and type II of bipolar disorder. *Australas. Phys. Eng. Sci. Med.* **2015**, *38*, 551–559. [CrossRef] [PubMed]
59. Erguzel, T.T.; Sayar, G.H.; Tarhan, N. Artificial intelligence approach to classify unipolar and bipolar depressive disorders. *Neural Comput. Appl.* **2016**, *27*, 1607–1616. [CrossRef]
60. Liao, S.C.; Wu, C.T.; Huang, H.C.; Cheng, W.T. Major depression detection from EEG signals using kernel eigen-filter-bank common spatial patterns. *Sensors* **2017**, *17*, 1385. [CrossRef] [PubMed]
61. Li, X.; La, R.; Wang, Y.; Niu, J.; Zeng, S.; Sun, S.; Zhu, J. EEG-based mild depression recognition using convolutional neural network. *Med. Biol. Eng. Comput.* **2019**, *57*, 1341–1352. [CrossRef] [PubMed]