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## Research article

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# Predicting Prognostic Effects of Acupuncture for Depression Using Electroencephalogram<sup>\*</sup>

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## ABSTRACT

**Background:** Depression is considered to be a major public health problem with significant implications for individuals and society. Patients with depression can be with complementary therapies such as acupuncture. Predicting the prognostic effects of acupuncture has a big significance of helping physicians to take early interventions for patients with depression and avoid malignant events.

**Methods:** In this work, a novel framework of predicting prognostic effects of acupuncture for depression based on electroencephalogram (EEG) recordings is presented. Specifically, EEG, as a widely used measurement to evaluate therapeutic effects of acupuncture, is utilized for predicting prognostic effects of acupuncture. Max-relevance and min-redundancy (mRMR), with merits of removing redundant information among selected features and remaining high relevance between selected features and response variable, is employed to select important lead-rhythm features extracted from EEG recordings. Then, according to the subjects' HAMD scores before and after acupuncture for 8 weeks, the reduction rate of HAMD score is calculated as a measure of the prognostic effects of acupuncture. Finally, five widely used machine learning methods are utilized for building the predicting models of prognostic effects of acupuncture for depression.

**Results:** Experimental results show that non-linear machine learning methods have better performance than linear ones on predicting prognostic effects of acupuncture using EEG recordings. Especially, the support vector machine with Gaussian kernel (SVM-RBF) can achieve the best and stable performance using the mRMR with both evaluating criteria of FCD and FCQ for feature selection. Both mRMR-FCD and mRMR-FCQ obtain the same best performance, where the accuracy and F1 score are 84.61 % and 86.67 %, respectively. What's more, lead-rhythm features selected by mRMR-FCD and mRMR-FCQ are analyzed. Top seven selected lead-rhythm features have much higher mRMR evaluating scores, which guarantee the good predicting performance for machine learning methods to some degree.

**Conclusion:** The presented framework in this work is effective in predicting prognostic effects of acupuncture for depression. It can be integrated into an intelligent medical system and provide the information of prognostic effects of acupuncture for physicians. Informed prognostic effects of acupuncture for depression in advance and taking interventions can greatly reduce the risk of malignant events for patients with mental disorders.

## 1. Introduction

Depression is one of the most common mental disorders, characterized by a persistent low mood, loss of interest or reduced energy. The person suffered from depression has serious impact on her/his study, work and social life. In a worst case, depression can cause the affected person to self-harm or even committing suicide when she/he is under long-lasting moderate or severe intensity [20]. According to the World Health Organization (WHO)'s report, over 264 million of persons in all ages suffer from depression [21].

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What's more, among of them, close to 800,000 persons are unnatural death due to suicide every year and the number of the suicide cohort is still increasing [15]. Depression becomes the world's second leading disease, imposing a heavy social and ethic burden on individuals, families, communities and countries.

Treatment of depression and control of the clinical symptoms are mainly depended on the antidepressants, which are currently the drugs used to various types of depression [18]. However, there are still many disadvantages of antidepressants, such as many side effects [4], drug dependence [8], poor compliance [33], high cost and single therapeutic target [27], which limit their clinical applications. In recent years, studies [34, 26, 10] have shown that acupuncture has a good clinical efficacy in the treatment of depression, with no side effects or adverse reactions. Acupuncture has been utilized by traditional Chinese medicine (TCM) to treat ailments and disorders more than 2000 years, however, the mechanism of acupuncture treatment is still controversial and there is still no objective evidence for the evaluation of its therapeutic

tic effects [5, 7]. The therapeutic effects of acupuncture are closely related to the selected acupoints and the techniques used. Generally, the acupuncture stimulates pain receptors around acupoints on the skin, it produces many reactions in various systems of body, especially in the nervous system [5]. Therefore, the therapeutic effects of acupuncture can be responded from central nervous system which is integrated in the brain.

Electroencephalogram (EEG) is a common tool to capture the changes of electrical activity caused by acupuncture [35]. Specifically, in the central nervous system of the human brain, there are many neurons. And those neurons will continuously produce potential changes. Through an EEG equipment, EEG signals can be acquired by recording the electrical activity of aforementioned neurons from the scalp [25]. Many researchers attempted to utilize EEG recordings to identifying depression [6, 31, 13, 1]. Hansu Cai et al. [6] presented a case-based reasoning model for identifying depression with three-electrode EEG signals. Axel Steiger et al. [31] analyzed EEG characteristics from an individual during wake and sleep phase, and provided a series of biomarkers to screen depression. Behshad Hosseinfard et al. [13] investigated a nonlinear analysis method for EEG signal to identify depression patients and normal individuals. U. Rajendra Acharya et al. [1] employed a state-of-the-art convolutional neural network (CNN) to screen patients with depression based on EEG signals. Meanwhile, researchers also utilized EEG signals to evaluate therapeutic effects of depression [19, 28]. Noemi Papp et al. [19] investigated the brain oscillations in the gamma frequency band of EEG signals, and evaluated the therapeutic effects with selective serotonin reuptake inhibitors (SSRIs) for depression. Shabah Mohammad Shadli et al. [28] studied the effects of ketamine on the EEG of patients with treatment-resistant generalized anxiety and social anxiety disorders. Since EEG has different signal morphological patterns on patients with depression or not [29, 2], it is shown from experiment and analysis results that all of aforementioned studies achieved a well performance using EEG recordings on screening patients with depression and evaluating therapeutic effectiveness of antidepressants. Therefore, EEG can be also utilized to evaluate the prognostic effects of acupuncture, which enables physicians to understand the prognosis and health conditions of patients in advance.

In this paper, we proposed a framework based on EEG recordings with machine learning methods for predicting prognostic effectiveness of acupuncture for depression. Specifically, lead-rhythm features extracted from EEG recordings are selected by max-relevance and min-redundancy (mRMR) with both evaluating criteria of FCD and FCQ. Then, according to the subjects' HAMD scores before and after acupuncture for 8 weeks, the reduction rate of HAMD score is calculated as a measure of the prognostic effects of acupuncture. Finally, popular machine learning methods of logistic regression (LR), random forest (RF), and support vector machine with linear kernel (SVM-Linear), poly kernel (SVM-Poly), and Gaussian kernel (SVM-RBF) are employed to build

8-week predicting models of prognostic effectiveness of acupuncture for depression. With the help of the predicting model of prognostic effects of acupuncture, physicians can learn about their patients' mental conditions in advance and take necessary interventions to reduce the risk of malignant events.

The main contributions of this paper are concluded as follows:

- We present a novel framework of predicting prognostic effectiveness of acupuncture for depression with EEG recordings.
- The mRMR with the advantages of removing redundant features and keeping maximum relevance with response variable is utilized to select important lead-rhythm features. Meanwhile, the reduction rate of HAMD score as a measure of prognostic effects of acupuncture is employed to produce the class labels with a threshold value of 0.5.
- Widely used machine learning methods of LR, RF, SVM-Linear, SVM-Poly and SVM-RBF are employed to built the 8-week predicting model of prognostic effects of acupuncture for depression.
- Experiment results show that the proposed framework with non-linear machine methods of RF, SVM-Poly, and SVM-RBF outperform that with linear machine learning methods of LR and SVM-Linear. Especially, the SVM-RBF performs the best and robust, where the best accuracy and  $F1$  score identically for both mRMR-FCD and mRMR-FCQ are 84.61 % and 86.67 %. Furthermore, selected lead-rhythm features from mRMR-FCD and mRMR-FCQ are analyzed for clinical functions related to depression.

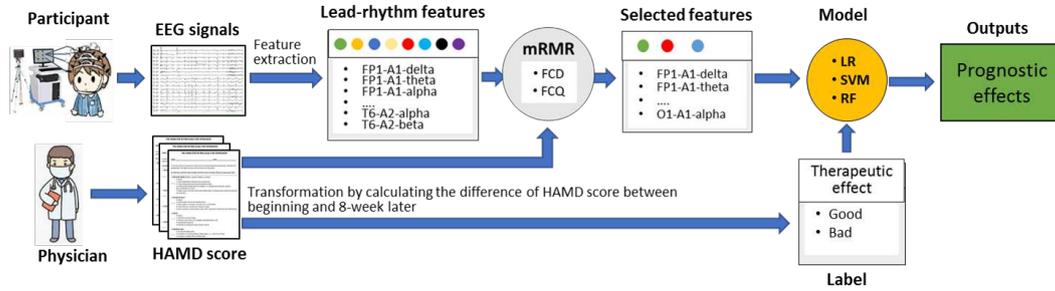
The rest of this paper are organized as follows: Section 2 introduce the criteria of recruited participants, feature selection, machine learning methods, and evaluation metrics. Section 3 demonstrates the experimental results. The selected lead-rhythm features are discussed in Section 4. Finally, conclusion is summarized in Section 5.

## 2. Methods and materials

Figure 1 shows the proposed predicting framework of prognostic effects of acupuncture for depression. It mainly consists of EEG recording acquisition, feature selection with the mRMR [30, 23], and predicting models built by widely used machine learning methods. The details are described as following:

### 2.1. Participants

Subjects with depression who were admitted to Shenzhen traditional Chinese medicine hospital for inclusion criteria were collected. This study was approved by the Ethics Committee of the Shenzhen Traditional Chinese Medicine Hospital with the IRB Number of 2017-8. All the patients signed informed consent and voluntarily participated in this clinical study.



**Figure 1:** Overview of predicting framework of prognostic effects of acupuncture for depression with EEG recordings

### 2.1.1. Inclusion criteria

For recruited participants, there are three inclusion criteria:

- Participants meet the western medical diagnostic criteria for digression, which requests the course of disorder is greater than or equal to two weeks.
- Participants who are conscious, have no aphasia or intellectual disorder, have certain ability of expression, and cooperate with the treatment.
- Participants of male or female are over 18 years old or under 65 years old.

### 2.1.2. Exclusion criteria

Meanwhile, to guarantee the study analysis, we defined five exclusion criteria based on clinical practice.

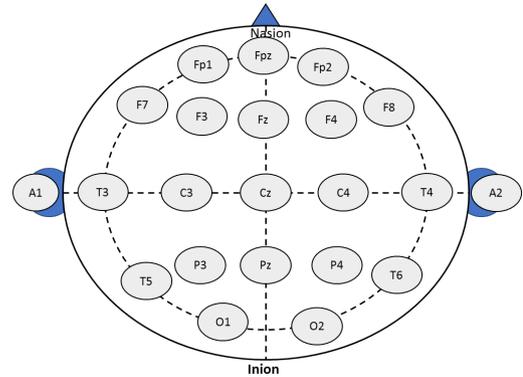
- Schizophrenia, and organic diseases and physical diseases that cause the symptoms of the disease.
- Participants with the age of under 18 or the age of over 65.
- Pregnant women.
- Participants with severe liver and kidney function, cardiovascular and cerebrovascular diseases, and hematopoietic system diseases.
- Participants who do not cooperate with acupuncture treatment and have poor drug compliance

### 2.1.3. Intervention with acupuncture

In this study, physicians employ acupuncture for depression treatment with the technique of transferring and regulating acupuncture [24], which is proposed by our research team. Five times a week, four weeks a course of treatment, a total of 2 courses of acupuncture treatment.

### 2.1.4. Depression assessment

The 17-item Hamilton depression scale (HAMD) [3] is the most widely used scale for depression assessment at present. It has good reliability and validity, and can reflect the changes of depression symptoms in a relatively sensitive manner. It is one of the best assessment tools in therapeutic research, and can better reflect the severity of depression. Therefore, we utilize HAMD-17 score to assess the prognostic effects of acupuncture for depression.



**Figure 2:** International "10-20" system, which describes the location of scalp electrodes of EEG signals.

## 2.2. EEG recordings acquisition

Nerron-spectrum-5 EEG device<sup>1</sup> manufactured by Neurosoft Ltd, Russia is used to collect EEG recordings from patients with depression syndrome. The room temperature is controlled at 18–25°C. Scalp electrodes are placed in accordance with the international 10/20 system electrode placement method (Figure 2), and bilateral ear lobes are used as the reference electrodes to record 19 conductive EEG signals. EEG was collected under the condition of quiet eye closure and relaxation. Steady EEG signals are collected before acupuncture.

## 2.3. Features

### 2.3.1. Feature description

Figure 2 shows the distribution of scalp electrodes of EEG signals. In this study, EEG recordings we collected consist of 19-lead signals, which are presented as FP1-A1, FP2-A2, F3-A1, F4-A2, FZ-A2, C3-A1, C4-A2, CZ-A1, P3-A1, P4-A2, PZ-A2, O1-A1, O2-A2, F7-A1, F8-A2, T3-A1, T4-A2, T5-A1, and T6-A2. Take FP1-A1 for example, it means the lead signal acquired from scalp electrodes of FP1 and A1. Four rhythm features (signal amplitude) of delta ( $\delta$ ), theta ( $\theta$ ), alpha ( $\alpha$ ), and beta ( $\beta$ ) are extracted by the embedded digital EEG system in Nerron-spectrum-5 EEG device. In this case, there are total of 76 lead-rhythm features for subsequent processing. The lead-rhythm features

<sup>1</sup> <https://www.medicaexpo.com/prod/neurosoft/product-69506-454186.html>

can be presented in the form of "(lead) - (rhythm)". For example, the four rhythm indexes of lead FP1-A1 can be described as FP1-A1-delta, FP1-A1-theta, FP1-A1-alpha, and FP1-A1-beta, respectively.

### 2.3.2. Prognostic effects evaluation

In this study, HAMD-17 rating scale (HRS) is utilized to assess depression conditions for each subject before acupuncture and acupuncture for eight weeks. To assess the prognostic effects of acupuncture for depression, the reduction rate  $R_{HRS}$  of HAMD scores with the difference of HAMD scores of two times on each subject is used to evaluate the prognostic therapeutic effects, which is defined as follows:

$$R_{HRS} = \frac{DScore_{pre} - DScore_{pos}}{DScore_{pre}} \quad (1)$$

where  $DScore_{pre}$  refers to the HAMD score before acupuncture and  $DScore_{pos}$  refers to the HAMD score of acupuncture for eight weeks. Here, to simplify the problem of predicting prognostic effects, the reduction rate of HAMD scores is mapped into binary values 0 and 1. If the  $R_{HRS}$  is greater than 0.5, the class label  $y$  of the prognostic effect is define to be 1, which means good prognostic effects. Otherwise, the  $y$  is define to be 0, which means bad prognostic effects.

### 2.3.3. Feature selection and normalization

Feature selection is a very important procedure before building a predicting model of prognostic effects of acupuncture for depression when the sample size is not more than the number of features. The mRMR [23], as one of the popular feature selection methods, is with the advantages of removing redundancy information among selected features and keeping high relevance between selected features and response variable. The relevance and redundancy information of mRMR can be measured by mutual information for category data features and class labels. For continuous data features and category labels, the relevance information is measured by F-statistic and Pearson correlation coefficients. In this study, the lead-rhythm features are continuous variables and class label of prognostic effects are binary category variable. Therefore, the mRMR in this study employs F-statistic and Pearson coefficients to measure the relevance and redundancy information among selected lead-rhythm features and class labels.

Generally, given two random vectors  $x$  and  $y$  with continuous values, the Pearson correlation coefficients  $P(f_i, f_j)$  can be defined to be:

$$P(f_i, f_j) = \frac{E(f_i f_j) - E(f_i)E(f_j)}{\sqrt{E(f_i^2) - E^2(f_i)}\sqrt{E(f_j^2) - E^2(f_j)}} \quad (2)$$

where  $f_i$  and  $f_j$  are one of features in selected lead-rhythm feature set. Therefore, minimum-redundancy information ( $MRed$ ) of selected lead-rhythm features  $S$  can be defined

as:

$$MRed(S) = \min \frac{1}{\|S\|^2} \sum_{f_i, f_j \in S} |P(f_i, f_j)| \quad (3)$$

To obtain maximum-relevance information  $MRel$  between selected features  $S$  and class label vector  $y$ , it can be defined as:

$$MRel(S, y) = \max \frac{1}{\|S\|} \sum_{f_i \in S} F(f_i, y) \quad (4)$$

where  $F$  is the F-statics, which can be defined as follows:

$$F(f_i, y) = \frac{(n - K) \sum_k n_k (\overline{m_{ik}} - \overline{m_i})^2}{(K - 1) \sum_k \sigma_k^2} \quad (5)$$

where  $m_{ik}$  is mean value of the  $i$ -th selected feature within the  $k$ -th class ( $k = 1, \dots, K$ ).  $m_i$  is the mean value across all entries in the  $i$ -th selected feature.  $\sigma_k$  is the variance of the  $k$ -th selected features across all data entries.  $n$  is the size of the whole data entries and  $n_k$  is the size of the data entries in the  $k$ -th class.  $K$  is the number of class labels. There are two ways to obtain maximum-relevance minimum-redundancy information, namely mRMR evaluating score, with F-test correlation difference ( $FCD$ ) and the F-test correlation quotient ( $FCQ$ ), which can be defined by equations of (6) and (7), respectively.

$$FCD = MRel(S, y) - MRed(S) \quad (6)$$

$$FCQ = MRel(S, y) \setminus MRed(S) \quad (7)$$

Due to a large of variation in terms of amplitudes among lead-rhythm selected features, it is necessary to utilize a normalization technique to map the selected features into a uniform range. In this study, the Min-Max normalization technique with the range from 0 to 1 is employed, which is defined as follows:

$$Norm(f_i) = \frac{f_i - f_{min}}{f_{max} - f_{min}} \quad (8)$$

where  $f_i$  is the  $i$ -th selected lead-rhythm feature. The  $f_{max}$  refers to the maximum value of the  $f_i$  and the  $f_{min}$  refers to the minimum value of the  $f_i$ .

## 2.4. Machine learning methods

In this study, popular machine learning methods of logistic regression, random forest, and support vector machine are utilized to build predicting model of prognostic effects of acupuncture for depression based on EEG recordings. The details are described as follows:

### 2.4.1. Logistic regression

Logistic regression (LR) is a classification method, which utilizes the Sigmoid function as a posterior probability distribution to classify the input data [22]. The LR can be used for both binary and multiple classification problems. On the other hand, the LR is easy to be implemented and can be applied to both distributed and real-time application scenarios. For a binary logistic regression model used in this study, mathematically, given input data  $x = \{x_1, x_2, \dots, x_n\}$ ,  $x_i \in R^m$  and binary class labels  $y = \{y_1, y_2, \dots, y_n\}$ ,  $y_i \in \{0, 1\}$ , the LR model can be defined by

$$\log \frac{\Pr(y_i = 1|x_i)}{1 - \Pr(y_i = 1|x_i)} = \beta_0 + \beta^T \cdot x_i \quad (9)$$

where  $\beta_0$  and  $\beta$  are the coefficients of the LR model.  $\Pr(y_i = 1|x_i)$  is the posterior possibility that the acupuncture operation achieves good prognostic effects for depression with the given lead-rhythm features  $x_i$ . Solving for  $p$  in equation (9), this gives

$$\Pr(y_i = 1|x_i) = \frac{1}{1 + \exp(-(\beta_0 + \beta^T \cdot x_i))} \quad (10)$$

In this study, we utilize the default threshold value of 0.5 to classify good and bad prognostic effects of acupuncture. Specifically, if  $\Pr(\cdot)$  is more than the threshold value of 0.5, the prognostic effect should be predicted to be  $y = 1$  (namely, good prognostic effect), otherwise,  $y = 0$  (namely, bad prognostic effect).

### 2.4.2. Random forest

Random forest (RF), as shown in Figure 3, is an ensemble classifier that contains multiple decision trees [16]. It is widely used for variant classification tasks and achieves quite well performance. Specifically, given a training dataset  $D$  with sample size  $N$ , the RF employs the bootstrap resampling technique to repeatedly extract  $k$  ( $k < N$ ) samples from the original training dataset. The extracted datasets is as the new training datasets for decision trees. If the dimension of each sample is  $M$ , specify a constant  $m$  ( $m \ll M$ ) and randomly select  $m$  feature subsets from  $M$  features. In this study, we employ the model of CART as the base decision tree model [17], which uses minimum criterion of gini index for optimal feature selection. The gini index is defined to be:

$$gini(D) = 1 - \sum_{i=1}^L \left( \frac{|C_i|}{|D|} \right)^2 \quad (11)$$

where  $C_i$  is the data subset belonged to the  $i$ -th group,  $L$  is the number of classes. Herewith, for specified feature  $F$ , we have the gini index of training dataset on the specific splitted feature  $F$ :

$$gini(D, F) = \sum_{i=1}^L \frac{|D_i|}{|D|} gini(D_i) \quad (12)$$

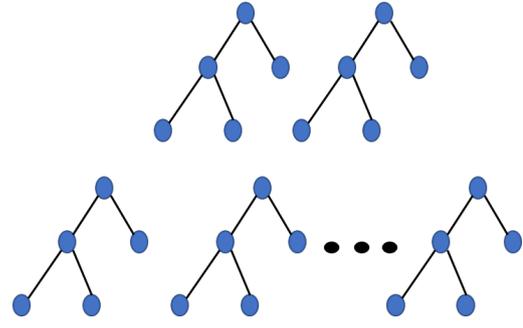


Figure 3: Schematic diagram of a random forest.

where  $D_i$  refers to the training data subset, which is splitted according to a threshold value of the specific feature. Train the base decision trees based on the new generated training data subsets, and the major voting method is utilized for all the base decision tree models to make final prediction.

### 2.4.3. Support vector machine

Support vector machine (SVM) is a binary classification model, which searches a hyperplane with the largest support vector margin in an affine high-dimensional feature space with kernel techniques [9]. Given a training dataset

$$D = \{(x_1, y_1), (x_2, y_2), \dots, (x_n, y_n)\}, y_i \in \{0, 1\}$$

, the SVM aims to search a separate hyperplane in terms of training dataset  $D$  to classify samples into their class groups as many as possible. In the affine feature space, the hyperplane can be defined as a linear equation:

$$w^T \cdot x + b = 0 \quad (13)$$

where  $w$  is the normal vector of the separate hyperplane, which determines the hyperplane's direction.  $b$  is the intercept, which determines the distance between the origin point and the hyperplane. Obviously, the separate hyperplane can be determined by normal vector  $w$  and intercept  $b$ . Mathematically, suppose the separate hyperplane is able to classify the training samples into their correct groups, namely, for a sample  $(x_i, y_i) \in D$ , we have

$$\begin{cases} w^T \cdot x_i + b \geq +1, & y_i = +1 \\ w^T \cdot x_i + b \leq -1, & y_i = -1. \end{cases} \quad (14)$$

where  $y_i = +1$  refers to good prognostic effect, and  $y_i = -1$  refers to bad prognostic effect. Hence, subject to the constraints of equation (14), the objective of the SVM is trying to find a largest margin of points in the support vector from two different classes, which is defined as follows.

$$\begin{aligned} & \max_{w, b} \frac{2}{\|w\|^2} \\ & \text{s.t. } y_i \cdot (w^T x_i + b) \geq 1, \quad i = 1, 2, \dots, n. \end{aligned} \quad (15)$$

**Table 1**  
Confusion matrix of four metrics for classification performance

Confusion matrix		Truth	
		Positive	Negative
Prediction	Positive	$TP$	$FP$
	Negative	$FN$	$TN$

where  $\frac{2}{\|w\|^2}$  is the margin between two support vectors,  $n$  refers to the size of training dataset. Furthermore, to map original data features to higher feature dimensions, totally three kinds of different kernels of linear, poly, and Gaussian are utilized for predicting prognostic effects in this paper, which are called SVM-Linear, SVM-Poly, and SVM-RBF in short, respectively.

### 2.5. Performance metrics

In this paper, four classification performance metrics of precision ( $Pre$ ), recall ( $Rec$ ), accuracy ( $Acc$ ), and  $F1$  score are employed to evaluate the predicting models of prognostic effects of acupuncture. As shown in Table 1,  $TP$  means the number of subjects with good prognostic effects predicted to be ones with good prognostic effects.  $FP$  means the number of subjects with bad prognostic effects predicted to be ones with good prognostic effects.  $FN$  means the number of subjects with good prognostic effects predicted to be ones with bad prognostic effects.  $TN$  means the number of subjects with bad prognostic effects predicted to be ones with bad prognostic effects. Therefore, aforementioned performance metrics can be defined to be:

$$\begin{aligned}
 Pre &= \frac{TP}{TP + FP} \\
 Rec &= \frac{TP}{TP + FN} \\
 Acc &= \frac{TP + TN}{TP + TN + FP + FN} \\
 F1 &= \frac{2 \cdot Pre \cdot Rec}{Pre + Rec}
 \end{aligned} \tag{16}$$

## 3. Results

### 3.1. Computing environment

All experiments are conducted on a computing server equipped with a 20-core Intel Xeon E2660 v2 processor and 252 GByte memory. Regarding the three machine learning methods, they run on machine learning platform of SKlearn V0.23.1, which is deployed in the CentOS 6.5 operation system.

### 3.2. Data source

In this paper, 92 subjects (age:  $37.58 \pm 10.99$  years, gender: 31 male and 61 female) satisfied inclusion criteria are recruited from Shenzhen Traditional Chinese Medicine Hospital to collect EEG data and HAMD scores. A physician of Shenzhen Traditional Chinese Medicine Hospital takes

charge of these data collection lasting almost one year from October, 2018 to May, 2019. Especially for HAMD scores collected, each subject have to be inquired with the HRS form two times. The first HAMD score is obtained before the acupuncture, the second one is obtained by a follow-up way after acupuncture for 8 weeks. However, most of recruited subjects are lost contacts or don't want to go to hospital to complete the test, only 26 subjects with completed EEG recordings and two times HAMD scores are remained. In other words, there are 26 observations we use to build the predicting model of prognostic effects of acupuncture in this paper.

### 3.3. Classification performance

In this section, leave-one-out cross validation is utilized to evaluate the classification performance of the predicting models of prognostic effect of acupuncture for depression. Specifically, only one observation is left at a time as the test dataset, and the remained observations as the training dataset are used for training predicting model of prognostic effect. Given the size of dataset is  $N$ , the predicting model of prognostic effect is needed to train  $N$  times and test  $N$  times. However, the classification performance of prognostic effects of acupuncture is calculated according to the accumulated test results from each validation test.

To train the predicting models of prognostic effects of acupuncture, five popular machine learning methods of LR, RF, SVM-Linear, SVM-Poly, and SVM-RBF are implemented with important hyper parameters listed in Table 2. Specifically, for the LR model, there are three hyper parameters of tolerance, solver, and iterated epochs. In order to obtain the best classification performance of LR model, tolerance is set to be  $1e^{-4}$  and the iterated epochs are to be 100. To overcome the small size problem, we utilize 'newton-cg' as the solver of the LR model. For the RF model, hyper parameters of number of estimators, split criterion, and number of features to train are important for its classification performance. In this study, they are set to be 100, 'gini', and 'sqrt', respectively. Regarding the SVM model, three respective kernels are employed to train a predicting model of prognostic effects of acupuncture. These three kernels are linear kernel, poly kernel, and Gaussian kernel. Excluding different kernels of the SVM-Linear, SVM-Poly, and SVM-RBF model, there are also some specified hyper parameters for each predicting model. For example, the SVM-Poly has the hyper parameter of degree to be set, which determines the order of the poly kernel. Here, we set the degree to be 3. For the SVM-RBF, it has a hyper parameter of gamma to be set. The gamma is mainly used to map the height of low-dimensional samples. The higher the gamma is, the higher the mapped dimension is. In this study, the gamma is set to be 'scale', which is defined as follows:

$$gamma = \frac{1}{N_{fea}\sigma} \tag{17}$$

where  $N_{fea}$  is the number of features,  $\sigma$  is variance of the training data.

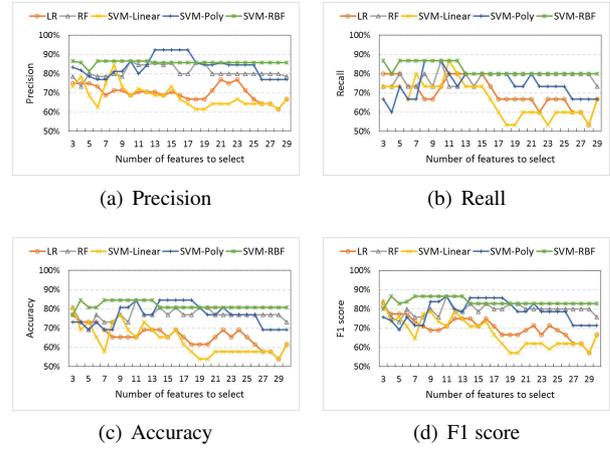
**Table 2**  
Hyper parameters configuration of machine learning methods

Methods	Optimized hyper parameters settings
LR	tolerance: $1e^{-4}$ ; solver:'newton-cg'; iterated epochs:100.
RF	no. of estimators:100; criterion='gini'; max features:'sqrt'.
SVM-Linear	kernel:'linear'; tolerance: $1e^{-3}$ .
SVM-Poly	kernel:'poly'; tolerance: $1e^{-3}$ ; degree: 3.
SVM-RBF	kernel:'rbf'; tolerance: $1e^{-3}$ ; gamma: 'scale'.

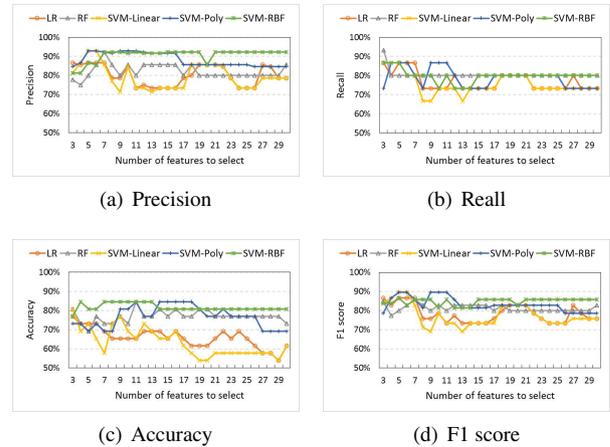
It is noted that the number of features to select is critical to the predicting models of prognostic effects of acupuncture. However, there does not exist a criteria to determine the number of selected features in the mRMR itself. Therefore, the number of selected features is determined by a wrapper technique with the predicting models. First of all, concerning sample size of training dataset, the number of selected features of the mRMR ranges from 3 to 30 in this work. Then, the selected lead-rhythm features are ranked in descending order according to the scores of mRMR. Finally, prognostic effect models of acupuncture are built with the machine learning methods of LR, RF, SVM-Linear, SVM-Poly, and SVM-RBF. As shown in Figure 4 and 5, classification performance of precision, recall, accuracy and F1 score vary a lot with the number of features to select using the mRMR of FCD and FCQ. Obviously, non-linear models of RF, SVM-Poly, and SVM-RBF are better than linear models of LR and SVM-Linear in predicting prognostic effects of acupuncture regardless of whether mRMR-FCD or mRMR-FCQ uses. What's more, among those non-linear models, the SVM-RBF can achieve better and stable classification performance. Specifically, the SVM-RBF can obtain its best performance with mRMR-FCD and mRMR-FCQ. For the mRMR-FCD, they are 86.66 % of precision, 86.66 % of recall, 84.61 % of accuracy, and 86.67 % of F1 score. Regarding the mRMR-FCQ, they are 92.30 % of precision, 86.66 % of recall, 84.61 %, and 86.67 % of F1 score. There dose not exist obvious difference of classification performance of the SVM-RBF with mRMR-FCD and mRMR-FCQ.

#### 4. Discussion

Figure 4 and 5 show that the SVM-RBF can achieve quite well classification performance when the number of features to select is 7 in both mRMR-FCD and mRMR-FCQ. As shown in Figure 6, most of lead-rhythm features with high mRMR scores, which are calculated by equation (6) and (7), are in the top 7. In terms of the mRMR-FCD, the top 7 features to select are 'CZ-A1-theta', 'F4-A2-theta', 'F3-A1-theta', 'C4-A2-theta', 'F3-A1-delta', 'FP2-A2-theta', and 'CZ-A1-delta'. For the mRMR-FCQ, the top 7 features to select are 'F7-A1-beta', 'CZ-A1-theta', 'T3-A1-alpha', 'FZ-A2-beta', 'F4-A2-theta', 'O1-A1-delta', and 'O1-A1-theta'. Among top 7 features to select, the lead-rhythm features of 'CZ-A1-theta' and 'F4-A2-theta' are selected by both mRMR-FCD and mRMR-

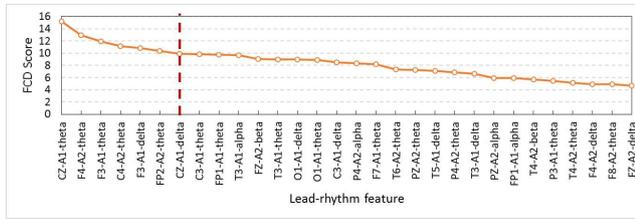


**Figure 4:** Classification performance of machine learning methods with the number of features to select using mRMR of FCD.

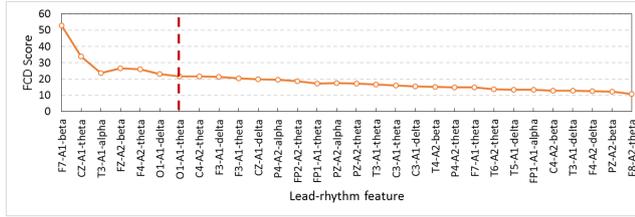


**Figure 5:** Classification performance of machine learning methods with the number of features to select using mRMR of FCQ.

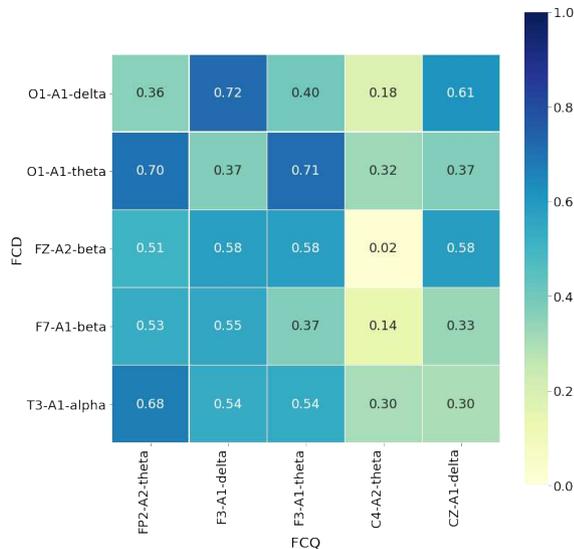
FCQ. As for the remained 10 different selected features, mRMR-FCD and mRMR-FCQ have five respective features each other. What's more, to learn about the causes of why mRMR-FCD and mRMR-FCQ select different lead-rhythm features, we investigate the relationship among the selected features from mRMR-FCD and mRMR-FCQ. According to the theory of the mRMR, it minimizes the redundancy among selected features. In other words, a selected feature can be substituted by another one if they have a high correlation between them. Therefore, correlation coefficients of selected features between mRMR-FCD and mRMR-FCQ are calculated, which is shown in Figure 7. It is noted that the selected features from mRMR-FCD have at least one feature selected by mRMR-FCQ with a high correlation coefficient. For instance, the selected feature 'O1-A1-delta' from mRMR-FCD has high relationship with the selected feature 'F3-A1-delta' from mRMR-FCQ, the correlation coefficient is 0.72. For the selected feature 'F7-A1-beta' from mRMR-FCD, there are two selected features of 'FP2-A2-theta' and 'F3-A1-delta' from mRMR-FCQ with high relationship. The correlation coefficients are



(a) FCD



(b) FCQ

**Figure 6:** Score trend chart of lead-rhythm features to select.**Figure 7:** Heatmap of correlation coefficients between selected lead-rhythm features with FCD and FCQ.

0.53 and 0.55, respectively. It means that the selected lead-rhythm features with high relationship can be replaced with each other to some degree. Namely, there does not exist a big difference between mRMR-FCD and mRMR-FCQ to select crucial lead-rhythm features even if they have respective mRMR score mechanisms.

Meanwhile, it is noted that most of the selected top lead-rhythm features using mRMR-FCD and mRMR-FCQ are with theta and delta rhythms, both of which belong to the slow wave. The theta rhythm is related to the amygdaloid nucleus, hippocampus, thalamus from the limbic system [32]. The occurrence of theta wave is a manifestation of central nervous system depression, which is closely related to mental state, cognition, and emotion. On the other hand, most of the selected important lead-rhythm features are from the leads of 'F3', 'F4', 'FP2', 'F7', and 'FZ', which are located at the

frontal and central region of a human brain. Prefrontal cortex plays a key role in determining psychopathological susceptibility [12]. For example, selected lead-rhythm features of 'F3-A1-theta' and 'F4-A2-theta' are located on the dorsolateral prefrontal cortex, which are verified to be significant to the occurrence of depression [11, 14].

## 5. Conclusion

In this paper, a novel framework for predicting the prognostic effects of acupuncture for depression with EEG recordings is presented. More specifically, the mRMR, with its merits of minimum redundancy among lead-rhythm features and maximum relevance between lead-rhythm features and prognostic effects, is utilized to select important lead-rhythm features. Meanwhile, the reduction rate of HAMD score is calculated and binarized to the prognostic effect label. Widely used machine learning methods of LR, RF, and SVM are employed to build the predicting models of prognostic effects of acupuncture. Extensive experiments show that the presented framework for predicting the prognostic effects of acupuncture can achieve well performance, where the best accuracy and F1 score are 84.61% and 86.67%, respectively. What's more, the selected important lead-rhythm features from mRMR-FCD and mRMR-FCQ are analyzed with the relationship technique, and we find there exist strong relationships between lead-rhythm features selected by mRMR-FCD and mRMR-FCQ. Therefore, the presented framework can help physicians and health providers to learn about patients' mental conditions in advance and take essential interventions to reduce the risk of malignant events.

## Authors' contribution

Xiaomao Fan takes charge of writing this manuscript and conducting corresponding data analysis. Xingxian Huang takes charge of recruiting participants and acquiring EEG recordings from Shenzhen Traditional Chinese Medicine hospital. Haibo Yu as a senior physician designs this study and discusses experimental results associated with medical clinical domain knowledge. Gansen Zhao guides the whole study and revises the manuscript.

## Declaration of competing interest

None

## Acknowledgment

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# Figures

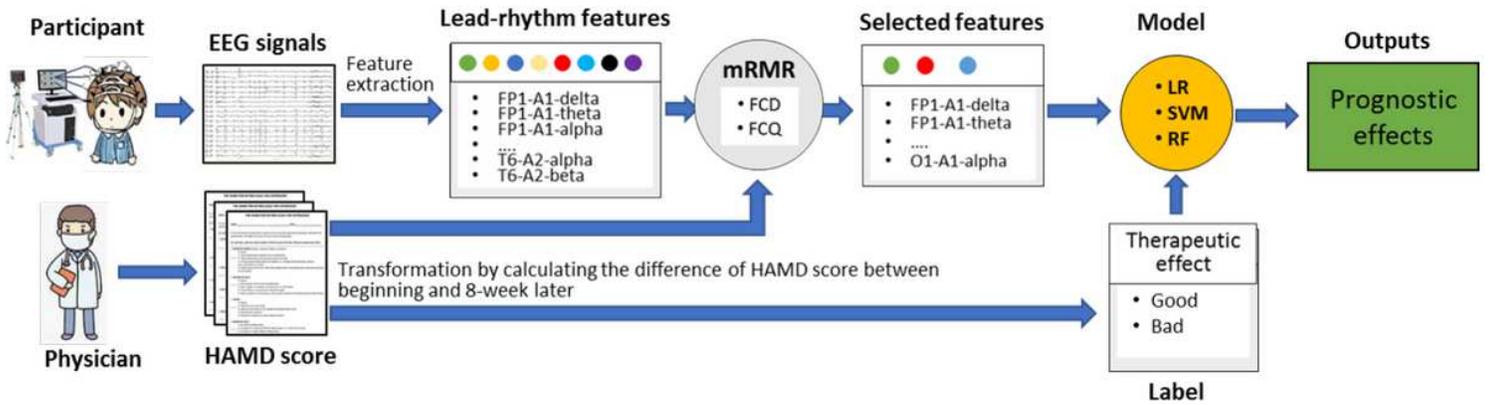


Figure 1

Overview of predicting framework of prognostic effects of acupuncture for depression with EEG recordings

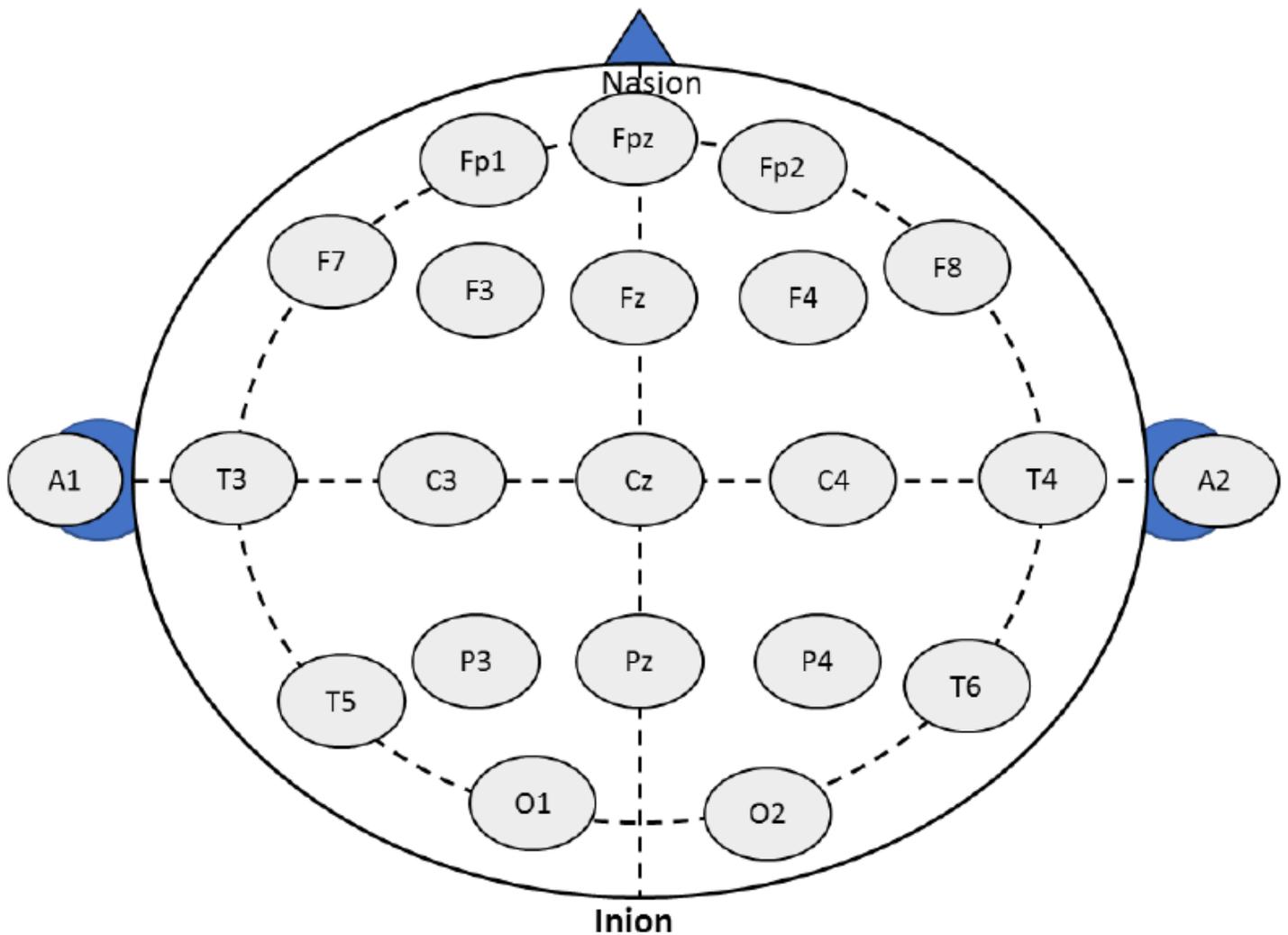
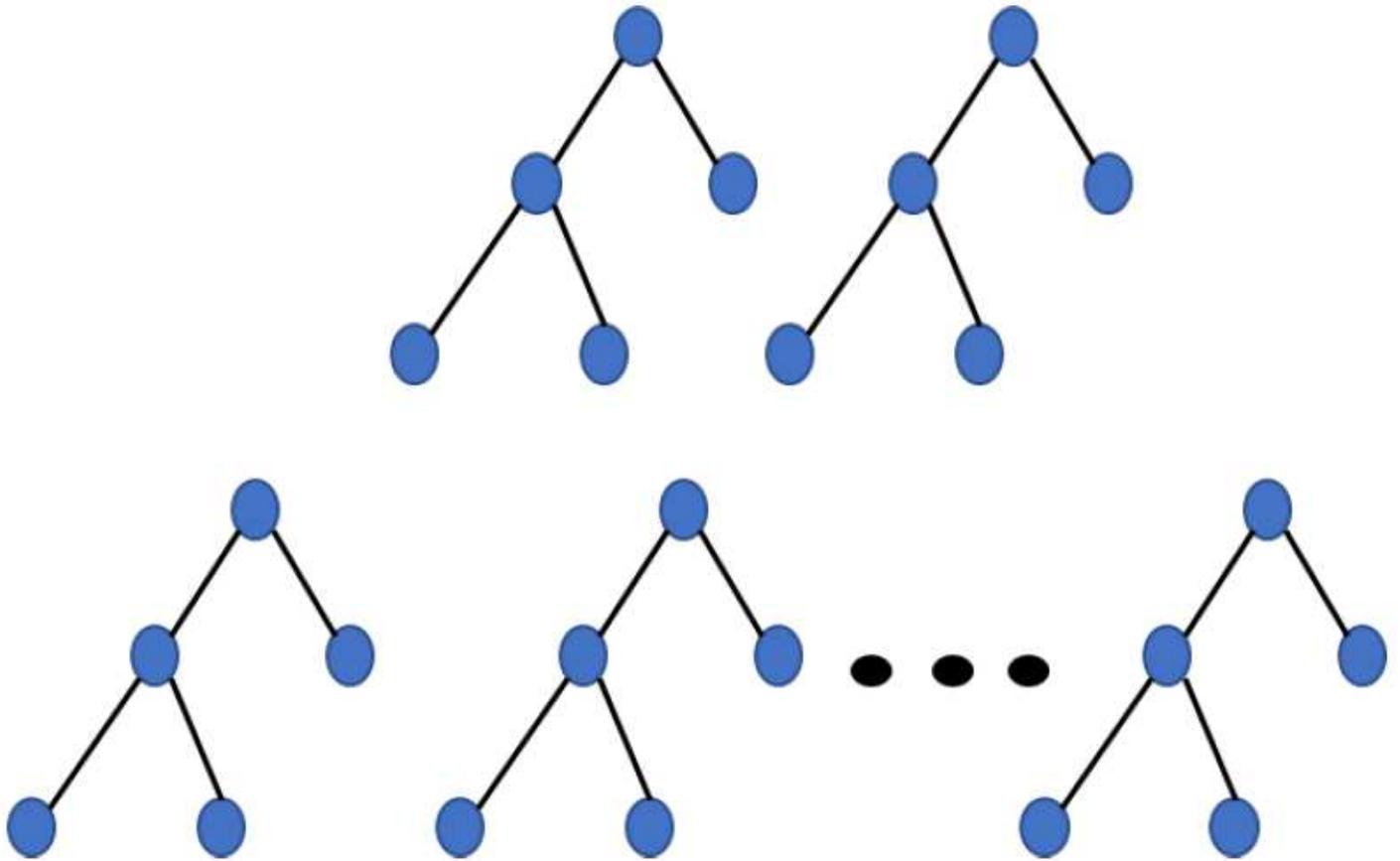


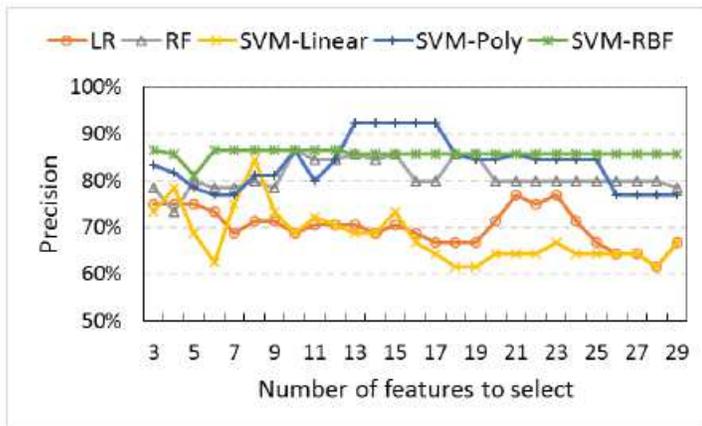
Figure 2

International "10-20" system, which describes the location of scalp electrodes of EEG signals.

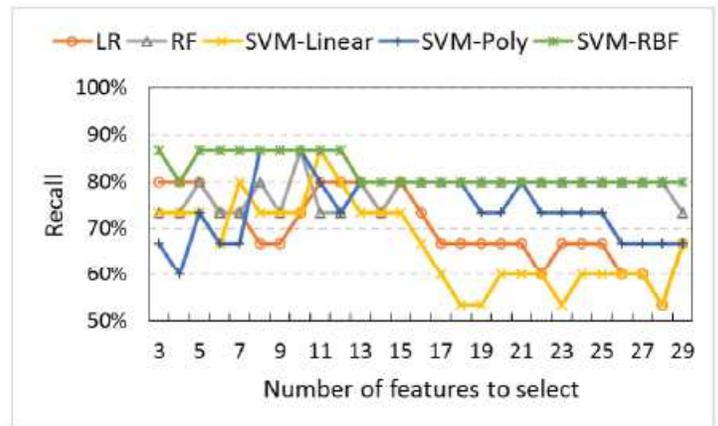


**Figure 3**

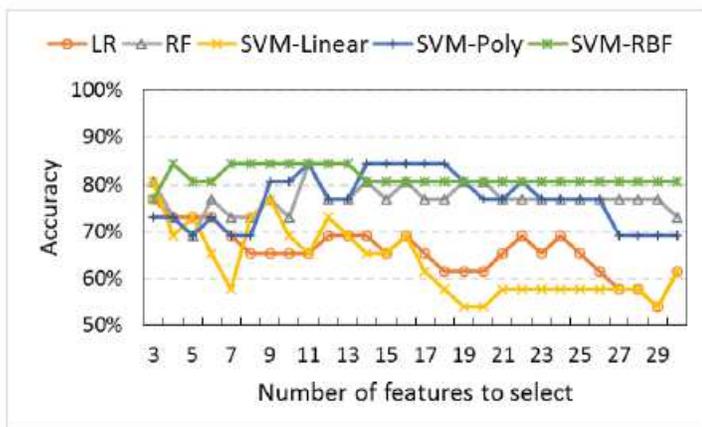
Schematic diagram of a random forest.



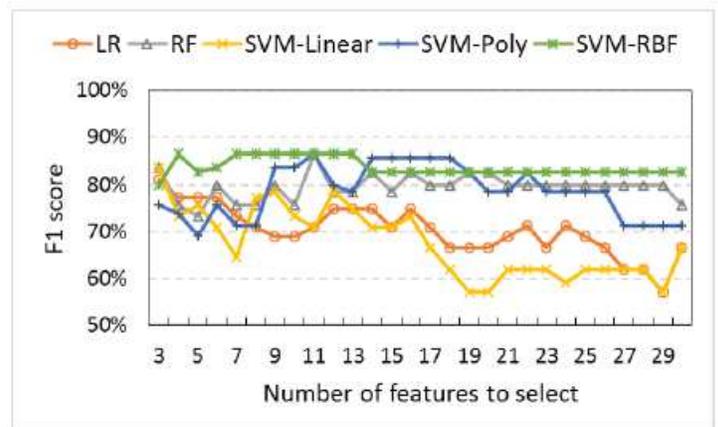
(a) Precision



(b) Reall



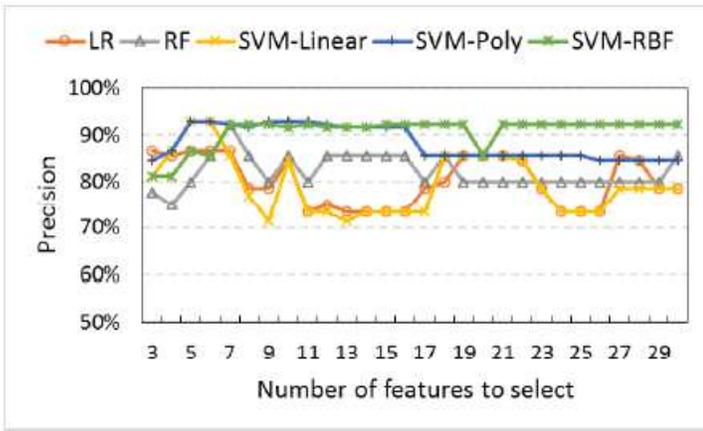
(c) Accuracy



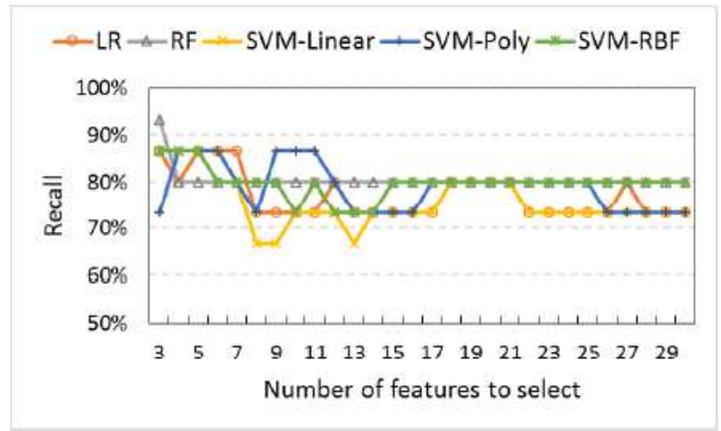
(d) F1 score

Figure 4

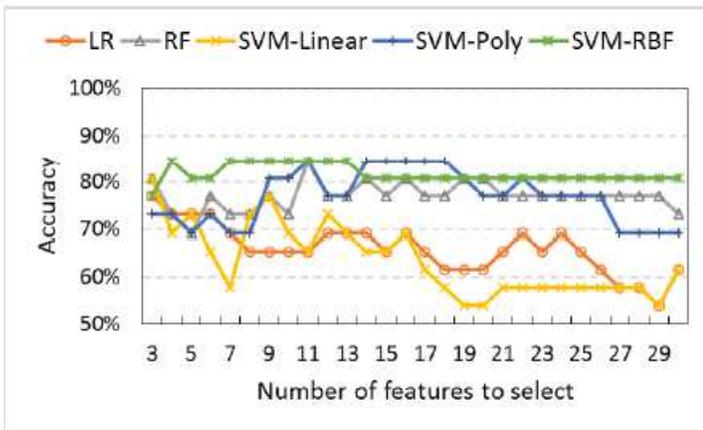
Classification performance of machine learning methods with the number of features to select using mRMR of FCD.



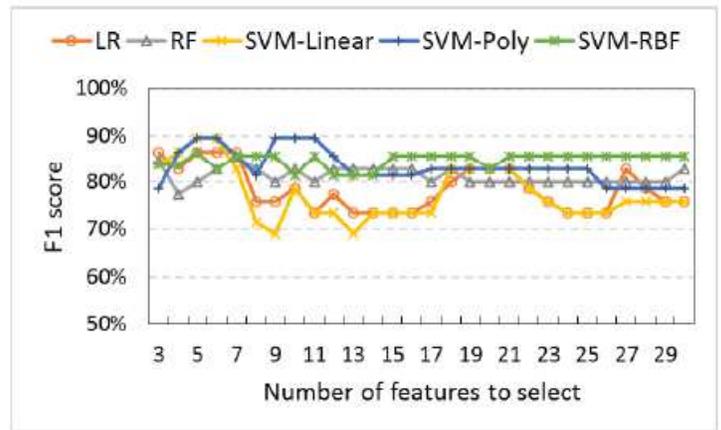
(a) Precision



(b) Recall



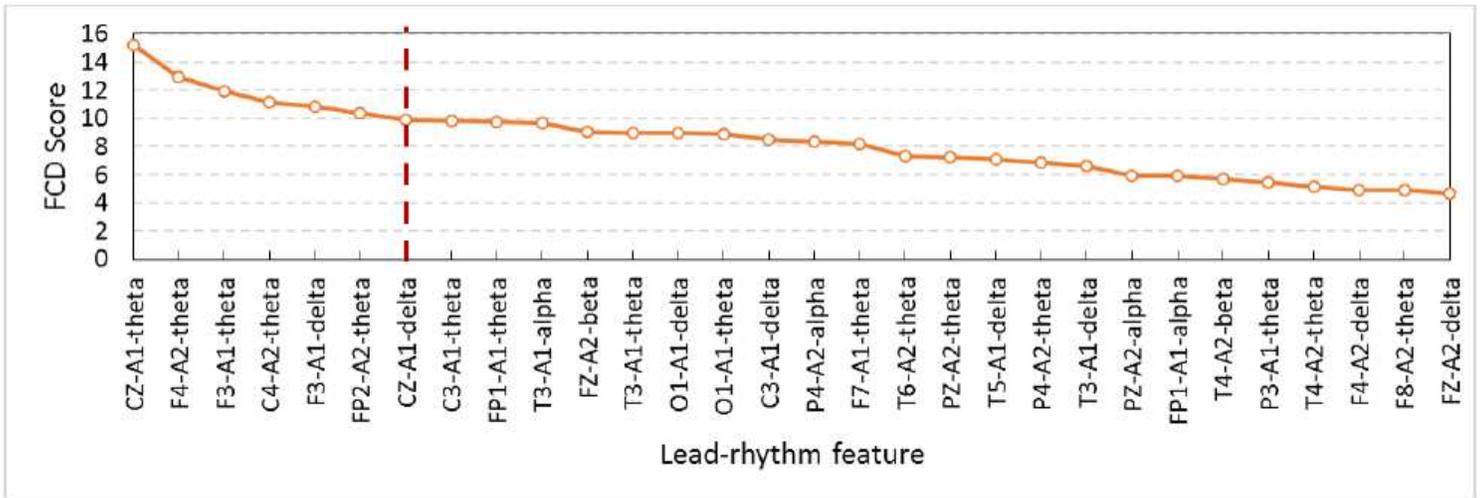
(c) Accuracy



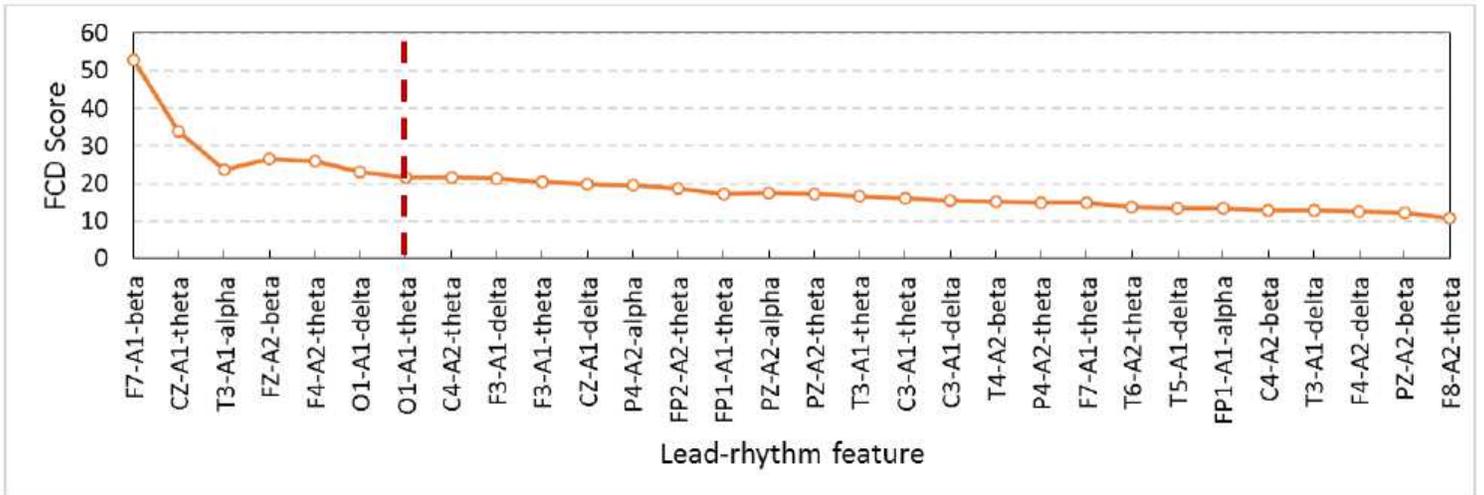
(d) F1 score

**Figure 5**

Classification performance of machine learning methods with the number of features to select using mRMR of FCQ.



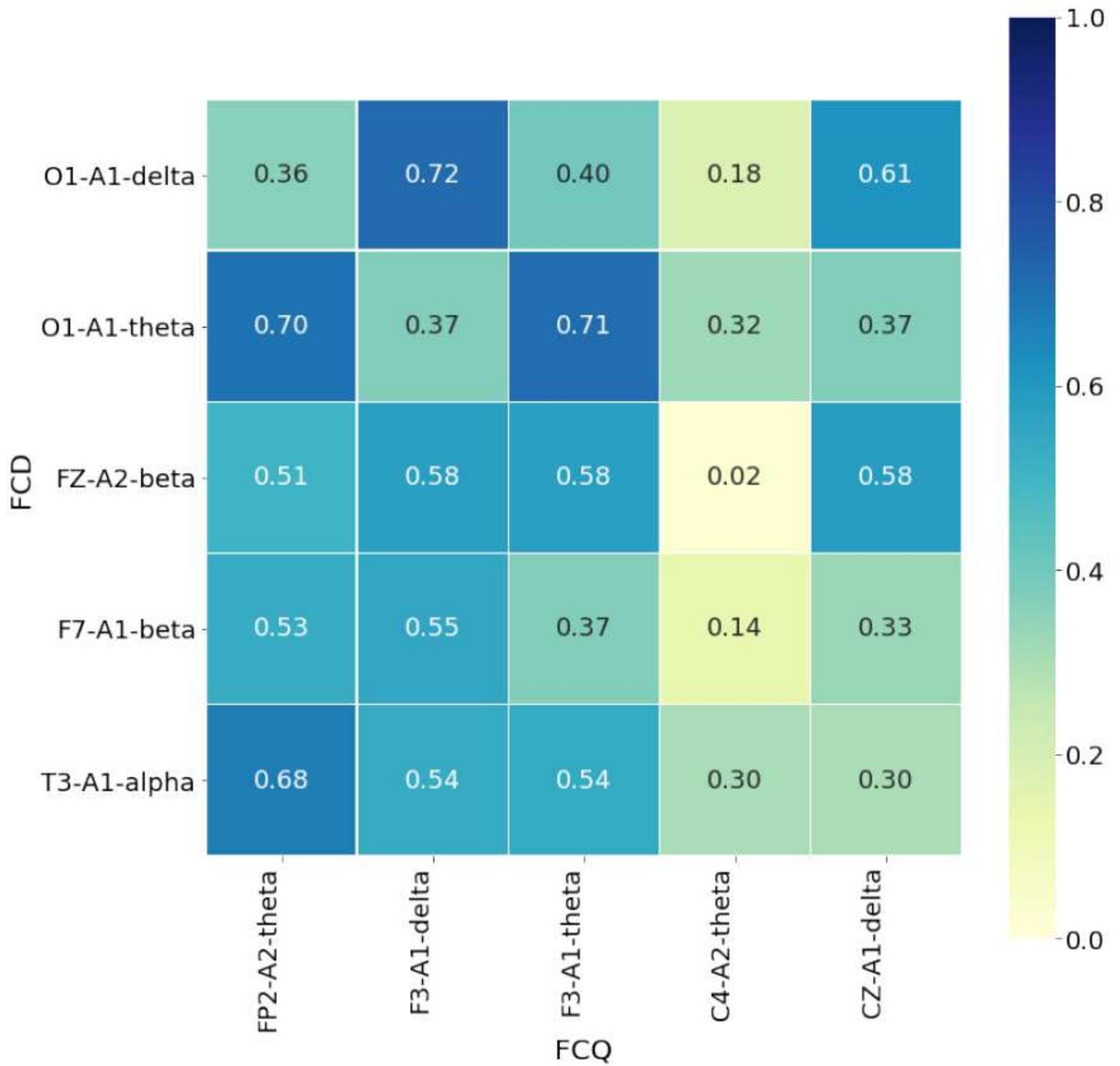
(a) FCD



(b) FCQ

Figure 6

Score trend chart of lead-rhythm features to select.



**Figure 7**

Heatmap of correlation coefficients between selected lead-rhythm features with FCD and FCQ.