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Task-State Heart Rate Variability Parameter-Based Depression Detection Model and Effect of Therapy on the Parameters

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ABSTRACT Depression is a common psychiatric disease. At present, psychometric scales are the main methods for detecting depression in patients and evaluating the clinical treatment effect of depression. However, the accuracy of the scales is influenced by the subjective factors of patients and doctors. This paper explored the construction of a depression detection model based on task-state heart rate variability (HRV) parameters and the effect of therapy on the related HRV parameters. The candidate HRV parameters were first extracted from the task-state electrocardiogram (ECG) collected before treatment and at three observation points during treatment. Then, a statistical t-test was used to screen those characteristic HRV parameters with a significant difference between the depressed and normal groups before treatment. The characteristic HRV parameters and a support-vector machine (SVM) were combined to construct the detection model. Finally, a score model was designed to reveal dynamic changes in the HRV parameters during the treatment process. This paper constructed an automatic, simple, and efficient depression detection model: peakHF+SVM. Detection accuracy reached 89.66%, and this model had comprehensive advantages compared with other related methods. During the entire treatment process, the change in the scores and the time to achieve the maximal scores were different among patients. The type and number of HRV parameters related to the maximal score of each patient also were different. The depression detection model has good application prospects in the objective, quantitative, and automatic detection of depression. The same curative method produced different effects on each patient with depression. The proposed score model may be helpful for the quantitative assessment of the therapeutic effect.

INDEX TERMS Depression, heart rate variability, task-state, detection, therapy.

I. INTRODUCTION

Depression is a common psychiatric disease characterized by high morbidity, recurrent attacks and a high mortality and disability rate. It not only seriously affects the work and life of patients but also places a great burden on society. Improving the accuracy of diagnosis and evaluating the therapeutic effect of depression have been challenging problems.

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At present, psychometric scales and behavioral observations are used to identify patients with depression. Statistical studies have confirmed that the accuracy rate of clinicians diagnosing depression by psychometric scales is only 47.3% [1]. In recent years, some researchers have extracted the characteristics from EEG signals [2], near-infrared spectral signals [3] and magnetic resonance images [4] to automatically detect and identify depression. The collection of EEG and near-infrared spectral signals is inconvenient and the signals are greatly affected by the scalp, skull and extra-brain tissue. In addition, the difficult spatial localization of electrodes leads to poor repeatability of results obtained by these two methods. Magnetic resonance imaging has the advantage of directly revealing the characteristics of depression but is expensive and thus less popular than other methods. Simpler and clearer objective indicators than those that are currently used are therefore urgently needed to detect depression automatically to improve diagnosis accuracy.

Traditionally, depression was mainly treated with medicine, psychology and physical methods [5], [6]. Acupuncture and moxibustion is a new treatment method for depression that has few side effects, low cost and no drug dependence. Studies have shown that this method can achieve the same effect as with drug treatment [7]–[12]. Currently, qualitative psychological scales are mostly used in clinical practice to evaluate the treatment effect of depression: scales such as the Hamilton Depression Scale (HAMD) [13], Beck Depression Inventory (BDI) [14], Self-Rating Depression Scale (SDS) [15]. However, these scales are time-consuming and complicated, with evaluation results closely related to the psychological state of the patient at the time of administration. In addition, the diverse manifestations, complicated aetiology and pathogenesis of depression may result in deviation between the scale and the actual results; therefore, many researchers [16]–[18] have extracted indicators from EEGs, MRIs and ECGs for quantitative evaluation of the curative effect of depression. The existing indicators of the curative effect are statistical parameters from a group of patients. There are individual differences among depressed patients, such as severity of depression and clinical response to treatment; therefore, the treatment plan for each patient to achieve the best curative effect may be very different. Only by evaluating the curative effect of each depressed individual can a doctor monitor the progress of treatment and make decisions for continuing or adjusting the original treatment plan.

Heart rate variability (HRV) is an accurate and non-invasive measure of the autonomic nervous system (ANS) that can reflect the physical condition of the individual. Existing studies show that the aetiology of depression is mostly related to changes in ANS function [19], [20]; therefore, some HRV parameters have been used to reflect the activity state of the ANS [21]–[23]. In the resting state, the sympathetic and parasympathetic nervous systems are relatively balanced. Under stimulation of different emotions, the balance of the ANS can be changed [24]. For example, positive emotions increase the activity of the parasympathetic nervous system whereas negative emotions can lead to parasympathetic inhibition and sympathetic activity [25]. Some studies have shown that depressed patients have biased emotional processing disorder, which is reflected by their tendency to recognize positive and neutral events as negative events [26], [27] and their decline in an ability to feel emotions (such as happiness or sadness.) [28], [29]. This illustrates that the HRV parameters collected in performing emotional tasks (defined as task-state HRV parameters) can more fully and accurately reflect changes in ANS and emotional disorders than resting-state HRV parameters; they can also better distinguish depressed patients from healthy individuals. In addition, the ECG signal is more convenient to be collected and HRV-related R waves in the ECGs are less susceptible to external interference than EEGs and EMGs [30]–[32].

In this paper, we first propose a depression detection model using task-state HRV parameters for automatically discriminating depressed patients from normal participants and providing objective evidence for a diagnosis of depression. Then, we focus on dynamic changes of the task-state HRV parameters during the treatment of each depressed individual, aiming at an objective assessment of the curative effect and guidance for an individual treatment plan. Finally, experimental data are used to validate the study.

II. MATERIALS AND METHODS

A. PARTICIPANTS

Fourteen depressed patients (six males, eight females) were recruited from the Affiliated Hospital of Chengdu University of Traditional Chinese Medicine (TCM) and Sichuan Provincial People's Hospital. The average age of the patients was 47±10.26 years and all were educated to senior middle school level or above.

In addition, all of the patients met the diagnostic criteria in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), and their HAMD24 scores were equal to or higher than 21 points. They had not used psychotropic drugs for the last 3 months and they had no circulatory system diseases (such as cardio-cerebrovascular diseases, diabetes, or stroke).

The 15 normal participants (8 males, 7 females) came from the community and the University of Electronic Science and Technology of China, and their average age was 41.47±11.67 years. All of them were educated to senior middle school level or above. Furthermore, their BDI-II scores were less than 13 points and there was no history of mental illness or family hereditary psychotic diseases. In addition, none of the participants had any circulatory system diseases such as cardio-cerebrovascular diseases, diabetes or stroke.

Before the experiment, all participants involved in this study gave their informed consent. Institutional review board approvals of the Affiliated Hospital of Chengdu University of TCM, Sichuan Provincial People's Hospital and University of Electronic Science and Technology of China were obtained for this study.

We performed a statistical t-test to find any difference between the depressed and healthy groups in terms of sex and age. The results showed that the p values for sex and age in the two groups were 0.589 and 0.201, respectively, both of which were much greater than 0.05. There was thus no significant difference between the two groups in terms of sex and age.

B. DESIGN OF EMOTIONAL IMAGE PROCESSING TASK

Unlike most traditional methods of ECG data collection, we collected ECG data when the participants performed an emotional image processing task to enhance the discrimination power between depressed and normal participants.

Emotional pictures with happy, sad and neutral expressions were randomly extracted from the Chinese emotional face system [33], then randomly matched by image processing software. In total, 30 happy and 30 sad expression pairs from the same person and from different people were edited, respectively. Similarly, 60 neutral expression pairs from the same person and from different people were edited, respectively [34].

A two-step stimulus experiment was performed during the collection of ECG data: the happy and neutral pictures first, then the sad and neutral pictures. In each step, the participants looked first at 10 pairs of emotional pictures and then at 10 pairs of neutral pictures, with each pair of pictures being visible for 3 s, a total of six times. The two pairings from the same person and from different people occurred randomly. The participant was asked, when looking at a pair of pictures, to determine if they were from the same person. This two-step stimulus experiment took a total of 12 min.

C. COLLECTION OF TASK-STATE ECGS BEFORE AND DURING THEREAPY

Before treatment, using battery-powered NINscan 4 (a wearable monitor) [35], we collected the ECG signals of 14 depressed patients and 15 normal controls while they completed the emotional image processing tasks. The sampling frequency of the task-state ECG signal was 250 Hz.

Among the 14 depressed patients, two chose medication, two chose psychotherapy, two chose physical therapy and eight chose acupuncture treatment. Because the sample size for the first three treatment methods was too small, the eight depressed patients who chose acupuncture treatment were included in the subsequent study on the effect of treatment on the HRV parameters.

Eight patients received acupuncture treatment for 8 weeks, three times a week, at the Affiliated Hospital of Chengdu University of TCM. The weekly treatment time was arranged on the mornings of Monday, Wednesday and Friday. To capture dynamic changes of the HRV parameters for each patient, we set up three therapeutic observation points in the acupuncture treatment process, one each at the second, fourth and eighth weeks.

At each observation time point during treatment, we collected the task-state ECGs of the eight depressed patients who received acupuncture treatment and the 15 healthy controls. The baseline drifts in the ECG signals were eliminated by the moving window median filtering method [36]. The algorithm proposed by Manriquez *et al.* [37] was used to locate the R waves for the RR interval sequences because this algorithm performed well on detecting the R waves.

D. SLECTION OF CANDIDATE HRV PARAMETERS

At present, HRV parameters have been well measured in time, frequency and non-linear domains. The physiological significance of these three types of HRV parameters is different. For example, the standard deviation of NN intervals (SDNN, a time domain HRV parameter) mainly reflects the overall HRV [38], the ratio of low frequency to high frequency (LF/HF, a frequency domain type) can reflect the balance of the sympathetic vagus nerve [39] and approximate entropy (ApEn) and sample entropy (SampEn), both non-linear types, reflect the complexity of the ECG time series [40]. To find those HRV indicators that can comprehensively and accurately reveal differences between depressed patients and healthy individuals and are influenced by therapy, we selected 9, 12 and 12 candidate HRV parameters from the time, frequency and non-linear domains, respectively. Details of the 33 candidate HRV parameters are shown in Table S1 in the Supplementary Material.

E. CONSTRUCTION OF THE DEPRESSION DETECTION MODEL

The HRV parameters from task-state ECGs are defined as task-state HRVs in this study. We first calculated all 33 task-state HRVs for each of 14 depressed patients and 15 normal controls, respectively. Then, a statistical t-test was used to screen those task-state HRVs that have a significant difference between the depression and healthy groups ($p < 0.05$). We supposed that M differential task-state HRVs were obtained and these were respectively combined from 1 to M into discrimination characteristics. A support vector machine (SVM) was used to classify the depressed patients and normal controls based on each discrimination characteristic. A leave-one-patient-out cross-validation (LOPOCV) was used to verify the performance of each detection model. The performance indices included the sensitivity (SE), specificity (SP), positive predictivity (PP), accuracy (ACC) and area under the curve (AUC) of the receiver operating characteristic (ROC). Finally, the discrimination characteristic with optimal detection performance was retained to construct the detection model.

F. QUANTITATIVE ESTIMATION OF THE EFFECT OF TREAMENT ON TASK-STATE HRVS

As mentioned in the Introduction, HRV parameters may be used to reveal the condition of depressed patients because the aetiology of depression is mostly related to changes in ANS function [19], [20]. The more the HRV parameters of a depressed patient change during therapy compared with a healthy participant, the greater the effect produced by the treatment method.

To find those HRV parameters that changed significantly during therapy and to comprehensively assess that change, we constructed a control matrix (denoted by $\mathbf{R}$) using the 33 task-state HRVs of N healthy people. Thus, the dimension of R is $33 \times N$ and the element r_{ij} of $\mathbf{R}$ represents the value of the i^{th} HRV parameter of the j^{th} healthy participant, where $i = 1, 2, \ldots, 33$, and $j = 1, 2, \ldots, N$.

Each raw vector of matrix $\mathbf{R}$ includes the same task-state HRV values of all N healthy participants. Correlations among the 33 HRVs of the control group can be established by calculating Pearson correlation coefficients (PCC) between the two raw vectors of matrix **R**, expressed by a correlation matrix of dimension 33 × 33 (denoted by $\mathbf{P_N}$).

Then, the 33 task-state HRVs of a depressed patient were taken as a column vector to add into **R**. A case-control matrix (denoted by $\mathbf{R_{+1}}$) of dimension 33 × (N + 1) was formed. Because there are possibly differences between the HRVs of depressed patients and healthy participants, the correlations among the 33 HRVs of the case-control matrix were changed. Similarly, we indicated the correlations using correlation matrix $\mathbf{P_{N+1}}$, which has the same dimension as $\mathbf{P_N}$.

Next, we constructed a difference matrix (denoted by $\mathbf{P_D}$) by subtracting the corresponding elements of $\mathbf{P_{N+1}}$ and PN, then tested the significance of each difference element in $\mathbf{P_D}$ using a t-test. It is not difficult to understand that those task-state HRVs associated with significant difference elements reveal differences in the ANS condition of a depressed patient compared with that of a healthy participant.

Furthermore, we quantitatively evaluated the difference between the task-state HRVs of a depressed patient and a healthy participant on two levels: difference in absolute values and correlation difference. Supposing there are Q significant difference elements in $\mathbf{P_D}$ and that K task-state HRVs are associated with these significant difference elements for a depressed patient, then the absolute difference ($AbsD$) is defined as:

$$AbsD = {}^{1}\!/_{K} \sum_{l=1}^{K} |r_{+1l} - r_l| \tag{1}$$

where r_{+1l} is the value of the l^{th} task-state HRV of a depressed patient and r_l is the average value of the l^{th} task-state HRVs of N healthy participants (i.e. the average value of the l^{th} raw vector in **R**). The correlation difference (CD) is defined as the average of Q significant difference element values in $\mathbf{P_D}$. Considering that Q significant difference elements and the K involved task-state HRVs are possibly different for different depressed individuals, we normalized CD by using the average of the non-significant difference element values in $\mathbf{P_D}$.

Finally, a score model was defined to comprehensively evaluate the difference between task-state HRVs of a depressed patient and a healthy participant, as follows:

$$S = AbsD \times NCD \tag{2}$$

where NCD is the normalized CD. Obviously, the higher the S value, the greater the variation of the task-state HRVs of a depressed patient compared with a healthy participant.

The effective treatment for depression can change the condition of the ANS, which is reflected by the changes in the HRV parameters for a depressed patient. Thus, the S score of a depressed patient will change dynamically with the progression of treatment.

TABLE 1. Three task-state HRV parameters with significant differences.

Name	Value in depression Group (Mean)	Value in healthy control group (Mean)	p-value
peakHF	0.235±0.065	0.296±0.058	0.017
aHF	260.867±138.385	407.887±276.390	0.048
DET	98.806±0.831	97.951±1.175	0.039

TABLE 2. The discrimination chracteristics and the performances of the detection model.

Discrimination characteristic	Performances of detection model				
	ACC (%)	SE (%)	SP (%)	PP (%)	AUC
peakHF	89.66	85.71	93.33	92.31	0.83
aHF	51.72	42.86	60.00	50.00	0.51
DET	6.90	7.14	6.67	6.67	0.07
peakHF、aHF	51.72	42.86	60.00	50.00	0.51
peakHF、DET	27.59	35.71	20.00	29.41	0.28
aHF、DET	51.72	42.86	60.00	50.00	0.51
peakHF、aHF、DET	51.72	42.86	60.00	50.00	0.51

III. RESULTS

A. CONSTRUCTED DEPRESSION DETECTION MODEL AND PERFORMANCES

From the 33 candidate task-state HRVs, we screened three (peakHF, aHF and DET) using a t-test that showed significant differences ($p < 0.05$) between the 14 patients with depression and 15 healthy control participants. Details of these three task-state HRVs are shown in Table 1.

The combination of three HRV parameters with significant differences formed seven discrimination characteristics (Table 2). An SVM was used to classify the depression and control samples based on each characteristic. The validation results of LOPOCV on 14 depressed patients and 15 controls for each detection model are also shown in Table 2.

As can be seen in Table 2, the peakHF+SVM model has the optimal performance and the least number of features of the seven combinations. The accuracy (ACC), sensitivity (SE), specificity (SP), positive prediction (PP) and area under ROC curve (AUC) of this model reached 89.66%, 85.71%, 93.33%, 92.31% and 0.83, respectively, which are much better values than those of the other six discrimination characteristics. Furthermore, we compared the performance of the peakHF+SVM model with that of the traditional k-Nearest Neighbor (KNN) model and two integrated learning classification methods—Ensembles for Boosting (EB) and Ensembles for Random Subspace (ERS)—as shown in Figure 1.

It can be seen from Figure 1 that the peakHF+SVM model outperforms the traditional KNN, EB and ERS classification methods. This illustrates that the task-state peakHF is a good parameter for revealing the difference between patients with depression and healthy people. Therefore, the peakHF+SVM model was proposed as a new method to detect depression.

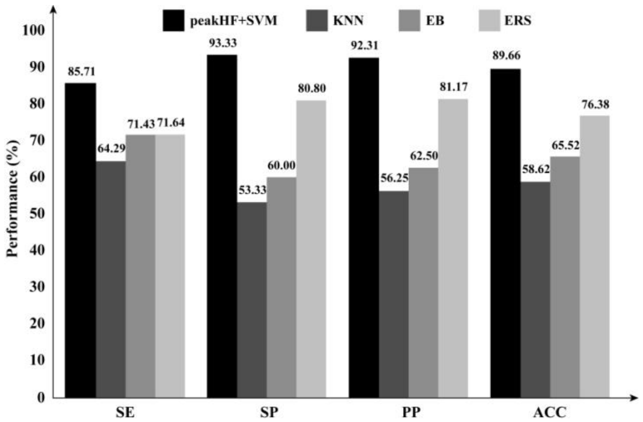

FIGURE 1. Performance comparison between the new and traditional detection methods.

TABLE 3. *S* scores of five depressed patients at each observation point.

Patient Observation point	Before treatment	After treatment		
		The 2th week	The 4th week	The 8th week
Cxp	53.44	285.79	92.70	391.15
Lsq	0.00	60.82	201.13	164.39
Wxy	66.58	111.43	120.94	129.01
Yxq	68.46	108.60	111.66	155.23
Zgy	0.00	192.51	238.14	33.40

B. EFFECT OF TREATMENT ON TASK-STATE HRVS FOR EACH PATIENT WITH DEPRESSION

The quality of the ECGs at four observation points (before treatment and treatment weeks 2, 4 and 8) for 8 patients with depression who received acupuncture treatment and 15 healthy controls was evaluated. We found that the ECG data for three of the patients with depression were incomplete because the electrodes fell off during treatment. Thus, 5 patients and 15 healthy controls with complete, good-quality ECG data were eventually included in the study.

Based on the healthy control group, the scores of the five patients with depression at each observation point were calculated respectively (Table 3). For each patient, the higher the value of S, the greater the impact of treatment on the task-state HRVs and the greater the possible change in ANS condition. The value of S was therefore conjectured to be associated with curative effects. Figure 2 used the S score to intuitively show the dynamic change in task-state HRVs for each patient with depression during treatment.

Clearly, during the entire treatment process, the dynamic change in S scores and the time to achieve maximal scores were different for each patient: Lsq and Zgy achieved maximal scores at week 4; Cxp, Wxy and Yxq achieved maximal scores at week 8. Furthermore, we analysed which task-state HRVs contributed to the maximal score for each patient, as shown in Table 4.

Table 4 shows that the type and number of HRV parameters related to the maximal score for each patient were not identical, with a minimum of 21 and a maximum of 32 HRV

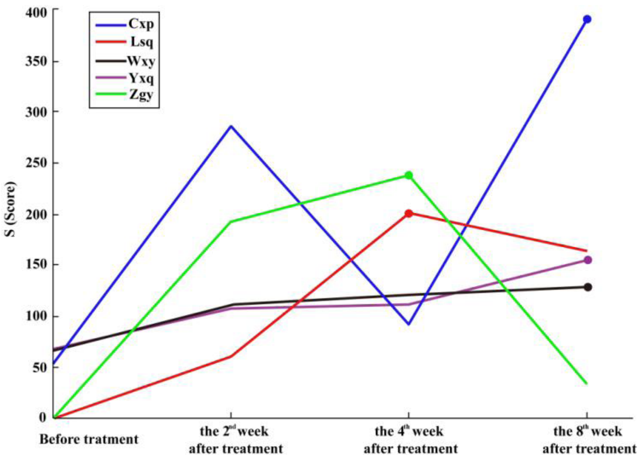

FIGURE 2. Dynamic change curves of task-state HRVs during treatment for five depressed individuals.

parameters, all involving at least half of the 33 HRV parameters. There were 12 common HRV parameters shared by the five patients (RMSSD, NN50, Pnn50, PeakVLF, PeakLF, aLF, aHF, SD1, D2, a2, Lmax, DET), with RMSSD, aLF, aHF and SD1 confirmed by the literature to be associated with depression [23], [41]–[43]. We analyze the potential clinical significance of the results of Figure 2 and Table 4 in the next section.

IV. DISCUSSION

Previous studies on the automatic detection of depression were mainly based on EEG, fNIRS and fMRI imaging features and rest-state HRV parameters. Using task-state HRV parameters, our study constructed an automatic, simple and efficient depression detection model: peakHF+SVM. The detection accuracy of this model reached 89.66%, with good prospects for clinical application.

There are few studies on the dynamic changes of task-state HRV parameters during the treatment of patients with depression. This study quantifies these changes for each patient with depression by constructing a score model, which can adaptively screen those HRV parameters that reveal the patients' depression for quantitative assessment of the therapeutic effect.

A. ACQUISITION AND SAMPLE CAPACITY OF TASK-STATE ECGS

In our study, we discarded traditional rest-state HRV parameters because the task-state HRV parameters acquired during emotional picture processing can more fully and accurately reflect ANS changes and emotional disorders. The wearable single-lead ECG acquisition device did not affect execution of the task, making collection of task-state ECGs feasible and convenient.

The study recruited 14 patients with depression and 15 healthy controls. The sample capacity meets the requirements of a statistical t-test for detecting depression and although, for various reasons, only five patients with

TABLE 4. The task-state HRV parameters contributing to the maximum score of each patient.

No.	HRV parameters	patients				
		Cxp	Lsq	Wxy	Yxq	Zgy
1	RR mean	√		√	√	√
2	SDNN	√	√	√	√	
3	HR mean	√		√	√	
4	HR SD	√	√	√		
5	RMSSD	√	√	√	√	√
6	NN50	√	√	√	√	√
7	pNN50	√	√	√	√	√
8	HRV triangular index	√	√	√		
9	TINN	√		√	√	
10	VLFp	√	√	√	√	√
11	LFp	√	√	√	√	√
12	HFp				√	
13	aVLF	√		√		
14	aLF	√	√	√	√	√
15	aHF	√	√	√	√	√
16	rVLF		√	√	√	√
17	rLF		√	√	√	√
18	rHF		√	√	√	√
19	LFn			√	√	√
20	HFn			√	√	√
21	LF/HF			√		
22	SD1	√	√	√	√	√
23	SD2	√	√	√		
24	Apen	√		√	√	
25	Sampen	√		√	√	√
26	D2	√	√	√	√	√
27	α1			√	√	√
28	α2	√	√	√	√	√
29	Lmean			√	√	√
30	Lmax	√	√	√	√	√
31	REC		√	√	√	
32	DET	√	√	√	√	√
33	ShanEn		√	√	√	√

Note: "√" indicates the HRV parameter associated with the maximum score. Bold font represents 12 common HRV parameters shared by the five patients.

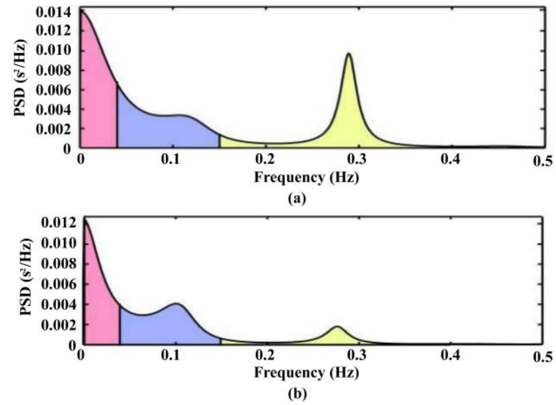

FIGURE 3. PSDs of RR interval sequences for healthy individuals and depressed patients. (a) Healthy individuals. (b) Patients with depression.

depression were available for assessing the dynamic changes of HRVs during treatment, the study was designed to analyze individualized samples. The small case sample size thus had no effect on the study results for the patients with depression, but it did affect the discovery of dynamic change rule in HRV during treatment. In future research, we will expand the sample size for quantitative assessment of the optimal curative effect.

B. DISCRIMINATION ABILITY OF TASK-STATE PEAKHP

We calculated the mean power spectral density (PSD) of RR interval sequences for the healthy and depression groups, as shown in Figure 3, finding a large difference between the power spectrum amplitudes of the two groups in the high-frequency band: the high-frequency amplitude of the depression group was significantly lower than that of the healthy group, and the frequency of the peak amplitude was also lower than that of the healthy group. This is because vagus nerve activity in depressed patients is lower than that in healthy participants and explains why the task-state peakHP parameter had high discriminating ability between the depression and healthy groups.

At present, the highest accuracy with EEG feature+SVM models for detecting depression can reach 94% [2], which is higher than the accuracy of our model (89.66%). However, compared with ECG, the EEG signal has a much smaller amplitude and is more susceptible to interference and distortion; furthermore, elimination of interference is more difficult and the EEG acquisition process is more complicated. Taking these factors into consideration, the discrete degree of accuracy for EEG-based models might be much larger than that of ECG-based models, but the average accuracy of the two models may be similar.

The accuracy of the fNIRS feature+SVM models in depression detection can reach 89.71% [3], which is almost equivalent to our model. However, the collection of fNIRS data is influenced by many factors (including scalp, skull and peripheral tissue); moreover, the result is poorly repeatable and feature extraction is difficult. Thus, there are still some obstacles in the clinical application of this method.

In addition to the methods above, image technology has non-invasive acquisition, intuitive results and high spatial resolution, thus attracting many researchers to use this technology to study the automatic detection of depression. For instance, Yoshida [4] used a kernel-based partial-least-squares algorithm (KPLS) to process resting-state fMRI data of patients with depression and healthy individuals, and used the extracted image features and linear discrimination analysis (LDA) to detect depression. The accuracy of their method reached 80.5%. This image-based detection method not only has lower accuracy than our method but also has a higher cost, thus limiting its popularity in practical clinical applications.

In summary, the method for detecting depression based on task-state HRV parameters proposed in this paper not only has the advantages of convenient ECG data collection and simple calculation of HRV parameters, but also achieves a high classification accuracy of 89.66%.

C. CLINICAL SIGNIFICANCE OF DYNAMIC CHANGE CURVES OF TASK-STATE HRVS

In the dynamic change curves of the task-state HRVs of Figure 2, the scores for patients Lsq and Zgy increased continuously after acupuncture treatment and reached a maximum by the fourth week, indicating that the first 3 weeks of acupuncture had good efficacy for these two patients and that efficacy was best at week 4. From the fourth to the eighth week, the score for Lsq decreased slightly whereas the score for Zgy decreased significantly. This means that the efficacy of acupuncture was reduced, suggesting that a 4-week treatment cycle could be used for Lsq and Zgy. The scores for patients Wxy, Yxq and Cxp reached a maximum at the eighth week of acupuncture treatment, but because there were no further observation points, we can only predict that the best efficacy of Wxy, Yxq and Cxp may be achieved either at the eighth week or after 8 weeks. The acupuncture treatment period for these three patients should therefore be at least 8 weeks. In fact, most existing clinical acupuncture treatment periods for patients with depression are set to 8 weeks. Furthermore, the dynamic change curves for Wxy and Yxq were similar and the scores increased gradually during the whole acupuncture treatment, indicating that acupuncture gradually produced curative effects. However, these curves were completely different from those of Cxp, which rose linearly after 2 weeks of acupuncture treatment, fell linearly at the fourth week and then rose to a maximum score at the eighth week; we describe this process as a fluctuating increase. Because of individual differences between patients with depression, the five patients can be classified into three categories based on the dynamic change curves: maximum at the fourth week (Lsq and Zgy); linear increase (Wxy and Yxq); and fluctuating increase (Cxp).

D. INDIVIDUALIZED DIFFERENCES REVEALED BY TASK-SATE HRVS

Table 4 shows that the type and number of HRV parameters related to the maximum score for each patient were not identical, with a minimum of 21 and a maximum of 32 HRV parameters, all involving at least half of the 33 HRV parameters. As already mentioned, only 12 HRV parameters (bold in Table 3) were shared by all five depressed patients, with most parameters being different. This illustrates that there is individual difference among the depressed patients, and that the same curative method possibly produced different curative effects.

In the future, we will establish the dynamic change patterns of task-state HRVs, assess the curative effect and explain the mechanism of optimal efficacy by increasing the number of samples and observation points (including post-treatment follow-up) and extending the treatment time as appropriate.

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