

# **Pulse Analysis in Bipolar Disordered and Nonpsychotic Human Subjects**

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## **Abstract**

The research literature indicates that patients with bipolar disorder (BPD) differ from healthy individuals in various ways that are also recognized in traditional Chinese medicine. The purpose of the current study was to analyze the pulse spectra in BPD patients to determine any differences from nonpsychotic healthy individuals. Sphygmography was used to measure the radial arterial pulse waves in all subjects. We analyzed the original waveforms and then transformed them into frequency spectra via Fourier transformation. The relative strength of each harmonic, believed to be connected to meridians in Chinese medicine, was identified from the frequency, and we compared the differences among the harmonics. A total of sixty individuals, thirty with BPD and thirty nonpsychotic healthy controls, participated in the study. The harmonic values of C4 (Lung Meridian) on the right hand,  $401.33 \pm 50.10$  vs.  $762.44 \pm 125.17$ , were significantly different ( $p < 0.05$ ) between the BPD group and the nonpsychotic healthy group. The harmonic percentage of C3 (Spleen Meridian) on the right hand,  $7.85 \pm 0.59\%$  vs.  $10.79 \pm 1.01\%$ , and C4 (Lung Meridian),  $1.80 \pm 0.15$  vs.  $3.24 \pm 0.43$ , was significantly different ( $p < 0.05$ ) between the two groups. The results were similar for the right and left hands. In this study, we objectively detected constitutional differences between BPD patients and healthy controls through arterial pulse analysis. The pulse spectrum analyzer is a noninvasive diagnostic tool that can be used to integrate scientific technology with traditional Chinese medicine diagnostics. We plan further study in this field to improve the accuracy of diagnosis in Chinese medicine.

**Keywords:** Arterial Pulse Analysis; Sphygmography; Traditional Chinese Medicine; TCM; Bipolar Disorder.

## **Introduction**

“Pulse diagnosis” is a unique diagnostic method used in Chinese medicine. Applied to only three fingers, this technique helps to identify problems with internal human organs (Wang, 1987). This traditional diagnostic art has been practiced in China for thousands of years and has attracted the attention of Western medicine. Traditional Chinese Medicine (TCM) relies on medical experience, and its treatments or prescriptions are often based on previous case studies. For many years, the Yellow Emperor's Classic of Medicine has been the primary reference for TCM treatment, and other classic texts such as "Shang Han Lun" or the "Compendium of Materia Medica" are also important references. Methods that are compatible with these classics are regarded as correct, whereas treatments that differ from the classics are regarded as incorrect. This convention limits the progress and innovation within TCM.

Subjectivity and lack of experience in a diagnostician can easily lead to misjudgment when the disease is diagnosed solely by measuring the pulse through three fingers. Sphygmography was developed to obtain objective data through the integration of computer technology and TCM pulse diagnosis (O'Rourke *et al.*, 2001). With the help of sphygmography and digital signal processing, we can more conclusively diagnosis the disease.

Bipolar disorder (BPD) is a psychiatric disorder that requires long-term treatment. In most cases, the symptoms occur in early adulthood and affect an individual's quality of life (Geldr *et al.*, 2001). Previous studies have found that BPD patients are genetically different from normal controls (Nanjing University of Chinese Medicine, 2007; He, 1995). Some classic Chinese references state that BPD patients differ from the general population with regard to their ambitions and feelings. Our intention is to establish a basic BPD pulse type by using scientific methods in a series of studies with BPD patients. Furthermore, we hope to define the relationship between the pulse type and the clinical symptoms. In the current study, we used sphygmography to analyze the differences in pulse frequencies between healthy people and BPD patients. The results of this clinical study are expected to be useful in clinical diagnosis and treatment.

## **Methodology**

### **Subjects**

The experiment was conducted from May 2009 to January 2010. Sixty participants were divided into two groups: 30 in the BPD group and 30 in the healthy group. The diagnostic criteria for BPD were consistent with the 1994 Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), whereas the healthy group

included individuals without mental illness or cardiovascular disease. We also excluded subjects with a family history of mental illness.

None of the subjects in the two groups had serious and chronic diseases, such as arrhythmia, cardiomyopathy, hypertension, diabetes, kidney failure, hyperthyroidism, severe asthma, or cancer. The two groups consisted of 16 males and 14 females; they were all older than eighteen years of age and ranged from 19.46 years to 55.08 years, with a mean of  $34.21 \pm 10.05$  years. The average age of the BPD and healthy groups was  $40.59 \pm 9.31$  years and  $27.84 \pm 5.88$  years, respectively. The BPD group was 12.75 years older, on average, than the healthy group.

### **Instruments**

The PDS-2000 Pulse 2 analysis system, developed by Cologne Technology Co., Ltd., Taiwan, with a DOH medical device system permit number of Zi 002302, was used in this study. This system for measuring the pulse and storing digital data was connected to a computer.

### **Procedures**

The experiment was approved by the Institutional Review Board (IRB) of China Medical University Hospital with the authorization number DMR98-IRB-074. All participants were examined in detail, which included an interview by a psychiatrist

about their history of mental illness. Upon examination, the participants were not suffering from respiratory infections, gastrointestinal illness, or other acute diseases.

After the psychiatrist's detailed examination and interview using a psychiatric history checklist, the participants were informed of the contents and procedures of the study, and they were asked to sign a voluntary consent form. In this study, the point for measuring the pulse was on the radial artery in the wrist at the TCM position of "guan." The probe pressure was adjusted to be between 40 mmHg and 60 mmHg. Each pulse was recorded for approximately 30 seconds. The time of day for the scheduled testing was between 9:00 and 11:00 or between 14:00 and 16:00. All participants were tested at the same location, and the room temperature was maintained between 25°C and 26°C. The right radial artery was recorded first, followed by the left radial artery.

### **Data Process**

The raw data from the pulse measurements were extracted in the time domain. We used the Fast Fourier Transform (FFT) function in the mathematical software Matlab 6.5.2 (MathWorks Inc.) to transform the raw data to their related frequency spectra and generate the spectrum figures.

Upon examination of the spectrum figures, we found the harmonic peaks at

different frequencies, and we named them C1, C2, C3, C4, C5, C6, C7, C8, C9 and C10, from the lowest to the 10<sup>th</sup> harmonic frequency. The central frequency of each harmonic was a multiple of the lowest harmonic frequency. By integrating the area under the spectrum curve, we obtained the power value for each harmonic. The values after the 11<sup>th</sup> peak were small enough to be ignored. Referring to Professor Wang's (2002) "organ resonance" hypothesis (Wang *et al.*, 1988; Wang *et al.*, 1988), these harmonics are thought to correspond to specific internal organs. For example, C1 corresponds to the liver, C2 to the kidney, C3 to the spleen, C4 to the lung, C5 to the stomach, C6 to the gallbladder, C7 to the bladder, C8 to the large intestine, C9 to the triple burner, and C10 to the small intestine (Wang, 2002). Calculation of the relative powers of the harmonics may provide insight into the status of the individual organs.

It must be noted that there is a discrepancy in Wang's hypothesis. Based on conjecture, Wang suggested that the first harmonic should be attributed to the liver meridian (Wang, 2002). However, on examining the results from the pulse spectrum, the resonance frequency of the first harmonic was the same as the heartbeat frequency. Only a correspondence with the heart could give rise to this effect of perfect resonance with the heartbeat frequency. According to Wang's hypothesis, the relationships among the harmonics are in order of the liver, kidney, spleen, and so on, as mentioned above (Liou *et al.*, 2011). However, according to the results of the pulse spectrum, the

first harmonic should be attributed to the heart, and the remainders are ordered similarly to Wang's hypothesis as liver, kidney, spleen, and so on (Wang *et al.*, 2003; Jan *et al.*, 2003; Chang *et al.*, 1995). In this study, we follow Wang's interpretation, i.e., that the first harmonic corresponds to the liver meridian.

### **Statistical Analysis**

The statistical software that we used was SPAS 17.0 for Windows (SPAS Inc.) For the BPD group and the healthy group, the variables for analysis included age, energy values of the harmonics, and relative percentage of the harmonic resonance. A two-sample *t*-test was employed for the comparison. In addition, a chi-squared test was used to analyze the gender distribution between the BPD group and the healthy group. For the harmonic resonance energy values and the relative percentages of the harmonics read from the right and left hands, we used a paired-sample *t*-test to compare the differences. Statistical significance was defined as  $p < 0.05$ .

### **Results**

Normally, Chinese medicine doctors diagnose the pulse pattern with their three fingers. They make diagnoses by detecting the pressure variation along the time flow. Therefore the sense of touch is mainly in the time domain. However, from the view of



a physicist, any periodic motion may cause resonance phenomenon. A certain response may be observed right at a specified frequency. We know the pulse wave vibrates periodically, so, as expected, it may have resonance effects connecting to its surroundings. That is the reason we want to transform the original pulse waveforms into frequency spectra to analyze the possible resonance effects, including the frequency and the intensity properties. Wang (Wang, 2002) proposed that the first resonance of the pulse wave referred to as the first harmonic, which is an index of liver, and the second, the index of kidney, and then the spleen, the lung, the stomach, and so on. Since in TCM, theories are always based on experience, Wang's hypothesis attempts to give an explanation of TCM with a physical meaning.

A two-sample *t*-test was employed to compare the harmonic spectra from the radial arteries of the BPD group with those from the healthy group. Table 1 shows the results of the harmonic spectrum of the right radial artery, and Table 2 shows the harmonic spectrum of the left radial artery.

The harmonics of the BPD group were lower than those in the healthy group for the right radial artery (Fig. 1A), and there was a significant difference for C4, which corresponds to the lung meridian.

The harmonics of the left radial artery showed similar results, except for C1 and C2. The harmonics of C1 and C2 in the BPD group were higher than those in the

healthy group, whereas for the other harmonics, the spectrum energy of the BPD group was lower than that of the healthy group (Fig. 1B). In addition, the  $p$  value for C3 between the two groups was 0.059, which approached significance.

Furthermore, when we transformed the energy of each harmonic into percentages of the total energy (see Tables 3, 4 and Fig. 2), the relationships of the energy percentages between the two groups differed, especially in C3 (spleen meridian) and C4 (lung meridian). The relative percentages of C3 and C4 of the BPD group were much lower than those of the healthy group ( $p=0.015$ ,  $p=0.003$ , respectively), whereas for C5 (the stomach meridian), the difference between the two groups was not significant ( $p = 0.069$ ). Similarly, using the measurements from the left hand, we found that in C3, C4, and C5, the relative percentages of the BPD group were much lower than those of the healthy group ( $p=0.018$ ,  $0.038$ ,  $0.014$ , respectively).

In this study, we found that in both hands, the C3 harmonics of the BPD group were less than those of the healthy group. For the right hand, the C3 harmonic in the healthy group was  $2,534.67 \times 10^5 \pm 324.47 \times 10^5$ , and the C3 harmonic in the BPD group was  $1,859.91 \times 10^5 \pm 262.61 \times 10^5$ ,  $p= 0.111$ . For the left hand, the C3 harmonic in the healthy group was  $2,324.74 \times 10^5 \pm 312.20 \times 10^5$ , and the C3 harmonic in the BPD group was  $1,626.04 \times 10^5 \pm 180.96 \times 10^5$ ,  $p=0.059$ .

The relative percentage of the individual harmonic in C3 (spleen meridian) was

different between the BPD group and the healthy group. The relative percentage of the harmonic in C3 was significantly lower in the BPD group than in the healthy group ( $p=0.018$ ). For the values of the right hand, the relative percentage of the harmonic was  $10.79\pm 1.01\%$  for the healthy group and  $7.85\pm 0.59\%$  for the BPD group ( $p=0.015$ ). Similarly, for the left hand, the relative percentage of the harmonic for the healthy group was  $9.88\pm 0.93\%$  and that for the BPD group was  $7.85\pm 0.59\%$  ( $p=0.018$ ).

When we compared the harmonic energy data from the right and the left hands, there was a significant difference in C5 (stomach meridian,  $p=0.042$ ). However, when we compared the relative energy percentages from the right and the left hands, no significant differences were found ( $p > 0.05$ ).

## **Discussion**

Although the symptoms of psychiatric diseases manifest in thinking, emotion and behavior, TCM theories indicate that psychiatric illnesses may be caused by dysfunction of the internal organs. TCM theories assume that the mechanism of BPD includes internal damage from seven emotions, improper dietary habits, and genetic inheritance. There are three possible factors that cause the abovementioned disorders. First, anger inflames the liver and damages the spirit. Second, sudden panic causes

manic psychosis. Third, thinking too much hurts the heart-spleen, or the phlegm and Qi depression causes depressive psychosis and depression.

TCM theories claim that the heart controls the spirit, organs, and mental behaviors. The “Five Elements” theory claims that the element of the heart is fire and the element of the spleen is earth. Because earth is produced from fire, the heart is the mother of the spleen. Therefore, heart disease will cause deterioration in the spleen, which explains the correlation of psychiatric disease with the spleen.

The measured harmonic and the relative percentage of the harmonic energy in C3 (the spleen meridian) was significantly different between the BPD group and the healthy group. In the BPD group, the energy of the spleen meridian was lower than that of the healthy group, which indicates that the relationship between the spleen meridian and BPD involves some stagnation in the spleen meridian in BPD patients.

Moreover, TCM theories presented in texts such as the Synopsis of the Gold Chamber (Jin-Kui-Yao-Lue) claim that the heart, the liver and the spleen regulate mood, i.e., joy is related to the heart, anger is related to the liver and worry is related to the spleen. We believe that the spleen affects the emotional changes seen in BPD patients, and we assert that the relative percentage of the harmonic in C3 (the spleen meridian) is related to the BPD syndromes. Another question is whether the harmonic

in C3 (the spleen meridian) may serve as an indicator to evaluate the status of the disorder (e.g., the response to drug treatment), and whether greater benefit would be obtained from treating a patient who has relatively less harmonic energy with spleen-regulating drugs. All of these topics warrant further investigation.

Through radial artery harmonic energy analysis, we found that the right C5 (stomach meridian) harmonic was  $331.37 \times 10^5 \pm 55.37 \times 10^5$  for the BPD group and  $436.29 \times 10^5 \pm 56.15 \times 10^5$  for the healthy group,  $p=0.189$ . The left C5 (stomach meridian) harmonic was  $265.76 \times 10^5 \pm 34.72 \times 10^5$  for the BPD group and  $360.81 \times 10^6 \pm 57.99 \times 10^6$  for the healthy group,  $p=0.165$ . Although these differences were not statistically significant, the energy of the BPD group overall was less than that of the healthy group. When we analyzed the energy percentages of the radial artery harmonics, there were statistically significant differences between the groups for the right C5 harmonic ( $1.40 \pm 0.15$  for the BPD group and  $1.93 \pm 0.24$  for the healthy group,  $p=0.069$ ) and the left C5 harmonic ( $1.40 \pm 0.15$  for the BPD group and  $1.59 \pm 0.17$  for the healthy group,  $p=0.014^*$ ). According to TCM theories, the spleen and the stomach share the same origin. When the spleen is weak, the stomach becomes weak, and the stomach meridian therefore decreases accordingly. Furthermore, when used as an acupuncture point, the stomach meridian can regulate mental conditions, which also confirms the relationship between the stomach meridian and BPD.

TCM theories indicate that psychiatric disorders are caused by the stagnation of the liver Qi and inflammation of the heart energy. According to the concept of the five elements, the element of the liver is wood, and the element of the spleen is earth. The controlling cycle of the five elements is also applicable to the five viscera. Table 2 and Figure 2 show that compared with the healthy group, the value of harmonic C1 (the liver meridian) was much higher in BPD patients, whereas the value of harmonic C3 (the spleen meridian) was lower. This finding suggests that the syndrome of BPD results from an increase in liver energy together with the stagnation of the spleen.

We also found relatively low energy in the C4 harmonic of both hands in the BPD group. The lung is considered to be the son of the spleen, and this finding provides evidence of an association between the lung meridian and the spleen meridian. The values of both C3 and C4 were lower in the BPD group than in the healthy group.

As expressed in TCM theories, the syndrome comprised of the ascendant hyperactivity of the liver yang, the repressed spleen Qi and the inflamed heart Qi could be regarded as the disease pattern of BPD. In this study, we confirmed an important relationship between C3 and BPD. TCM proposes that obsessively worrying for a long time or thinking too much causes many disorders in a process called the “internal damage of seven emotions.” Being highly obsessed with work may damage the spleen and the stomach and may also cause Qi stagnation. The patient experiences lassitude, somnolence and poor concentration. In Western

medicine, during a manic episode, the patient experiences the flight of ideas, whereas during a depressive episode, the patient becomes inert and slow. Referring to the theory of five viscera, Western medicine seems to share similar concepts with TCM.

In this study, we used sphygmography and digital signal processing analyses to confirm the important relationship between C3 (the spleen meridian) and BPD under TCM theory. We have also used these methods to investigate psychiatric diseases. We intend to establish a basic set of data for BPD patients to establish the relationship of pulse diagnosis to clinical features. Furthermore, in the future, we hope to set the criteria for evaluating the prognosis of mental disorders using pulse diagnosis and to provide new references for drug responses.

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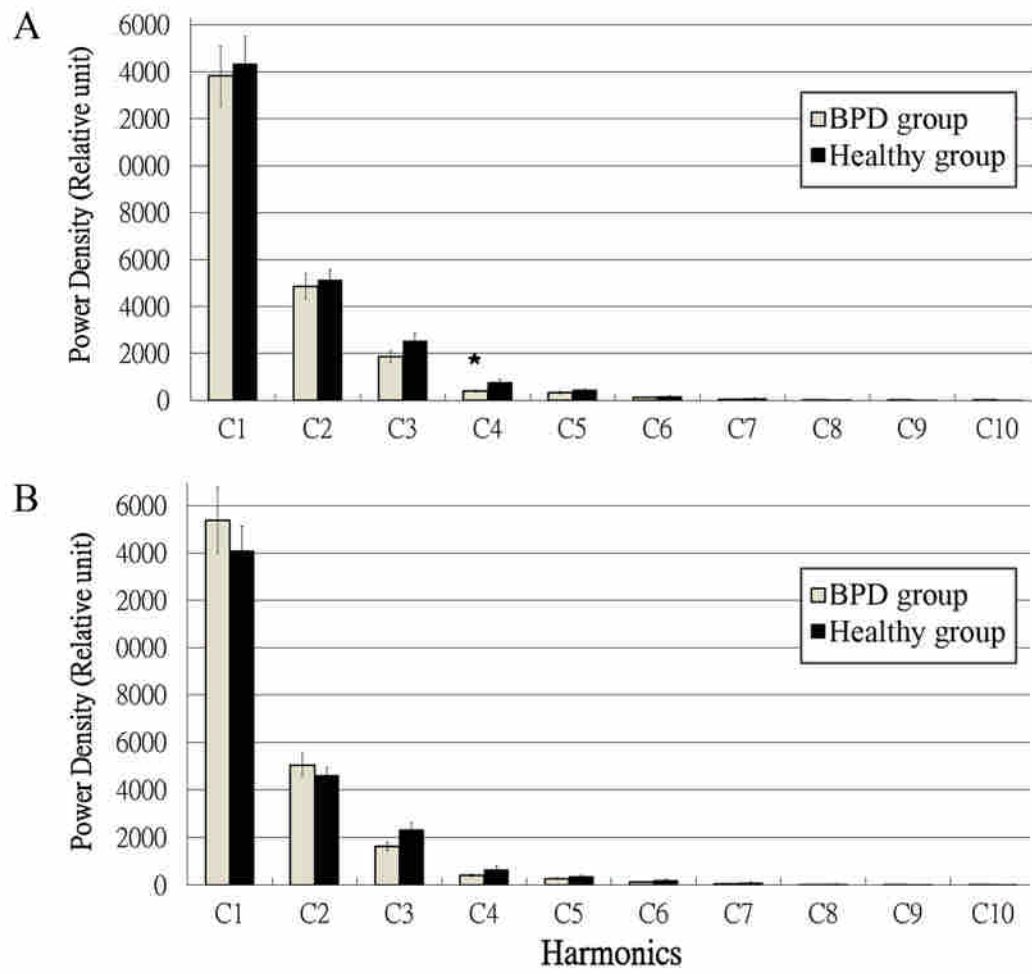
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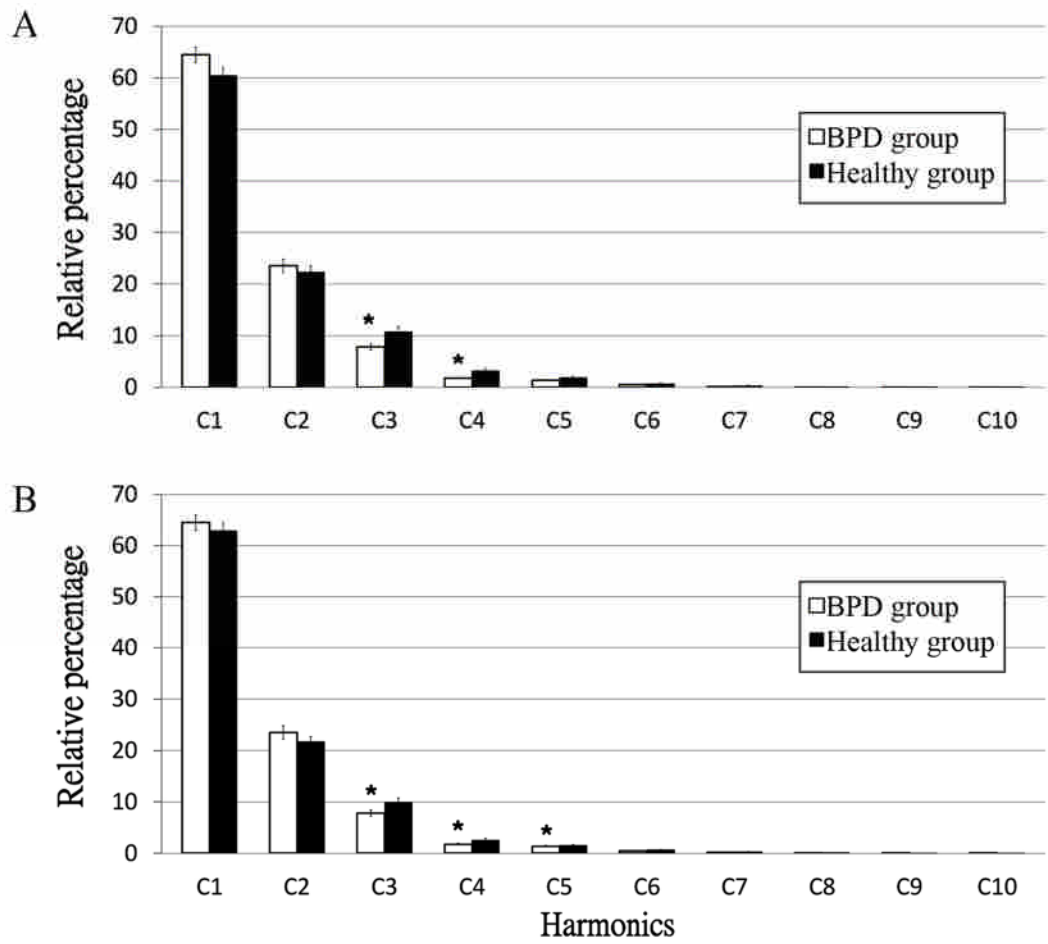
### ***Figure legends***

Fig.1. Harmonic energies of the BPD group and the healthy group. A) is for the right hands. B) is for the left hands. \* indicates statistical significance between the two groups ( $p < 0.05$ ).

Fig 2. Relative Percentages of the Harmonics of the BPD group and the healthy group. A) is for the right hands. B) is for the left hands. \* indicates statistical significance between the two groups ( $p < 0.05$ ).



**Figure 1**



**Figure 2**

Table 1. Spectrum Harmonic of the Right Radial Artery Pulse (in relative units)

	bipolar disorder ( $\times 10^5$ ) Mean $\pm$ SD	sub-healthy ( $\times 10^5$ ) Mean $\pm$ SD	<i>p</i> value
C1	13823.11 $\pm$ 1281.38	14350.17 $\pm$ 1155.66	0.761
C2	4865.38 $\pm$ 532.75	5145.59 $\pm$ 436.83	0.686
C3	1859.91 $\pm$ 262.61	2534.67 $\pm$ 324.47	0.111
C4	401.33 $\pm$ 50.10	762.44 $\pm$ 125.17	0.011*
C5	331.37 $\pm$ 55.37	436.29 $\pm$ 56.15	0.189
C6	135.85 $\pm$ 26.83	176.70 $\pm$ 27.60	0.293
C7	43.83 $\pm$ 8.49	78.66 $\pm$ 25.52	0.200
C8	21.90 $\pm$ 5.07	27.83 $\pm$ 6.36	0.469
C9	13.26 $\pm$ 2.77	12.84 $\pm$ 2.17	0.904
C10	7.94 $\pm$ 1.80	9.10 $\pm$ 1.46	0.619

Table 2. Spectrum Harmonic of the Left Radial Artery Pulse (in relative units)

	bipolar disorder ( $\times 10^5$ ) Mean $\pm$ SD	sub-healthy ( $\times 10^5$ ) Mean $\pm$ SD	<i>p</i> value
C1	15380.28 $\pm$ 1401.08	14092.21 $\pm$ 1046.44	0.464
C2	5042.91 $\pm$ 478.25	4617.55 $\pm$ 316.44	0.461
C3	1626.04 $\pm$ 180.96	2324.74 $\pm$ 312.20	0.059
C4	400.27 $\pm$ 56.74	649.97 $\pm$ 158.44	0.143
C5	265.76 $\pm$ 34.72	360.81 $\pm$ 57.99	0.165
C6	116.47 $\pm$ 24.15	189.40 $\pm$ 53.06	0.216
C7	49.98 $\pm$ 13.88	98.41 $\pm$ 46.80	0.325
C8	18.17 $\pm$ 2.96	37.47 $\pm$ 15.74	0.233
C9	11.34 $\pm$ 2.15	16.33 $\pm$ 3.73	0.251
C10	8.73 $\pm$ 2.63	10.73 $\pm$ 2.86	0.608

Table 3. Relative Percentages of the Harmonics in the Right Radial Artery Pulse

	<b>BPD (%)</b> <b>Mean±SD</b>	<b>Sub-healthy(%)</b> <b>Mean±SD</b>	<b><i>p</i> value</b>
C1	64.50±1.54	60.46±1.63	0.071
C2	23.51±1.33	22.31±1.14	0.498
C3	7.85±0.59	10.79±1.01	0.015*
C4	1.80±0.15	3.24±0.43	0.003*
C5	1.40±0.15	1.93±0.24	0.069
C6	0.53±0.07	0.75±0.10	0.092
C7	0.17±0.02	0.32±0.09	0.089
C8	0.08±0.01	0.12±0.02	0.165
C9	0.05±0.01	0.06±0.01	0.492
C10	0.03±0.004	0.04±0.01	0.176

Table 4. Relative Percentages of the Harmonics in the Left Radial Artery Pulse

	<b>BPD (%)</b>	<b>Sub-healthy(%)</b>	<i>p</i> value
	<b>Mean±SD</b>	<b>Mean±SD</b>	
C1	64.58±1.54	62.96±1.53	0.083
C2	23.51±1.33	21.73±0.98	0.506
C3	7.85±0.59	9.88±0.93	0.018*
C4	1.80±0.15	2.60±0.34	0.038*
C5	1.40±0.15	1.59±0.17	0.014*
C6	0.53±0.07	0.68±0.11	0.337
C7	0.17±0.02	0.31±0.09	0.263
C8	0.08±0.01	0.13±0.03	0.093
C9	0.05±0.01	0.07±0.01	0.142
C10	0.03±0.004	0.04±0.01	0.999