Investigation of Heart Rate Variability using Wavelet Packet Transform in Major Depressive Disorder

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Abstract
Depression is a common mood disorder that is characterized by impairment of mood regulation, and loss of interest in enjoyable activities. According to the previous studies, it has been reported that this disorder is related with elevated rates of cardiovascular morbidity and mortality. Therefore, as an important indicator for diagnosis and classification of cardiac dysfunctions, heart rate variability (HRV) has been widely used in depression. Differ from the previous studies in this field, wavelet packet transform (WPT) is used for determination of effective very low frequency (VLF), low frequency (LF), and high frequency (HF) bands in HRV signals of depressed patients in this study. Twenty patients who met the DSM-IV criteria for major depressive disorder and age, gender-matched twenty healthy controls were participated for this study. HRV data of these participants were first were recorded using the Brainamp ExG data acquisition system and then decomposed into sub-bands including VLF, LF, HF using WPT with 9 level Daubechies (db4) family and variations of energy in these bands were analyzed in MATLAB. The HRV measures as each sub-band average energy and sympathovagal balance (LF/HF ratio) were compared statistically between patients and controls. The results of this study indicates that especially the mean energy values of sub-frequency ranges in VLF band for each participant are higher than that the values of other bands as LF and HF. In addition, the mean energy values of the regions in LF band of control subjects are significantly lower than the same measure of patients. In contrast, in comparison with control subjects, patients with major depression exhibited low HF band energy. Finally, results indicate that sympathovagal balance that reflects the equilibrium between sympathetic and parasympathetic activity of the autonomic nervous system in patients was higher than that of control subjects indicating autonomic dysfunction throughout the entire experiment. It can be conclude that low cardiovagal activity in patients with major depression may contribute to the higher cardiac dysregulations of these patients.

Keywords: major depressive disorder, heart rate variability, wavelet packet transform, sympathovagal balance

Introduction
Major depressive disorder is a common psychiatric condition comprising depression, loss of interest, pleasure and other symptoms [1]. Related to autonomic nervous system (ANS) dysfunction in patients, individuals suffering from depression often have decreased vagal tone, increased heart rate, fatigue, sleep disturbance, and sympathetic arousal [2]. Moreover, it has been reported that the existence of depressive disorder is associated with cardiovascular morbidity and mortality [3,4]. Therefore, as a cost-effective and non-invasive procedure, heart rate variability (HRV) analysis has been widely used for assessing the cardiac autonomic modulation.

However, inconsistent results have been reported in these studies investigating HRV in depressive patients. In some of these studies, depressive patients show a reduction of HRV [5,6] or no HRV difference compared to controls [7]. On the other hand, consistent with altered cardiac ANS function, increased heart rates have been reported in patients with depression and this situation has been suggested as an important risk factor for sudden cardiac death [4]. In most of these studies, ECG has been used for HRV analysis. Besides, as an easy, noninvasive and optical method, photoplethysmography (PPG) have also been proposed for HRV analysis in numerous studies [8,9]. It has been reported that instead of the RR intervals of ECG signals, the peak-to-peak (PP) intervals in the PPG can be used for HRV analysis. In the frequency domain HRV analysis, the PPG data can be divided into very low frequency (VLF), low frequency (LF), and high frequency (HF)
bands. Among them, the LF band (0.04-0.15 Hz) reflects both sympathetic and parasympathetic activities and the HF band (0.15-0.40 Hz) is only associated to parasympathetic activity [10]. Moreover, the ratio of the LF to HF power (LF/HF) that is an important characteristic for evaluating sympathovagal balance widely used another frequency domain HRV measures. The purpose of this study was to analyze frequency domain HRV features of depressive patients and healthy control subjects using PPG data. Unlike the previous researches in this field, wavelet packet transform (WPT) is used for determination VLF, LF, and HF bands and LF/HF ratio in PPG based HRV analysis of patients.

**Patients and Methods**

20 depressed patients and 20 age and gender-matched healthy controls were studied in this research (Table 1). The patients with major depressive disorder, diagnosed by the Structured Clinical Interview for DSM-IV Axis-I Disorders, were recruited from Psychiatry Department of Fatih University, Sema Hospital. Fatih University ethics committee approved the study and an informed consent was obtained from all participants before the study. Patients with prior history of cardiovascular, pulmonary or other psychiatric diseases were excluded from the study.

Data acquisition was started after a resting, adaptation period of approximately 3 min. PPG data were acquired for all subjects while they were instructed to sit on a chair without moving. For data collection, Brainamp ExG data acquisition system (Brain Products GmbH, Munich, Germany) and the associated software were used. The blood pulse sensor was strapped on to the index finger of subject’s non-dominant hand and data were recorded for 5 minutes and sampled with 250 Hz.

**Data Analysis**

The data analysis was performed in MATLAB 7.6® software package. The obtained PPG signals were first preprocessed using the Butterworth filters as 8th order low-pass with 8 Hz cutoff frequency and 4th order high-pass with 10 Hz cutoff frequency in order to eliminate any motion artifact or noise. Then, an algorithm was implemented to find the peak-to-peak (PP) intervals of the data. The PP interval data were interpolated with a cubic spline interpolation and resampled with 4 Hz sampling frequency. In the last step of preprocessing, a sliding window average filter was used to select only the normal-to-normal beats of the data for HRV analysis without any occasional ectopies and/or arrhythmic beats. Finally, the data were decomposed into sub-bands with a 9 level db4 (daubechies) WPT. As a generalization of discrete wavelet transform, in WPT, both the approximation and detail coefficients are further decomposed at each level (Figure 1).

Therefore, using these decomposition 512 wavelet packets was obtained and between 1-9th nodes were defined as very low frequency, between 10-38th nodes were defined as low frequency (LF) and between 39-102th nodes were defined as high frequency (HF) bands.

In these frequency bands, the mean RMS energy values of nodes were calculated using the following formula [12]

$$W_{rms,m,j} = \frac{1}{N} \sum |W_{m,j}(f)|^2$$  (1)
where $m$ denotes the decomposition level, $n$ shows total number of elements in the packet, $j$ is the index of node in each level, and $r$ is an index for elements of the packet. The total energy was calculated as

$$E_{w_{rms,m}} = \sum_{j=0}^{M} |w_{rms,m,j}|^2$$  (2)

where $M$ is the last decomposition level. Then, the average energy values in each node were calculated for both patients and controls. The HRV measures as each sub-band average energy and sympathovagal balance (LF/HF ratio) were calculated in patients and controls.

**Statistical Analysis**

The results were evaluated statistically using the SPSS® (version 20.0) statistical software package. Levene’s test was used to test the homogeneity of groups’ variances. According to this test results, comparisons of HRV features between the patients and controls were compared using an independent sample Student’s t-test.

**RESULTS**

In this study, PPG data were recorded from patients with depression and healthy controls to investigate frequency domain HRV features. A sample PPG data obtained from a patient is shown in Figure 2. In this figure, while horizontal axis shows time, the vertical axis illustrates PP intervals (PPint).

Table 2 lists the calculated frequency domain HRV measures between depressive patients and control subjects. We found statistically significant differences in extracted frequency domain measures of HRV between patients and control subjects.

Table 2. Obtained HRV measures in patients and controls

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>LF energy</td>
<td>$0.6576 \pm 0.34$</td>
<td>$0.4668 \pm 0.19$</td>
</tr>
<tr>
<td>HF energy</td>
<td>$0.9273 \pm 0.41$</td>
<td>$0.9819 \pm 0.48$</td>
</tr>
<tr>
<td>LF/HF ratio</td>
<td>$0.729 \pm 4.14$</td>
<td>$0.551 \pm 5.72$</td>
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</tbody>
</table>

**DISCUSSION AND CONCLUSION**

It has been reported that altered autonomic function is related to higher rates of cardiac disease and morbidity in patients with depression. Therefore, HRV analysis has become a powerful and useful tool in clinical research to assess ANS dysfunction in these patients. We aimed to investigate the PPG based HRV frequency parameters using WPT. It was found that depressive patients had higher LF band energies and lower HF energy as compared to the control subjects’ values as shown in Figure 3. Frequency domain analyses reveal that the patient group also exhibited significantly increased LF/HF ratio when compared to healthy subjects.

**DECLARATION OF INTEREST**

The authors declare no conflict of interest for this study.
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REFERENCES


