The Analysis of Youngster with Fever by Using Instantaneous Pulse Rate Variability

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***Abstract*—Body temperature is an important homeothermic autoregulation of humans. Body temperature is usually controlled by autonomic nervous system (ANS). When a person has suffered a virus or bacterial infection, it causes fever. The ANS rises the body temperature by tachycardia and cutaneous vasomotion. The common non-invasive indication for ANS is based on heart rate variability (HRV) and pulse rate variability (PRV). However, these two methods are limited by the timescale of time series. Instantaneous PRV (iPRV) was proposed as a surrogate of HRV in frequency domain and breaks the restriction of timescale. In this paper, thirty subjects were recruited for the study; the body temperature and the photoplethysmography (PPG) signal were acquired in supine position for ten minutes. Fifteen fever subjects, whose body temperature was higher than 37.9 °C, are in Group Fev., the others are in Group Ctr. The results show that the power of iPRV in normalized low frequency (nLF) in Group Fev.(0.63±0.13, $p<0.05$) was significantly higher than that in Group Ctr.(0.47±0.16). And the power of iPRV in normalized high frequency (nHF) in Group Fev.(0.38 ±0.13, $p<0.05$) was significantly lower than that in Group Ctr.(0.54±0.16). Besides, the nVHF might have a potential for indicating the peripheral circulation and providing more information about body regulation.**

Keywords-photoplethysmography; instantaneous pulse rate variability; body temperature; fever; autonomic nervous system; peripheral circulation.

I. INTRODUCTION

Body temperature, which usually refers to the rectal temperature in animals, is an important homeothermic autoregulation of humans. In many mammals, the preoptic area (POA), a region of hypothalamus, is considered as the thermoregulatory center. The normal body temperature is about 36.5°C~37.5 °C and it is affected by the environmental temperature. When the receptor receives an environment temperature change, POA controls some organs activities or reaction to regulate the body temperature, and then the body temperature also sends feedback to POA for maintaining the body temperature. Sometimes, an abnormal rise in body temperature occurs, which is higher than normal body temperature, and we call it fever. It is usually caused by infection of bacterium or virus. When a person gets fever, the hypothalamus changes the set point to the higher temperature and it makes the body feel cold because the body temperature is lower than the set point. Therefore, POA tries to rise the body temperature [1].

There are many mechanisms to regulate the body temperature like cutaneous vasomotion, tachycardia, etc. Most of them are controlled by the autonomic nervous system (ANS), which is dominated by POA. So, the body temperature regulation can be observed by ANS activities [2].

Heart rate variability (HRV) [3], a common assessment for cardiovascular circulation in clinic, has been widely used as an ANS activities observation. It is measured by a non-invasion instrument, electrocardiogram (ECG), and calculated by beat-to-beat interval (RRI, which is the interval between R peaks in ECG.) series to get time domain or frequency domain index. However, the study of HRV is limited by timescale because of RRI (Fig 1(a)).

Pulse rate variability (PRV), another non-invasive method, was proposed for replacing HRV to provide not only ANS activities but also the information of peripheral circulation (Fig. 1(b)). PRV is measured by photoplethysmography (PPG) and calculated by peak-to-peak interval (PPI) instead of ECG and RRI. Previous studies have determined that PRV acts as a surrogate of HRV during non-stationary conditions [4][5]. Nevertheless, timescale of PPI still restricted the study of PRV.

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Because both HRV and PRV have timescale restrictions, a new measurement named instantaneous pulse rate variability (iPRV) was proposed [6]. iPRV adopts the PRV technique and the Hilbert-Huang transform (HHT) [7] for breaking the timescale limitation. However, there is a problem called mode-mixing problem that occurs during the process of empirical mode decomposition (EMD) in the HHT. For solving this problem, ensemble EMD, a noise-assisted technique, was proposed [8]. Previous studies have determined that iPRV is reliable by using PPG during non-stationary condition [9][10], and iPRV can not only observe ANS activities like HRV and PRV, but also provide higher frequency band information [6]. Nevertheless, the meaning of this frequency band still is undetermined.

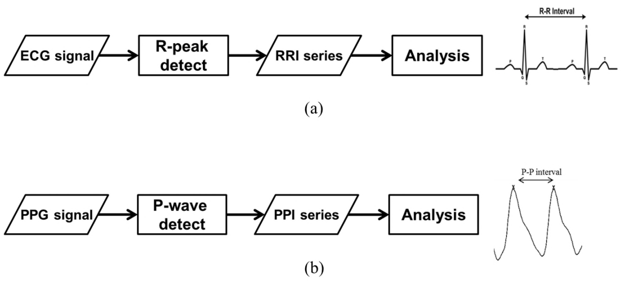


Figure 1. The steps of HRV and PRV: (a) HRV analysis and R-R interval. (b) PRV analysis and P-P interval

Body temperature is part of a mechanism of body regulation. We can assess the health status of a person by observing the variety of body reactions, such as ANS activities and peripheral circulation, when body temperature change. Peripheral blood vessels constrict when a person gets fever. It is possible to observe the regulation of peripheral blood vessels in VHF. This paper applied the iPRV method to compare the difference between fever patients and others and to find out the meaning of the index calculated by iPRV.

II. METHOD

A. Subjects and data collection

The experiment was carried out in Yo-Yo Clinic, Kaohsiung, Taiwan. The body temperature was measured by ear thermometer (Radiant TH889, Radiant Innovation Inc.) and the signal was acquired by PPG (Nonin 8500, Nonin Medical Inc.) with 200 Hz sampling rate.

Thirty subjects (19 males; age 10.5±2.9), whose ages were 7 to 18 years old, were recruited in this study. Fifteen subjects (10 males; age 10.1±2.4) with fever, whose body temperature was higher than 37.9 °C, served as Group Fev. and the others served as Group Ctr. We measured the body temperature of all recruited subjects before the experiment. Then participants wore the PPG sensor on the right index finger and rested quietly in supine position for 10 minutes. This experiment was approved by the institutional review board of the National Chiao Tung University. Informed consent was obtained from all subjects before the experiment.

B. iPRV procedure

iPRV applies the frequency extension method based on HHT [7] to PRV for the continuous-time heart rate rhythm. There is an important process during HHT called EMD. The steps of EMD are shown in Fig. 2. First, find the local maximum and local minimum, compute upper envelope and lower envelope by cubic spline and calculate the mean of these two envelopes. Then use the input data to subtract the average envelope. The above steps make up what is called the sifting process. After the sifting process, use the input data to subtract the average envelope and determine if the result is intrinsic mode functions (IMF) or not. It is IMF if the data satisfies by following two requirements: one is that the number of local extrema must be equal to the number of zero-crossings or differ at most by one, and two, is that, at any point, the value of the average envelope must approximately equal to zero. If it is not IMF, replace the input data by the result and redo the sifting process. Else, output the IMF and subtract the input data by this IMF to get the residue. Determine if the residue is a monotonic function or not. If it is not monotonic function, let residue be the input

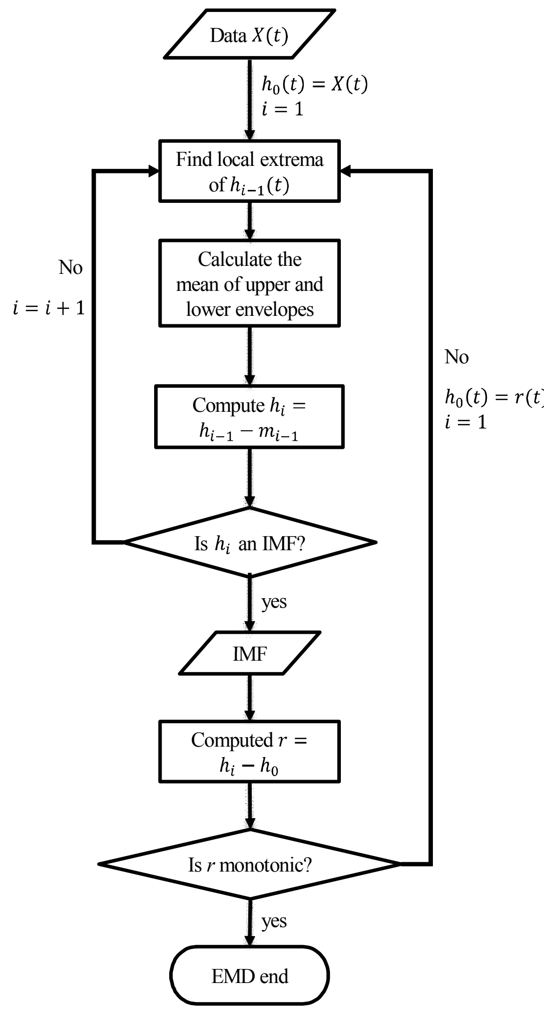


Figure 2. The EMD algorithm.

data and redo the above steps. Otherwise, the EMD finishes, and there are many IMFs decomposed by EMD.

However, there is a problem called the mode-mixing problem that may occur during the EMD process. For solving it, the ensemble EMD method (EEMD) was proposed [8]. EEMD is similar to EMD, but it adds white noise before the sifting process to solve the mode-mixing problem. In addition, EEMD does many times the EMD and averages the output IMFs and average the output IMFs to reduce the effect of white noise (Fig. 3).

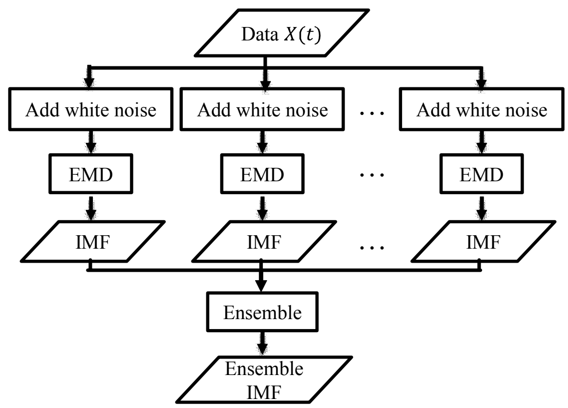


Figure 3. The EEMD algorithm.

After the EEMD process, one of the IMFs which is sinusoid-like is considered as the heartbeats component and is used for calculating the instantaneous frequency (IF) by normalized direct quadrature (NDQ) [11].

The steps of iPRV are shown in Fig 4. One of the IMFs extracted from the input PPG data by using EEMD is used as continuous-time heart rate rhythm. The IF is computed by NDQ and gets the instantaneous period (iPeriod) estimated by the inversion of IF of IMF. The Fast Fourier transform (FFT) is applied for power spectral analysis to estimate each frequency band including low frequency (LF, 0.04 to 0.15 Hz), high frequency (HF, 0.15 to 0.4 Hz) and very high frequency (VHF, 0.4 to 0.9 Hz) [3][6]. Besides, the iPRV spectrum can find the heartbeats peak in much higher frequency band (Fig. 5). The spectral analysis programs in this study were developed by using a commercial software platform (LabVIEW version 2013, National Instruments Corp., Austin, USA).

The normalized LF power (nLF) and normalized HF power (nHF) without VHF is calculated as in

$$nLF = LF / (TP - VHF) \tag{1}$$

$$nHF = HF / (TP - VHF) \tag{2}$$

where TP means total power and is computed as

$$TP = LF + HF + VHF \tag{3}$$

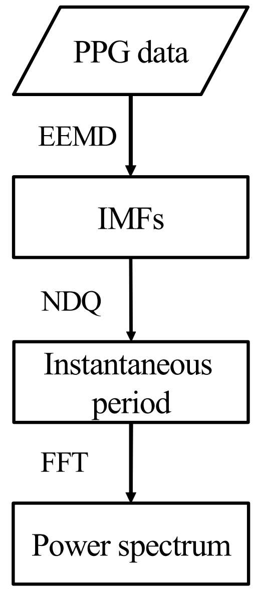
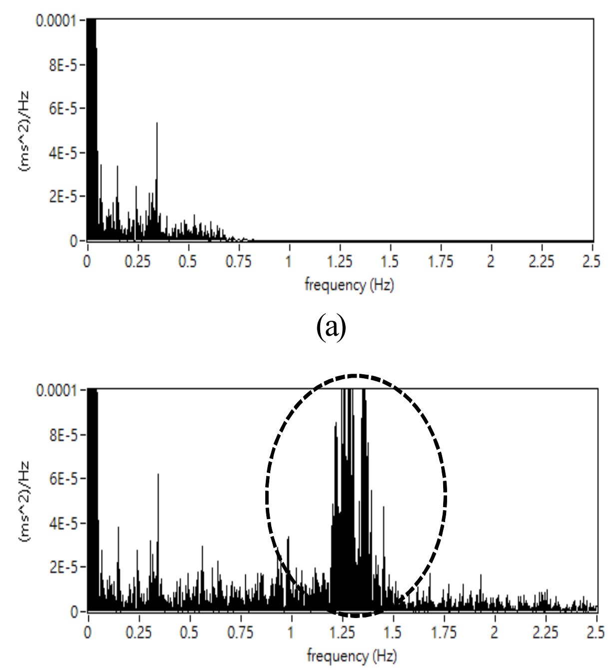


Figure 4. The iPRV procedure.



(a)

(b)

Figure 5. The comparision between PRV and iPRV spectrum: (a) PRV spectrum. (b) iPRV spectrum, which can observe the heartbeats peak on spectrum.

And, if we calculate the normalized power including the VHF, the representation is as follow

$$nLF \text{ (including VHF)} = LF / TP \tag{4}$$

$$\text{nHF (including VHF)} = \text{HF} / \text{TP} \tag{5}$$

$$\text{nVHF (including VHF)} = \text{VHF} / \text{TP} \tag{6}$$

LF to HF ratio is computed as in

$$\text{LF-HF ratio} = \text{LF} / \text{HF} \tag{7}$$

III. RESULTS

The results of the body temperature, heartbeats per second and power spectral analysis between the two groups are shown in Table 1. The processing of the iPRV analysis between Group Fev. and Group Ctr. is illustrated in Fig. 6.

TABLE I. THE RESULT BETWEEN TWO GROUPS

	Group Fev.(15)	*Group Ctr.(15)*
Body temperature (℃)	38.41±0.46	36.33±0.32*
Heartbeats (Hz)	1.92±0.18	1.5±0.22*
nLF	0.63±0.13	0.47±0.16*
nHF	0.38 ±0.13	0.54±0.16*
nLF (including VHF)	0.33 ±0.12	0.26±0.11
nHF (including VHF)	0.19 ±0.07	0.31±0.12*
nVHF (including VHF)	0.49 ±0.14	0.43 ±0.1
LF-HF ratio	2.08 ±1.36	1.1±0.87*

The form is (mean ± standard deviation), * means p-value<0.05 compared with Group Fev.

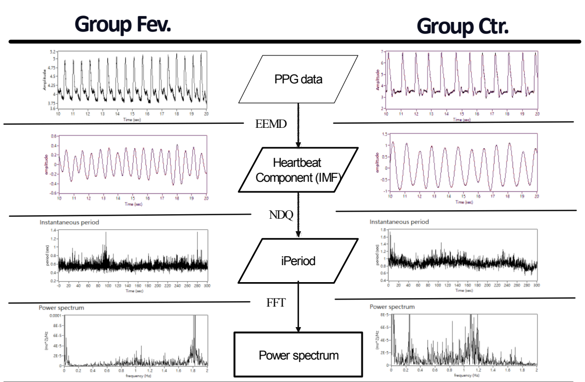


Figure 6. The iPRV analysis between two groups

The body temperatures in Group Fev.(38.41±0.46, $p<0.05$) are significantly higher than those in Group Ctr.(36.33±0.32). The heart rates in Group Fev.(1.92±0.18, $p<0.05$) are also significantly higher than those in Group Ctr. (1.5±0.22).

In frequency domain analysis, the nLF values in Group Fev.(0.63±0.13, $p<0.05$) are significantly higher than those in Group Ctr.(0.47±0.16) . The LF-HF ratios in Group Fev.(2.08 ±1.36, $p<0.05$) are also significantly higher than those in Group Ctr.(1.1±0.87). On the other hand, nHF values in Group Fev.(0.38 ±0.13, $p<0.05$) are significantly lower than those in Group Ctr.(0.54±0.16). If we calculate the normalized power including VHF, nHF values (including VHF) in Group Fev.(0.19±0.07, $p<0.05$) are significantly lower than those in Group Ctr.(0.31±0.12). In the nLF values (including VHF) and nVHF values (including VHF) can be observed a trend, and that trend is that the mean values of nLF (including VHF) in Group Fev.(0.33±0.12) are higher than those in Group Ctr.(0.26±0.11) and the mean of nVHF values (including VHF) in Group Fev.(0.49±0.14) are lower than those in Group Ctr.(0.43 ±0.1).

IV. DISCUSSION

This study compares the difference between Group Fev. and Group Ctr. by iPRV analysis. The result shows that the person whose body temperature is higher usually had higher number of heartbeats. The relationship between body temperature and heartbeats per second is drawn in Fig 7. However, it is not absolute because the heart rate is not only influenced by body temperature. It is also influenced by the environment temperature, others diseases, age and gender. Nonetheless, the body temperature is still an important factor to affect the heart rate.

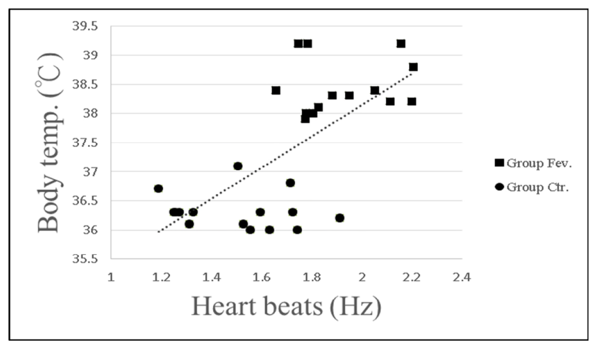


Figure 7. The relationship between body temperatur and heartbeats per second in all subjects.

Heart activities are usually dominated by ANS. It is considered that the heart rate increases because the sympathetic system is more excited than the parasympathetic system, and, on the contrary, the heart rate decrease because the parasympathetic system is more excited than the sympathetic system. The conventional HRV analysis in frequency domain is usually used for the ANS activity observation. The nLF is the percentage of LF in the sum of LF and HF is usually thought as the activities of sympathetic, and the nHF is the percentage of HF in the sum of LF and HF is usually considered as the activities of parasympathetic. The ratio of LF to HF is considered as the regulation of sympathetic [3]. The correlation of iPRV and HRV in the frequency domain analysis during non-stationary conditions has been examined in LF and HF [6][9]. HRV analysis in frequency domain rarely uses VHF because of the timescale problem, but iPRV breaks the restriction and provides more information in VHF.

The ANS rises the body temperature when someone has fever [1][2]. Therefore, the sympathetic is more excited than the parasympathetic. Regarding the results in Table 1., the value of nLF and LF-HF ratio in Group Fev. is significantly higher than Group Ctr. This means that the sympathetic is actually more excited in fever patients. This result is the same as the hypothesis.

If calculating the normalized power including VHF, only the nHF values (including VHF) in Group Fev. are significantly lower than those in Group Ctr. There is a trend, and that trend is that the mean value of the nLF (including VHF) and nVHF (including VHF) are larger in Group Fev., though this is not significant. Maybe the nLF values (including VHF) and the nHF values (including VHF) do not only represent the activities of sympathetic and parasympathetic, but have more regulation mixed in them. For VHF, maybe there is too much information to indicate the difference between the two groups. The meaning of these normalized powers need further research to examine.

For the new frequency band, VHF proposed by iPRV, previous studies have assumed that VHF has possible meaning of cardiac output or peripheral circulation [6][12][13]. In this study, the fever patients have the constriction of peripheral blood vessels, and it increases blood pressure. These situations cannot be observed in LF and HF by conventional HRV analysis. So, the VHF band might also contain information of regulation between the peripheral blood vessels and blood pressure, and the normalized power calculated including VHF might contain the regulation of ANS and peripheral circulation. The VHF bandwidth is very wide (0.4 to 0.9 Hz), it is possible to find more useful information by separating the band into more numbers of narrow bandwidth. It needs further research and investigation for verification.

V. Conclusion

This study compares the difference between the fever patients and people without fever by iPRV analysis and the results showed that iPRV can explore ANS function as conventional HRV analysis and, furthermore, provides more information owing to the new frequency band (VHF). The VHF has a possibility to indicate the regulation between the peripheral blood vessel and blood pressure or more regulation among ANS activities, heart activities and peripheral circulation. Nevertheless, it still needs further work to verify its feasibility. Even so, it still has the potential to be a useful indicator for healthcare by iPRV analysis.

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