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Spectral Analysis of Pulse Transit Time Variability and Its Coherence with Other Cardiovascular Variabilities

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Abstract—**Pulse transit time (PTT) has been reported correlated with heart rate (HR) and blood pressure (BP), however, the results are not consistent in different investigations. Towards a better understanding of the underlying mechanisms of the PTT changes, this study compares the power spectrum density of the variability in PTT with that in HR and BP under rest and post-exercise physiological conditions. Coherence function is also examined to quantify the strength of coupling between paired variabilities. The results show that the pulse transit time variability (PTTV) has significant coherence (>0.5) with heart rate variability (HRV) and blood pressure variability (BPV) under all physiological conditions at high frequency (HF). However, at the low frequency (LF) band, the coherence reduced to insignificance immediately after the exercise (≤5 minutes after exercise) and then return back to significant level 9 minutes after the exercise. The results show that PTTV is strongly coupled with HRV and BPV at the HF, indicating that the parasympathetic modulation could be the main cause of PTTV. The unstable coupling relationship of PTTV with BPV at LF should raise caution in the beat-to-beat BP estimation by PTT in the dynamic situation.**

I. Introduction

It is well known that the variation of some cardiovascular parameters, such as heart rate variability (HRV) and blood pressure variability (BPV), at different frequency bands are attributed to various autonomic control mechanisms. The established understanding of HRV and BPV has provided useful information to predict abnormalities in hemodynamics and prevent cardiovascular mortality [1-5]. Analysis on the power spectrum density (PSD) is one most frequently used approach to investigate autonomic control on cardiovascular system. Two major components around 0.1 Hz (LF) and 0.25 Hz (HF) were mostly investigated since 1) the HF component corresponding to the respiratory rhythm is a marker of vagal modulation, 2) the LF component indicates the sympathetic activities, and 3) the reciprocal relationship between these two rhythms would characterize the sympathovagal balance [6]. Under the same scenario, other cardiovascular variables could also be regulated by the similar regulative mechanisms of HRV and BPV.

Pulse transit time (PTT), defined as the time interval for a blood pressure (BP) pulse to travel from one arterial site to another, also shows a spontaneous fluctuation. In common practice, PTT is obtained at periphery, usually finger or toe, and timed from the R-wave of ECG to the arrival of the BP pulse, which is represented by the foot of photoplethysmographic (PPG) signal. As PTT to the large extent depends on the arterial properties, which is related to BP level, it has been employed for BP estimation [7, 8] and adopted for the studies of sleep-apnea [9] and vascular reactivity [10]. Although the regulative mechanism underlying PTT variation would be important for clinical applications, it has not been systematically studied yet. The purpose of this paper is to study the PTT regulation mechanism.

Recent studies revealed that the spontaneous fluctuation in PTT was associated with HRV [11] and highly correlated with BPV [12] in time domain. Taking advantage of the known autonomic regulations reflected by variability power spectrum, we investigate the PSD of PTTV and its coherence with HRV and BPV under different physiological conditions. Specifically, the coherence spectrum is adopted to quantify the strength of the coupling between PTTV and HRV and BPV for understanding the possible underlying mechanisms of PTT variations. The analysis is based on the experimental data collected from 12 healthy subjects under rest and post-exercise statuses.

II. Methodology

A. Data Acquisition

Twelve healthy volunteers (4 females and 8 males), aged 21-28 years old without known cardiovascular abnormalities, participated in this study. Each subject submitted an informed consent before conducting the experiment. Upon their arrival, subjects were asked to sit down and relax for 10 minutes to stabilize their BP level. For the data collection, continuous BP was recorded from the middle finger of right hand by Finometer (FMS, Finapres Medical System BV, The Netherlands); standard lead I ECG signal was collected by an ECG machine (GRASS, Astro-med, Inc.); and reflective PPG signal was detected at the index fingertip of right hand by a self-designed sensor.

Each subject contributed 15 sets of data in total under three physiological conditions: rest, immediately after exercise (≤5 minutes after exercise), and post-exercise recovery (9~60 minutes after exercise). After three successive trials at rest, the subject was introduced to a treadmill running for 4 minutes at the speed of 10km/h. Immediately after the dynamic exercise, a 5-minute recording was carried out as the 4^{th} trial. During the 9^{th}~60^{th} minute after the exercise, another eleven 20-second recordings were conducted. The whole

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experimental procedure was summarized by Table 1.

TABLE 1
EXPERIMENT PROCEDURE

Physiological conditions	Trial No	Time	Recording length
Rest	1	1st min	20 s
	2	2nd min	20 s
	3	3rd min	20 s
Dynamic exercise (4-minute running at 10km/h)			
Immediately after exercise	4	0 min	5 mins
Post-exercise recovery	5	9th min	20 s
	6	11th min	20 s
	7	13th min	20 s
	8	15th min	20 s
	9	20th min	20 s
	10	25th min	20 s
	11	30th min	20 s
	12	40th min	20 s
	13	50th min	20 s
	14	55th min	20 s
	15	60th min	20 s

In each trial, continuous BP, ECG and PPG signal were measured simultaneously. All of the collected signals were sampled at 1 kHz and stored for off-line analysis. A manual mercury sphygmomanometer (TXJ-10, Desk Model, Japan), as the "golden standard", was operated by a registered nurse at brachial arteries in the 1st and 3rd trials for validating the effectiveness of the measurements. Data from two subjects were rejected because of too frequent recalibration by Finometer in the BP recording in the 4th trial, where the beat-to-beat information was hard to be extracted. Finally, data of 150 trails from 10 subjects were analyzed.

B. Parameter Extraction

The raw data were first processed by a sliding window with window length of 10 milliseconds. The beat-to-beat parameters were extracted as shown in Fig.1. Specifically, pulse transit time (*ptt*) is defined as the time interval between the R-wave of ECG and the frontal foot of the PPG pulse within in the same cardiac cycle; systolic BP (*sbp*) and diastolic BP (*dbp*) are the peak and foot values of the BP pulse, respectively. The variability in each parameter was calculated as the beat-to-beat difference of the successive values. The HRV was represented by the beat-to-beat variability in the R-R intervals from ECG.

C. Power Spectrum Estimation

Before the PSD estimation, each series of beat-to-beat variability was first interpolated to an evenly sampled signal with sampling frequency of 2.5 Hz. Weltch method was adopted to estimate the PSD of the investigated variabilities.

The squared coherence spectrum $K^2(f)$, a measure of the coupling strength between two signals in frequency domain, was estimated for paired PTTV and HRV and BPV, respectively.

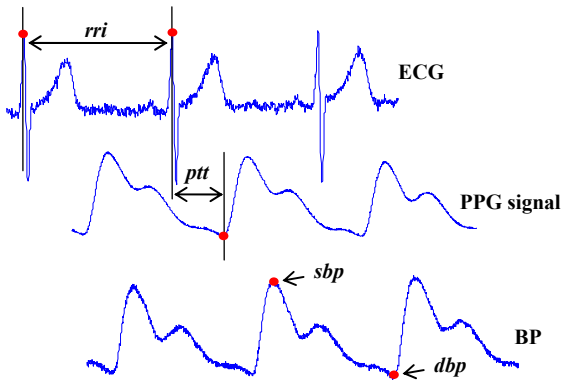

Fig.1 Variables extracted from the raw data

The squared coherence $K^2(f)$ of two variable (x and y) has the value between 0 to 1 and is defined as

$$K^2(f) = \frac{|P_{xy}(f)|^2}{|P_{xx}(f)||P_{yy}(f)|} \quad (1)$$

where $P_{xy}(f) = X^*(f)Y(f)$ is the cross-spectrum of x and y (* denotes the complex conjugate); and $P_{xx}(f)$ and $P_{yy}(f)$ are the PSD of x and y, respectively.

III. RESULTS

As the HF and LF components were usually investigated to reveal autonomic regulations, this study also focused on the comparison among PTTV, HRV, and BPV spectra at these two frequency bands. Specifically, the LF band was defined as [0.04Hz, 0.15Hz]. Considering the respiratory frequency could be significantly different after dynamic exercise, the HF band was chosen as the [HF_{ct}-0.055Hz, HF_{ct}+0.055Hz], where HF_{ct} is the center frequency of the HRV within 0.15~0.5 Hz. In such a way, the frequency span for both HF and LF is 0.11Hz.

By visual observation, a distinctive peak at HF can be clearly detected in all the PSD of HRV, BPV, and PTTV. However, no substantial conclusion can be made on the appearance of the peak at LF. Figure 2 presents representative PSD of the investigated variabilities from one subject under different physiological conditions. In this individual case, it showed that the LF power in the PSD of SBPV and DBPV was enhanced immediately after the exercise, while, no corresponding change presented in the PSD of HRV and PTTV.

In order to reveal possible mechanisms of PTT variation, we applied the coherence function between PTTV and HRV or BPV, the latter two of which have been frequently used to indicate cardiovascular regulations. Specifically, 0.5 is regarded as significant coherence as adopted in previous studies [13].

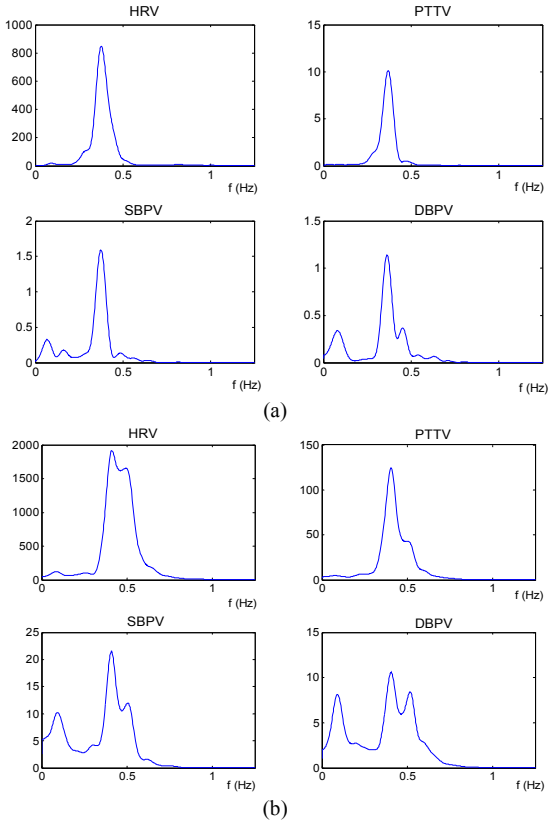

Fig.2 Representative PSD of the investigated variability signals (a) at rest and (b) immediately after dynamic exercise.

Figure 3 gives example of the squared coherence spectra, which correspond to the signals shown in Fig.2. As expected, the absence of the peak at LF in the PTTV spectra results in low coherence between PTTV and both SBPV and DBPV, especially immediately after the exercise. In addition, the mean squared coherences at different frequency are summarized in Table 2.

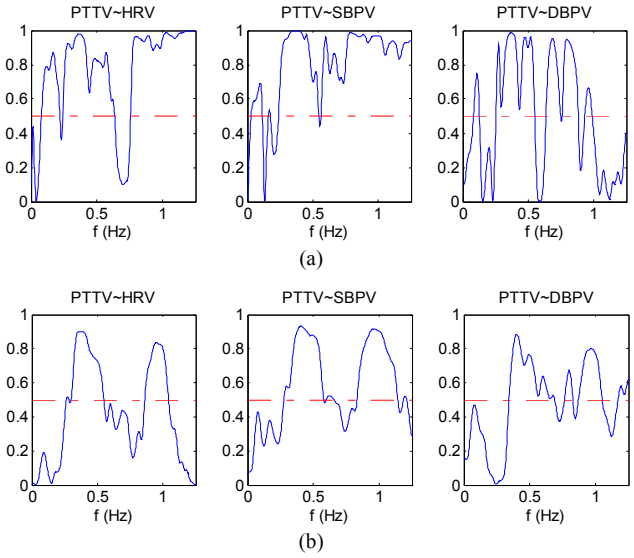

Fig.4 Representative squared coherence spectra between paired cardiovascular variabilities (a) at rest and (b) immediately after dynamic exercise.

TABLE 2
MEAN SQUARED COHERENCE (K^2) BETWEEN PAIRED VARIABILITIES

		whole fre.[1]	LF	HF
PTTV~HRV	R^2	0.64±0.09	0.71±0.17	0.88±0.12
	IAE[3]	0.38±0.13	0.33±0.18	0.76±0.21
	Rec[4]	0.63±0.08	0.68±0.19	0.87±0.12
	all[5]	0.62±0.11	0.66±0.21	0.87±0.13
PTTV~SBPV	R	0.68±0.11	0.62±0.17	0.85±0.15
	IAE	0.31±0.12	0.28±0.14	0.78±0.12
	Rec	0.65±0.11	0.68±0.18	0.82±0.17
	all	0.63±0.14	0.64±0.2	0.82±0.17
PTTV~DBPV	R	0.64±0.09	0.60±0.19	0.80±0.19
	IAE	0.25±0.1	0.28±0.16	0.52±0.23
	Rec	0.61±0.09	0.65±0.18	0.76±0.16
	all	0.59±0.13	0.62±0.21	0.75±0.18

Notes:
1. the whole investigated frequency band: 0~1.25Hz
2. trials at rest: 1st~3rd trails
3. trials immediately after exercise: 4th trial
4. trials at recovering stage: 5th ~ 15th trials (5~60 minutes after exercise)
5. all investigated trials (15 trials for each subject)

IV. DISCUSSIONS AND CONLUSIONS

The dynamic interplay between ongoing perturbations to the circulation reflects the responsible regulation mechanisms mediated by autonomic nervous system, which could be indicated by the PSD of HRV or BPV. It was suggested: 1) HF component (around 0.25 HZ), corresponding to the respiratory rhythm, is governed exclusively by the parasympathetic nervous system that is mediated by vagus nerves, and 2) LF fluctuations (around 0.1 Hz) are jointly mediated by the β-sympathetic and parasympathetic nervous systems [6, 14]. As summarized in a review paper [15], some previous studies suggested that the pattern of PTT changes due to the respiratory events are stable. From the spectral examination in this study, it is evident that the power of PTTV is centered at HF, at which PTTV also has significant coherence (>0.5) with HRV and BPV. Such results imply that PTTV is mainly caused by the parasympathetic regulations.

From physiological point of view, the PTT investigated in this study includes two components, the pre-ejection period (PEP) and the pulse propagation time in artery. A previous study concluded that during an inspiratory effort, the afterload on the heart increase would prolong the time between electrical depolarization and aortic valve opening that enlarges PEP [16], hence possibly leading to an increase in PTT. On the other hand, the respiratory activity mechanically induces inter-beat variations in intrathoracic pressure resulting in changes in arterial BP [14], and thereby alters the arterial elasticity and the pulse wave velocity (PWV). Equations 2 (Moens-Korteweg model [7]) and 3 (Hughes model [17]) illustrate the relationship between PWV and BP.

$$c = \sqrt{\frac{gEh}{2r\rho}} \tag{2}$$

where c is PWV; g is the gravitational constant; h is the wall thickness; r is the arterial radius; ρ is the density of the blood, and E is the Young's modulus of the artery that is associated with the BP level as

$$E = E_0 e^{\alpha P} \quad (3)$$

where E_0 is the zero-pressure modulus and α is a constant which depends on the vessel properties. As the pulse wave propagation time is inversely proportional to the PWV, changes in BP will also cause PTT variations. Since both components of PTT are influenced by the respiratory activity, the distinctive peak at HF of PTTV can be reasonably attributed to the same mechanisms of HRV and BPV at HF, i.e. the parasympathetic regulation.

It is well known that when the baseline conditions of human body are altered, the functional adaptation of the cardiovascular system is achieved by varying the autonomic control patterns. Dynamic exercise is one typical way to change such baseline. The withdrawal of the parasympathetic nerve outflow and the increase in sympathetic nerve stimulation to the heart are the main causes for the exercise tachycardia [18]. Table 2 illustrates that all the coherences decreased immediately after the exercise, and then returned to the baseline level during the recovery period. Specifically, the investigated coherences at LF were all reduced into insignificance (<0.5), while, they kept at significant level at HF. It may be postulated that the varied sympatho-vagal balance caused by dynamic exercise would lower the coupling relationship of PTTV with HRV and BPV, especially in LF component.

Because cardiovascular system is maintained by a complex control loop, fluctuations in PTT, HR, and BP may result from different interactions of the respective autonomic controls. The results of this preliminary study demonstrate that PTTV is mainly caused by parasympathetic regulations and significantly coupled with HRV and BPV at HF. The results further support the application of PTTV as an indicator of respiratory effort. Besides, caution should be raised for BPV estimation by PTTV, especially in LF component, due to instable coherence between them under dynamic conditions.

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REFERENCES

[1] S. L. Dawson, B. N. Manktelow, T. G. Robinson, R. B. Panerai, and J. F. Potter, "Which parameters of beat-to-beat blood pressure and variability best predict early outcome after acute ischemic stroke?," *Stroke*, vol. 31, pp. 463-468, 2000.

[2] P. v. D. Borne, N. Montano, K. Narkiewicz, J. P. Degaute, A. Malliani, M. Pagani, and V. K. Somers, "Importance of ventilation in modulating interaction between sympathetic drive and cardiovascular variability," *Am. J. Physiol. Heart Circ. Physiol.*, vol. 280, pp. H722-H729, 2001.

[3] D.-F. Su and C.-Y. Miao, "Blood pressure variability and organ damage," *Clinical and Experimental Pharmacology and Physiology*, vol. 28, pp. 709-715, 2001.

[4] M. Pagani, "Circadian heart rate and blood pressure variability considered for research and patient care," *International Journal of Cardiology*, vol. 87, pp. 29-30, 2003.

[5] G. Piccirillo, C. Naso, A. Moise, M. Lionetti, M. Nocco, S. d. Carlo, T. d. Laurentis, D. Magri, M. Carriafesta, and V. Marigliano, "Heart rate and blood pressure variability in subjects with vasovagal syncope," *Clinical Science*, vol. 107, pp. 55-61, 2004.

[6] A. Malliani, M. Pagani, F. Lombardi, and S. Cerutti, "Cardiovascular neural regulation explored in the frequency domain," *Circulation*, vol. 84, pp. 482-492, 1991.

[7] W. Chen, T. Tobahashi, S. Ichikawa, Y. Takeuchi, and T. Togawa, "Continuous estimation of systolic blood pressure using the pulse arrival time and intermittent calibration," *Med. & Biol. Eng. & Comput.*, vol. 38, pp. 569-574, 2000.

[8] C. C. Y. Poon and Y. T. Zhang, "Cuff-less and noninvasive measurements of arterial blood pressure by pulse transit time," presented at the 27th IEEE Int. Conf. of Engineering in Medicine and Biology Society, Shanghai, China, 2005.

[9] D. J. Pitson, A. Sandell, R. v. d. Hout, and J. R. Stradling, "Use of pulse transit time as a measure of inspiratory effort in patients with obstructive sleep apnoea," *Eur. Respir. J*, vol. 8, pp. 1669-1674, 1995.

[10] J. E. Naschitz, R. Itzhak, N. Shaviv, I. Khorshidi, S. S. Isseroff, M. Fields, R. M. Priselac, D. Yeshurun, and E. Sabo, "Assessment of cardiovascular reactivity by fractal and recurrence quantification analysis of heart rate and pulse transit time," *Journal of Human Hypertension*, vol. 17, pp. 111-118, 2003.

[11] M. J. Drinnan, J. Allen, and A. Murray, "Relation between heart rate and pulse transit time during paced respiration," *Physiological Measurement*, vol. 22, pp. 425-432, 2001.

[12] T. Ma and Y. T. Zhang, "A Correlation Study on the Variabilities in Pulse Transit Time, Blood Pressure, and Heart Rate Recorded Simultaneously from Healthy Subjects," presented at The 27th Annual Conference of IEEE Engineering in Medicine and Biology Society, Shanghai, China, 2005.

[13] R. W. deBoer and J. M. Karemaker, "Relationship between short-term blood-pressure fluctuations and heart-rate variabiliity in resting subjects I: a spectral analysis approach," *Med. & Biol. Eng. & Comput.*, vol. 23, pp. 352-364, 1985.

[14] S. Akselrod, D. Gordon, F. A. Ubel, D. C. Shannon, A. C. Berger, and R. J. Cohen, "Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control," *Science*, vol. 213, pp. 220-222, 1981.

[15] R. P. Smith, J. Argod, J.-L. Pepin, and P. A. Levy, "Pulse transit time: an appraisal of potential clinical applications," *Thorax*, vol. 54, pp. 452-458, 1999.

[16] J. Brock, D. Pitson, and J. Stradling, "Use of pulse transit time as a measure of changes in inspiratory effort," *J. Ambul. Monit.*, vol. 6, pp. 295-302, 1993.

[17] D. J. Hughes, C. F. Babbs, L. A. Geddes, and J. D. Bourland, "Measurement of Young's modulus of elasticity of the canine aorta with ultrasound," *Ultrasonic Imaging*, vol. 1, pp. 356-367, 1979.

[18] P. Terziotti, F. Schena, G. Gulli, and A. Cevese, "Post-exercise recovery of autonomic cardiovascular control: a study by spectrum and cross-spectrum analysis in humans," *Eur. J. Appl. Physiol.*, vol. 84, pp. 187-194, 2001.