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Heart Rate Variability and Multi-Site Pulse Rate Variability for the Assessment of Autonomic Responses to Whole-Body Cold Exposure

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***Abstract*— Heart rate variability (HRV) is a noninvasive marker of cardiac autonomic activity and has been used in different circumstances to assess the autonomic responses of the body. Pulse rate variability (PRV), a similar variable obtained from pulse waves, has been used in recent years as a valid surrogate of HRV. However, the effect that localized changes in autonomic activity have in the relationship between HRV and PRV has not been entirely understood. In this study, a whole-body cold exposure protocol was performed to generate localized changes in autonomic activity, and HRV and PRV from different body sites were obtained. PRV measured from the earlobe and the finger was shown to differ from HRV, and the correlation between these variables was affected by the cold. Also, it was found that PRV from the finger was more affected by cold exposure than PRV from the earlobe. In conclusion, PRV is affected differently to HRV when localized changes in autonomic activity occur. Hence, PRV should not be considered as a valid surrogate of HRV under certain circumstances.**

***Clinical Relevance*— This indicates that pulse rate variability is affected differently to heart rate variability when autonomic activity is modified and suggests that pulse rate variability is not always a valid surrogate of heart rate variability.**

I. Introduction

Heart Rate Variability (HRV) measures the dynamics of heart rate (HR) through time, and has been widely used as a noninvasive alternative to understand the autonomic activity and to assess the balance between the parasympathetic and sympathetic branches of the autonomic nervous system (ANS), [1]. HRV is usually measured from an electrocardiogram (ECG), by identifying the QRS complexes of the signal and measuring the time difference between consecutive R peaks [1]. HRV has been shown to reflect the regulation of autonomic balance, blood pressure, gas exchange, and gut, heart, and vascular tone, among others. Also, an optimal level of variation in HR has been related to health and self-regulatory capacity, and adaptability to different and changing environmental conditions [2].

In an attempt to minimise the complexity of the systems used to obtain HRV information by ECG, several researchers have aimed to explore different signals from which the cardiac cycle information can be retrieved. Photoplethysmography (PPG) has then been suggested as the logical alternative, due to its simplicity, widespread use, noninvasive nature, and cost-effectiveness [3]. From this pulsatile signal, which optically measures the changes in blood volume in tissue [4], the pulse rate (PR) can be estimated, and the variability of this PR can be obtained. This variability is usually referred to as Pulse Rate Variability (PRV) and has been applied in different studies as a validate surrogate of HRV, in areas such as sleep studies, mental health, and cardiovascular diseases. However, the relationship between HRV and PRV is not entirely understood, and although some researchers claim that PRV can be used as a surrogate of HRV [6, 7], it has been stated that this is only true when the subjects under investigation are healthy, young, and in resting states [7]. PRV has been found to be influenced by technical factors, such as the fiducial points used for measuring the cardiac cycles [8], and the sampling rate of the PPG signal [9]; as well as by physiological aspects, such as the variability of the pulse transit time [10], the nature of the PPG and ECG signals [7], and changes in cardiovascular behaviour [11].

It has been shown that whole-body cold exposure causes localised alterations in the autonomic responses when measured using multi-site PPG signals [12]. Hence, this study aims to evaluate if these changes affect the relationship between PRV and HRV when the former is measured from different body locations. It was hypothesized that PRV reflects localised changes, similarly to what was concluded in [12], generating differences in the relationship between HRV and PRV due to cold exposure and body location.

II. Materials and Methods

A. Experimental protocol

Twenty healthy volunteers (11 male, 30.3 ± 10.4 years old) were recruited to take part in the study. All subjects were normotensive, normothermic, and did not take any medication at the time of the study. The subjects were asked to refrain from ingesting beverages with caffeine and alcohol, and not to exercise or smoke at least 2 hours before the test. To maximize the effect of cold temperatures on the vasculature, subjects were asked to wear only one layer of clothes during the data acquisition session. The study protocol was approved by the City, Senate Research Ethics Committee, and all subjects gave informed consent before taking part in the study.

Left index finger (F) and earlobe (EL) PPG, both based on infrared light (peak emission wavelength of 870 nm), and ECG signals, were obtained from each subject during the recording phase of the study. PPG and ECG measurements were acquired using a research PPG acquisition system (ZenPPG),

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developed in the Research Centre for Biomedical Engineering, from City, University of London [13]. All signals were acquired at a sampling rate of 1 kHz.

Upon arrival, subjects were seated for at least 10 minutes in a room maintained at 24 ± 1 °C and after this period, the sensors for acquiring the signals were attached to the subject. The measurement started with a 2-min baseline measurement (BM), in which signals were recorded from the subjects while the room temperature was kept at 24 ± 1 °C. Once the 2 minutes were over, the volunteers were moved to an adjacent, controlled-temperature room, maintained at 10 ± 1 °C. Subjects remained in this room for 10 minutes (CE). Finally, the volunteers were moved back to the original room at 24 ± 1 °C for an additional 10 minutes (CR). After this time, the sensors were removed from the subjects. During each phase of the measurement protocol, subjects were seated in a comfortable chair, with both hands resting at an approximate heart level.

B. Signal acquisition and processing

The signals were down-sampled to 100 Hz to restrict the bandwidth of the signals and remove any unwanted noise. PPG signals were detrended, whereas the first and last 10 seconds of each stage of the protocol were removed. Then, PPG signals were filtered using a fourth-order bandpass Butterworth filter, with cut-off frequencies of 0.1 and 2 Hz. Different fiducial points such as systolic peaks, onsets of the pulse, maximum slope point, and the intersection point between tangent lines from the onset and the maximum slope point were obtained from each PPG signal. Using signal quality indices, the fiducial point that better segmented the pulses of each PPG signal was selected and used for measuring PRV.

The first 20 samples of the ECG signals in each stage were removed, and R peaks were identified applying the algorithm proposed in [14]. HRV was obtained by measuring the time difference between consecutive R peaks. Both from HRV and PRV data, time- (SDNN, RMSSD, and pNN50), frequency-domain (nLF, nHF, and LF/HF), and nonlinear (SD1, SD2, and SD1/SD2 from Poincaré plots) indices were extracted.

C. Statistical analysis

Normality of data was determined using a Shapiro-Wilk test and a significance level of 5% (p-value > 0.05) was considered significant for all analyses. Correlation analyses and Friedman rank sum tests were used for assessing how the relationship between HRV and PRV was affected by cold exposure. If results from the Friedman rank sum test showed a significant difference between HRV and PRV, post hoc tests were performed using Nemenyi's test. Spearman or Pearson correlation coefficients were considered for normally and non-normally-distributed data, respectively.

III. RESULTS

Fig. 1 illustrates the behaviour of the different indices measured from HRV, earlobe PRV and finger PRV, during each of the three stages, and results from the correlation analyses are shown in Table 1. Stronger correlations were obtained when PRV was measured from the earlobe, and pNN50 was the time-domain index with stronger correlations during all stages. Frequency-domain indices also showed strong correlations. Nevertheless, nonsignificant correlations were observed when PRV was measured from the finger, both in time-domain and nonlinear indices. Table 2 shows the results from the Friedman rank sum tests and its related post hoc analyses. Only comparisons between HRV and PRV from the earlobe and the finger are shown, denoted as MC-EL, and MC-F, respectively. It can be seen from these results that, during the three stages most indices measured from PRV differ from those measured from HRV, regardless of the location of the PPG sensor. It is also evident that cold exposure affects PRV both during and after the exposure to the low temperatures, but under resting, normal conditions, earlobe-derived PRV has more similar behaviour to HRV, than finger-derived PRV.

TABLE I. CORRELATION ANALYSIS RESULTS FOR THE COMPARISON BETWEEN HRV AND ECG DURING BASAL MEASUREMENT (BM), COLD EXPOSURE (CE) AND COLD RECOVERY (CR). HRV WAS OBTAINED FROM ECG SIGNALS, WHILE PRV WAS MEASURED FROM EARLOBE (EL) AND FINGER (F) PPG SIGNALS. | ρ |: CORRELATION COEFFICIENT. BOLDED VALUES INDICATE STATISTICALLY SIGNIFICANT CORRELATIONS.

Stage	**Index**	**HRV vs EL PRV**		**HRV vs F PRV**	
		| ρ |	***p – value***	***| ρ |***	***p – value***
BM	SDNN	**0.748**	**< 0.001**	0.378	0.101
	RMSSD	**0.578**	**0.008**	0.136	0.567
	pNN50	**0.905**	**< 0.001**	**0.614**	**0.005**
	nLF	**0.799**	**< 0.001**	0.417	0.069
	nHF	**0.477**	**0.034**	0.096	0.688
	LF/HF	**0.818**	**< 0.001**	0.152	0.521
	SD1	**0.578**	**0.008**	0.136	0.567
	SD2	**0.999**	**< 0.001**	**0.974**	**< 0.001**
	SD1/SD2	**0.554**	**0.011**	0.041	0.862
CE	SDNN	**0.798**	**< 0.001**	0.154	0.517
	RMSSD	**0.789**	**< 0.001**	0.295	0.207
	pNN50	**0.911**	**< 0.001**	**0.733**	**< 0.001**
	nLF	**0.642**	**0.003**	**0.753**	**< 0.001**
	nHF	**0.576**	**0.008**	**0.729**	**< 0.001**
	LF/HF	**0.690**	**0.001**	**0.753**	**< 0.001**
	SD1	**0.789**	**< 0.001**	0.295	0.207
	SD2	**0.949**	**< 0.001**	**0.861**	**< 0.001**
	SD1/SD2	**0.800**	**< 0.001**	0.244	0.299
CR	SDNN	**0.839**	**< 0.001**	0.126	0.594
	RMSSD	**0.767**	**< 0.001**	0.275	0.239
	pNN50	**0.905**	**< 0.001**	**0.499**	**0.027**
	nLF	**0.902**	**< 0.001**	**0.556**	**0.011**
	nHF	**0.815**	**< 0.001**	**0.651**	**0.002**
	LF/HF	**0.877**	**< 0.001**	**0.632**	**0.003**
	SD1	**0.767**	**< 0.001**	0.275	0.239
	SD2	**0.998**	**< 0.001**	**0.650**	**0.002**
	SD1/SD2	**0.722**	**< 0.001**	0.198	0.402

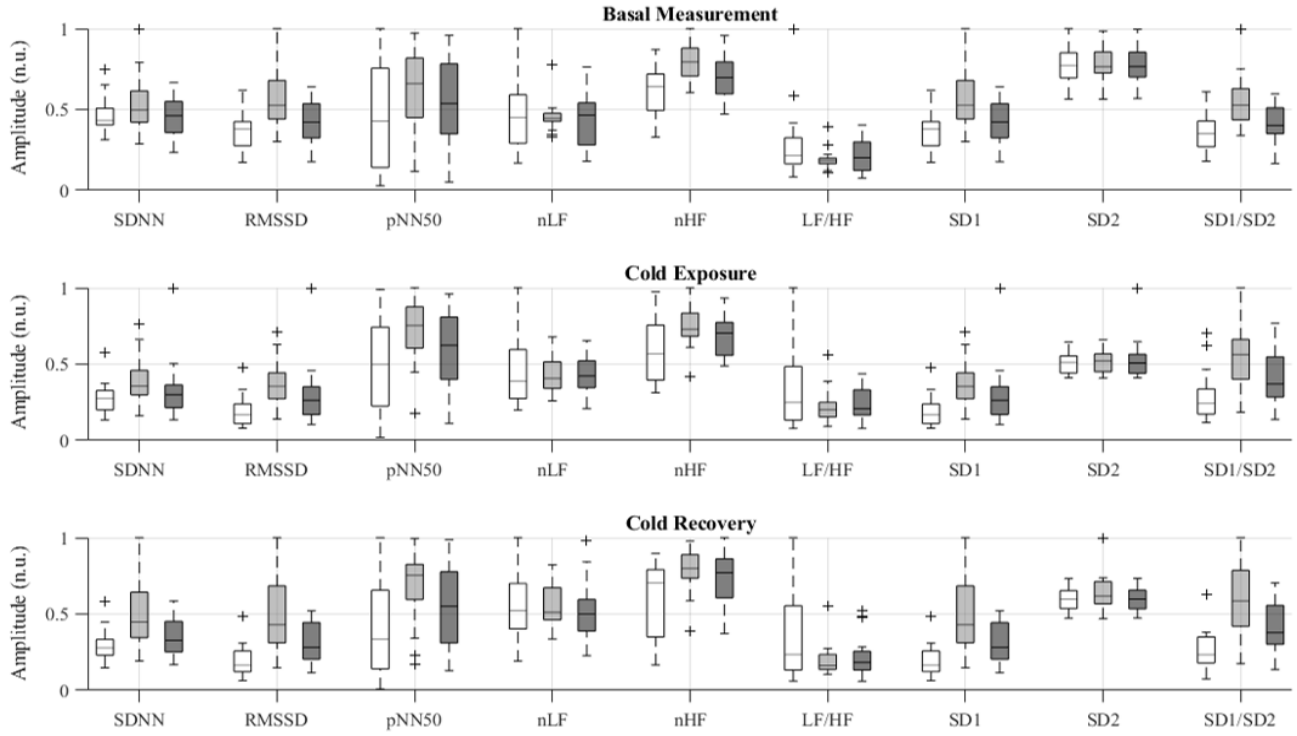

Figure 1. The behaviour of the time- (SDNN, RMSSD, pNN50), frequency-domain (nLF, nHF, LF/HF), and nonlinear (SD1, SD2, SD1/SD2) parameters obtained during each of the three stages of the test. White boxes: HRV-related information. Light grey boxes: Finger PRV-related information. Dark grey boxes: Earlobe PRV-related information.

The former does not show any significant difference after post-hoc analyses in any index. It is interesting to observe that nLF, LF/HF, and SD2 did not show any statistically significant difference between PRV and HRV in any of the temperature conditions. Additionally, SDNN was statistically similar between HRV and PRV from both locations during BM.

IV. Discussion

HRV is a valuable tool to understand the complex behaviour of the cardiac autonomic system [2]. PRV, a similar variable which describes the changes in time of PR, has gained important attention and several studies have applied PRV to obtain HRV-related information. However, the relationship between HRV and PRV is not fully understood, and several factors may affect it. One of the key factors that influences PRV results is the location at which the PPG signals are acquired. In an attempt to understand how localised alterations of autonomic activity may affect the relationship between HRV and PRV, a cold exposure study was carried out where PRV was measured from finger and ear lobe and HRV using the ECG. The whole-body cold exposure experiment was performed with 20 healthy volunteers.

Correlation analyses showed that, although it was expected to obtain significant correlations in every case, time-domain and Poincaré plot indices behaviour differed between HRV and PRV, when PRV was obtained from a peripheral tissue such as the finger. One of the main reasons for which PRV has been employed as a valid surrogate of HRV is the fact that HR is highly correlated with PR [7]. Nonetheless, these findings suggest that the relationship between PR and HR variabilities is not always linear, and that care should be taken when obtaining PRV from peripheral tissue under certain circumstances. Interestingly, frequency-domain indices did not show any nonsignificant correlations. This, however, could be explained by the short measurements taken during the study, especially during the basal measurement (2 minutes). The comparison between HRV and PRV, which was done using Friedman rank sum tests, showed that both PRV from the earlobe and the finger have statistically significant differences to HRV. These differences did not occur during any of the three stages of the test on nLF, LF/HF, and SD2, which are considered as long-term recordings [2]. Hence, PRV is mainly affected by changes that alter the short-term behaviour of localised ANS. It is worth remarking that, although SD1/SD2 and LF/HF indices have been considered to contain similar information regarding the sympathovagal balance [2], their behaviour is not the same, and SD1/SD2 shows differences between PRV and HRV that are not observable in frequency-domain. This could be due to the nature of the nonlinear indices obtained from Poincaré plot, and the fact that, since ANS behaves as a nonlinear, complex system, these indices may reflect the dynamic of the system more properly [15].

The differences observed between PRV and HRV may originate from physiological factors or from technical aspects. It is evident that the identification of pulses from a pulse wave such as the PPG can be less accurate than the detection of high-frequency R peaks from the ECG. Also, due to cold exposure, the morphology and quality of the PPG signal can be affected, making it harder to obtain reliable segmentation of the pulses. However, physiological factors such as pulse transit time and blood pressure variability have been proposed as a probable explanation of the differences between HRV and PRV [7]. Cold exposure alters vasoconstriction and blood pressure,

which could both affect the physiological origin of PRV, and the quality of the PPG signals obtained. If a robust processing of the PPG signal is performed, and the extracted PRV information is verified, then the differences between HRV and PRV may be considered mainly as physiologically based.

TABLE II. FRIEDMAN RANK SUM TEST AND DERIVED POST-HOC ANALYSES FOR THE COMPARISON BETWEEN HRV AND PRV, DURING BASAL MEASUREMENT (BM), COLD EXPOSURE (CE) AND COLD RECOVERY (CR). MULTIPLE COMPARISONS BETWEEN VALUES OBTAINED FROM HRV AND EARLOBE PRV (MC-EL), AND HRV AND FINGER PRV (MC-F) ARE SHOWN. BOLDED VALUES INDICATE STATISTICALLY SIGNIFICANT DIFFERENCES IN THE DISTRIBUTION OF DATA.

Stage	**Index**	**Friedman rank sum test**		**Nemenyi's test p-values (Multiple comparisons)**	
		χ^2	***p – value***	***MC- EL***	***MC-F***
BM	SDNN	4.300	0.116	0.415	0.709
	RMSSD	18.100	**< 0.001**	0.510	**< 0.001**
	pNN50	6.700	**0.035**	0.191	**0.031**
	nLF	0.300	0.861	1.000	0.883
	nHF	9.100	**0.011**	0.191	**0.008**
	LF/HF	1.900	0.387	0.415	0.510
	SD1	18.100	**< 0.001**	0.510	**< 0.001**
	SD2	1.300	0.522	0.946	0.709
	SD1/SD2	18.100	**< 0.001**	0.510	**< 0.001**
CE	SDNN	13.900	**0.001**	**0.031**	**0.001**
	RMSSD	19.600	**< 0.001**	**0.001**	**< 0.001**
	pNN50	16.300	**< 0.001**	**0.020**	**< 0.001**
	nLF	2.700	0.259	1.000	0.329
	nHF	12.700	**0.002**	**0.008**	**0.004**
	LF/HF	3.100	0.212	0.191	0.510
	SD1	19.600	**< 0.001**	**0.001**	**< 0.001**
	SD2	2.800	0.247	0.415	0.254
	SD1/SD2	20.100	**< 0.001**	**0.003**	**< 0.001**
CR	SDNN	16.900	**< 0.001**	**0.001**	**0.001**
	RMSSD	28.300	**< 0.001**	**< 0.001**	**< 0.001**
	pNN50	17.500	**< 0.001**	**0.004**	**< 0.001**
	nLF	0.900	0.638	0.609	0.883
	nHF	21.700	**< 0.001**	**< 0.001**	**< 0.001**
	LF/HF	4.900	0.086	0.099	0.191
	SD1	28.300	**< 0.001**	**< 0.001**	**< 0.001**
	SD2	3.215	0.200	0.290	0.254
	SD1/SD2	28.300	**< 0.001**	**< 0.001**	**< 0.001**

Hence, care should be taken before using PRV as a valid surrogate of HRV, and its applicability depends on the circumstances in which it is to be studied. When localised changes in the ANS activity could occur, PRV should not be considered as a valid surrogate of HRV information. Future studies should aim to better understand the agreement between HRV and PRV and to explain the physiological and technical factors that could be related to the difference between these variables. This study has limitations that should be considered when analysing the results. As mentioned before, the quality of the signals obtained, especially during the cold exposure, was low, due to the physiological changes that modify the PPG signal under low temperatures. However, signals were filtered and processed to achieve a good performance in the identification of fiducial points and the measurement of PRV, and the outliers in the detected pulses were manually corrected. Also, the recording time was short, which restricts further analysis of the obtained indices, especially during BM and from frequency-domain information. Finally, the sample size was small and restricted to a certain population. However, the results presented in this study show that PRV is affected by low temperatures in a different way than HRV and that there may be differences between the different body locations from which PRV is obtained.

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