Reliability of Pulse Rate Variability in Elderly Men and Women: an Application of Cross-Mapping Approach

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Abstract— **Photoplethysmography (PPG) is a completely non-invasive, optical method of assessing blood flow dynamics in peripheral vasculature. Wearable devices for PPG recording are becoming increasingly popular, due to their cost-effectiveness and ease of use. For these reasons, many recent scientific studies have proposed the use of pulse rate variability (PRV) extracted from PPG as a surrogate for heart rate variability (HRV), in monitoring autonomic activity and cardiovascular health.**
In this work, we used a cross-mapping approach, a methodology based on chaos theory, to compare PRV and HRV dynamics, and investigate their agreement according to age and gender of healthy subjects. We used ECG and PPG data acquired from 57 subjects (41 young and 16 elderly) during resting state in the supine position. Signals were gathered from the publicly available VORTAL dataset. Our results showed a statistically significant decrease of PRV reliability as an HRV surrogate in old participants, which was confirmed as significant when only men subjects were analyzed (p-value$<$0.01).
Our findings, although preliminary, suggest greater caution in the use of PPG devices for monitoring cardiovascular health, especially in elderly men.

I. Introduction

The use of wearable devices for the acquisition of photoplethysmography (PPG) signals to monitor cardiovascular health is increasingly widespread. This rapid boost in the demand and consequent production of these devices is due to a multiplicity of factors, e.g., their non-invasiveness, cost-effectiveness, and easiness of connection.
PPG signals acquired with such wearable devices have been used to analyze the heart rate variability (HRV): the gold standard signal to investigate the autonomic nervous system. However, several previous studies have shown controversial results on the reliability of pulse rate variability (PRV) obtained from PPG signal, as a surrogate for HRV signal extracted from the ECG [1]–[7]. Specifically, the reliability of PRV was found to be influenced by several factors, including physical activity [4], stress and emotions [8], [9], cold exposure and acquisition site [9], [10]. The hypothesis of using PRV indexes as surrogates for HRV features was investigated also in subjects affected by cardiovascular diseases (such as hypertension, acute infarction, heart failure, and coronary artery disease) [5] and ischemic stroke [11]. Under these pathological conditions, the agreement between HRV and PRV was lower than in healthy subjects and caution was recommended when using PRV for cardiovascular health monitoring. Pathologies such as cardiovascular disorders or ischemic strokes are much more frequent in the elderly population, characterized by a physiological weakening of the heart system and by pathologies such as hypertension and diabetes, which can affect its regular activity.
This study aims to investigate how aging can influence the agreement between PRV and HRV, in healthy subjects. The possible effects of aging on PRV due to vascular changes was already hypothesized in previous literature [1]. The age-related increase of artery stiffness can in fact influence the morphology of PPG signal and was demonstrated to be inversely correlated with sympathetic baroreflex sensitivity, an indicator of cardiac autonomic regulation [12]. Moreover, several studies highlighted that gender affects baroreflex sensitivity and the incidence of specific cardiovascular diseases [12], [13]. The factors behind this difference are still being investigated, although one of them could be related to different exposure to sex hormones [14].
We compared the quality of the PRV signal extracted from the PPG of healthy elderly subjects with that of healthy young subjects. We used data contained in the public VORTAL dataset [15]–[17], consisting of ECG and finger-PPG signals acquired from 41 young healthy subjects and 16 elderly healthy subjects. All participants were monitored in the supine position for at least 9 minutes. In order to compare PRV and HRV dynamics we used the approach we proposed in [9], based on cross-mapping method [18], [19]. This approach studies and compare nonlinear dynamics of HRV and PRV signals in the phase space, and allowed us to unveil relevant differences in the quality of PRV when acquired from wrist and finger, overcoming the performance of a simple linear correlation between the signals [9]. We started from the hypothesis that in order to consider PRV as a good surrogate of HRV, the attractors described by PRV and HRV time series after the phase space reconstruction have to follow the same dynamics. Finally, statistical analysis was carried out to compare PRV and HRV signals in the two groups of subjects, i.e. young and elderly, by using the indexes of agreement obtained with the cross mapping approach.

II. Materials and Methods

A. Data description

The VORTAL dataset contains data from a total of 57 healthy participants: 41 young subjects (21 women, aged 26-31) and 16 elderly subjects (9 women, aged 72-78) [15]–[17].

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All the participants provided written informed consent for the study. The dataset was collected during the VORTAL study (National Clinical Trial 01472133), at St Thomas' Hospital, London, UK. Ethical approval was obtained from the London Westminster Research Ethics Committee (11/LO/1667). The Vortal dataset contains simultaneous ECG, finger-PPG, ear-PPG, oral-nasal air pressure and impedance pneumography signals acquired during a resting state session of about 10 minutes in supine position. For this study, according to the minimum duration of the acquisitions, we used the first 9 minutes of ECG and PPG signals. PPG signals were recorded from the finger of each participant, which is considered the gold-standard location for PPG acquisition. Lead II ECG signals were acquired using an adapted 3-lead M1510A ECG cable (Philips Medical Systems, Boeblingen, Germany) and PPG signals were recorded by using the MLT1020FC finger clip infrared reflection plethysmograph sensor (Braebon Medical Corporation, Kantata, ON, Canada). A sampling rate of 500 Hz was used.

B. Signal pre-processing

In this study, we applied the cross-mapping procedure to compare HRV series and PRV series of young and elderly healthy subjects. HRV and PRV were extracted from simultaneously acquired ECG and PPG signals, respectively. Interbeat interval series (RR series) were extracted from ECG signals, by using the Pan-Tompkins algorithm to automatically detect the QRS complexes [20]. The pulse detector algorithm described in [21] was used to extract the pulse-to-pulse (PP) series. Then, two uniformly-sampled HRV and PRV series were obtained for each subject through a shape-preserving piecewise cubic interpolation at the standard rate of 4 Hz.

C. Cross-Mapping

Before applying cross-mapping method the attractors of PRV and HRV time series have to be reconstructed according to Takens' theorem, using time-delayed embedding [22]. For each time series, we identified the appropriate time delay τ, as the minimum of the mutual information function, and the embedding dimension m, using the false nearest neighbor (FNN) method [23]–[25].

Given two time series $[x(1), x(2), ..., x(n)]$ and $[y(1), y(2), ..., y(n)]$, representing the observation functions of the same dynamic process and describing the diffeomorphic attractors, the cross-mapping method can be applied following the procedure described in [18], [19]. An estimate of Y can be generated from a reconstructed manifold or "shadow manifold" M_X, derived from X. The estimate of each point of Y is called $\hat{Y}(t)|M_X$, and is found through a simple projection: a nearest-neighbor algorithm based on exponentially weighted distances from nearby points on M_X. Specifically, in order to find $\hat{Y}(t)|M_X$ starting from the shadow manifold M_X, the corresponding point over time in M_X has to be identified, i.e., $X(t)$. Then, a small region of $E+1$ points around $X(t)$ has to be used to map a corresponding small region around $Y(t)$, where E was chosen as the maximum value among the embedding dimensions of the two time series [18], [26]. This means that the points $[X(t_1), X(t_2), ..., X(t_{E+1})]$ ordered from the nearest to the farthest, are used to map the corresponding points $[Y(t_1), Y(t_2), ..., Y(t_{E+1})]$, and the of estimate $Y(t)$ is found as follows:

$$\hat{Y}(t)|M_X = \sum_{i=1}^{E+1} w_i Y(t_i) \tag{1}$$

The weights w_i are calculated using the Euclidean distances between $X(t)$ and the nearest $E+1$ points ($\| \cdot \|$ indicates the Euclidean distance in $\mathbb{R}^E$):

$$w_i = \frac{u_i}{\sum_{j=1}^{E+1} u_j} \tag{2}$$

$$u_i = \exp\left(-\frac{\| X(t) - X(t_i) \|}{\| X(t) - X(t_1) \|}\right) \tag{3}$$

Finally, the Pearson correlation coefficient is computed to compare the time series obtained applying the cross-mapping and the original series.

Here, we used the points of the attractor related to the PRV series to estimate the points of the attractor of the HRV series. Then we compared the estimate of HRV series obtained using the PRV attractor with the real HRV signal, by using Pearson correlation indicated as ρ_{M_X}. The higher the ρ_{M_X} coefficient value, the higher the reliability of PRV signal as a surrogate of HRV.

D. Statistical analysis

The Mann-Whitney non-parametric test was used to statistically compare group-wise medians between ρ_{M_X} values obtained after the application of cross-mapping procedure. Specifically, the statistical analysis consisted in identifying the presence of significant differences in the ρ_{M_X} values between young and old participants starting from three different groups of subjects: all participants, all men, all women. A p-value<0.05 was considered significant. The use of non-parametric tests was justified by the non-gaussian distribution of samples ($p < 0.05$ from the Shapiro-Wilk test).

III. RESULTS

Figure 1 shows the values of the correlation coefficient ρ_{M_X} obtained after the application of cross mapping approach to cardiovascular signals of Vortal dataset. Results are presented in the form of boxplots referred to three pools of participants: for all the subjects grouped according to the age (young vs. elderly), and for all the women and all the men grouped in the same way. In the first case, when we used the Mann-Whitney test to analyze the statistical difference between young and elderly regardless of the gender of the participants, we found a significant p-value i.e., p=0.028. The median value of ρ_{M_X} coefficients was higher in the group of young subjects when compared to the median value of correlation coefficients computed for the group of old participants.

On the other hand, studying males and females separately, only males presented significant differences in ρ_{M_X} values according to the age. Elderly men were associated with lower correlation coefficients with respect to young males.

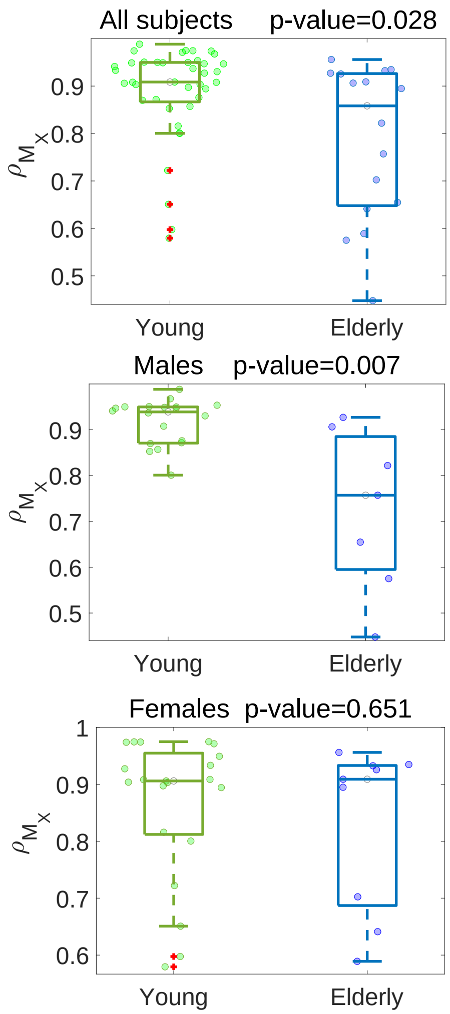

Fig. 1. Boxplots of ρ_{M_X} coefficient values obtained after the application of cross-mapping method on Vortal ECG and PPG data, considering the following three groups: all subjects, males and females. Boxplots related to young subjects are colored by green, whereas boxplots associated with elderly subjects are colored by blue. The p-value of the Mann-Whitney statistical test between ρ_{M_X} values of young and elderly subjects is reported above the corresponding subfigure.

IV. Discussion and Conclusion

The convenience and practicality of using wearable devices for PPG signal monitoring have led to an in-depth study on the reliability of PRV signal extracted from it, as a surrogate of HRV signal. According to recent literature, PRV should be used with caution as a diagnostic tool in old subjects affected by cardiovascular diseases and stroke [5], [11].

This study reports on the investigation of statistical differences in PRV and HRV agreement according to the age in both male and female healthy subjects. In fact, aging plays a crucial role in characterizing cardiovascular dynamics also in healthy population [13], [27], and physiological factors, e.g. sex-related hormones and biochemical processes, can influence the development of several cardiac pathologies [14]. We used data gathered from the public available VORTAL dataset [15]–[17]. ECG and PPG signals lasting nine minutes were simultaneously recorded from 57 subjects in supine position, grouped according to the age: 41 young and 16 old participants. In order to compare HRV and PRV dynamics, we used the cross-mapping, a methodology based on chaos theory and used to evaluate time correlation and causality between two time series [9], [18], [26]. Nonlinear analysis of cardiovascular univariate and multivariate time series has already been shown to be an effective tool for the detection of age-dependent changes in complex autonomic dynamics [25], [28]. The results obtained after the application of cross-mapping approach showed a decrease of agreement between PRV and HRV in elderly participants. Mann-Whitney non-parametric statistical test revealed a significant statistical difference between the median values of the correlation coefficient ρ_{M_X} related to young and old subjects (p-value$<$0.05). When we investigated gender effects on our analysis, we did not find significant differences if only the signals of female participants were taken into account. On the other hand, a significant p-value, i.e. p$<$0.01, was obtained when only the PRV and HRV signals recorded from men were considered.

Our outcomes suggest that the reliability of PRV signal decreases according to the age of subjects and is affected by gender, showing a statistically significant reduction of the agreement with HRV in men. The results are in line with previous literature. In fact, PPG signal was demonstrated to be affected by aging [29], [30]. Furthermore, gender differences in cardiovascular metrics extracted from elderly were already found, showing higher values of parasympathetic indexes and more complex dynamics in women than men [31], [32]. The quality of PRV was already analyzed in patients affected by several diseases, specially cardiovascular disorders [5]. However our results, obtained on a population of healthy subjects and not on patients as in the previous studies, suggest caution on the use of the PRV signal not only in the prognosis of diseases, but also in the diagnosis and monitoring. The analysis of gender differences added new and relevant information, showing a worse reliability in elderly men than in women.

Future works will be addressed towards an increase of sample size to study more thoroughly gender dependence, and an investigation of the reliability of PRV also in case of short and ultra-short time series, i.e., series with a duration less than or equal to five minutes.

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