Validation of the PR-RR Hysteresis Phenomenon

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Abstract

Previous studies on ECG recorded under exercise conditions on sedentary and athlete subjects lead to following results: 1) the subjects can be characterized according to their training level studying the PR slope in the early recovery phase, and 2) it exists a non-linear relationship between PR and RR intervals which exhibits a clockwise hysteresis shape when data from exercise and its recovery are compared. The main drawback of these studies is that they were performed on a small size data set. As the understanding of the PR-RR hysteresis phenomenon may lead to improvement of pacemaker's design, the aim of this study is to check the PR-RR hysteresis on a larger data set.

1. Introduction

The problem of estimation of the heart periods, and consequently the problem of the understanding of the neural activity during exercise and recovery is still interesting since it could lead to innovations in the field of pacemaker's design. Although the PR intervals are difficult to extract and process especially during exercise where T-P fusion occurs during higher heart rates, only few works about the PR interval estimation and analysis have been proposed until now. Recent methods have been proposed to estimate the PR intervals on ECG recorded in exercise: we have proposed a time delay estimation method that take into account the potentially parasite T wave which overlaps the P one at high heart rate, and proposed different modellings for the T wave [1]. Applying this method on real stress ECG, new findings have been revealed : i) it exists a non-linear relation between PR and RR intervals which exhibits a hysteresis shape (which was unknown until now whereas the hysteresis on QT/RR is widely investigated), ii) it is possible to characterize the subjects according to their training level studying the PR interval slope in the early recovery phase [1–3]. But these studies have been performed on small databases. Before understanding these phenomena at the physiological point of view, we want first to check their presence on a larger data set.

The remainder of the report is organized as follows. Section 2 deals with the method. It includes the experimental design (subjects and protocol) and the signal processing analysis. In Section 3, the results on the real ECG database are presented. Finally, we conclude and some perspectives are suggested in Section 4.

2. Methods

2.1. Experimental design

Study population

Forty one subjects participated in the present study. Subjects were classified into different groups:

- W: 7 Women non-ischaemic with negative clinical and electrical exercise test, aged 61 ± 10 years,
- M: 12 Men non-ischaemic with negative clinical and electrical exercise test, aged 46 ± 14 years,
- S: 5 healthy Sedentary men, aged 32.5 ± 11 years,
- MM: 2 Military Men, asymptomatic volunteers from the Spanish Army who underwent an exercise test with negative results for coronary artery disease, aged 35 ± 0 years,
- ATH: 7 healthy ATHlete men, aged 26.5 ± 4.5 years,
- Isc: 3 Ill men who presented ischemia since the coronary angiography has revealed significant stenoses at least one major coronary artery,
- TrL3: 3 TRansplanted men for Less than 3 years, aged 38 ± 15 years,
- TrM3: 2 TRansplanted men for More than 3 years, aged 63 ± 1 years.

Protocols

The protocol of the stress test differed from each group of subjects since the records were provided by different structures.

For the W, M, MM and Isc groups, the ECG were recorded in the University Hospital 'Lozano Blesa' of Zaragoza, Spain, and refereed for a treadmill exercise test following the Bruce protocol. Standard leads and RV4 were digitally recorded at 1,000 Hz sampling rate. For the treatment, the lead which exhibits the higher P wave amplitude has been chosen (usually the V5).

For the S and ATH groups, the ECG were recorded in the University Hospital 'Pasteur' of Nice, France, and refereed

for a maximal graded exercise test on a cycle ergometer. The initial load was fixed at 75 W for sedentary subjects or 150 W for athletes and increased by 37.5 W every 2 minutes until exhaustion. The pedaling rate was kept constant at 75 and 90 revolutions/min for the S and ATH group respectively. During the exercise test and the preceding 5 minutes (rest), a one-lead ECG was recorded and digitized on-line by a 12-bit analog-to-digital converter at a sampling rate of 1,000 Hz on a personal computer. The lead is placed collinearly to the standard DII derivation directly on the chest in order to avoid limbs motion artifacts. The DII lead is chosen because it exhibits the highest amplitude of the P wave. Besides, it assures the T wave of being positive and monophasic, and it minimizes the presence of the U wave.
For the TrL3 and TrM3 groups, the ECG refereed for a maximal graded exercise test on a cycle ergometer recorded by the society Brainware, La Valette du Var, France. The initial load was fixed at 20 W and increased by 15 W every 2 minutes.

2.2. Signal processing

2.2.1. Cardiac period extraction

Body motion could distort the ECG signal during stress test recordings, and then could bias the method of RR interval estimation [4]. To limit the potential artifacts due to body motion, a robust R-peak occurrence calculation method was used [2]. A double threshold-crossing technique applied on the high-pass filtered and demodulated ECG refines the estimation of the R-peak time occurrence t_k. The used high-pass filtering is a 500^{th} order FIR filter designed with a hamming window and a cut off frequency equal to 5 Hertz. The successive RR intervals, RR(k), were calculated as the difference:

$$RR(k) = t_k - t_{k-1}$$

The RR interval series were visually inspected. In case of artifacts due to an undetected R-wave, the inaccurate RR interval was replaced by the mean of the two neighbor RR interval values. Note that those artifacts were not common in our data set.

2.2.2. PR intervals estimation

Pre-processing

Segments including each expected P wave and its corresponding R wave in sequence were formed time-locked with the t_k. The length of the segments was fixed for all beats, and depended of the subject. For each heart rate, the left boundary of the segment was adjusted in order to get only the decreasing part of the T wave (supposed monophasic and positive in the chosen lead, see section 2.1), and to ensure that the whole P wave is encompassed. In a real case, this condition was readily achieved and the T wave should not be present in the observation window for low heart rate.

The PR interval estimation is biased by the presence of baseline corresponding to the respiration and other artifacts. Then, to provide accurate detection of PR intervals, a baseline removal approach based on an order one polynomial substraction was used [2].

Note that the instantaneous, or time course, of PR intervals is not in the scope of this paper since we focus on the PR interval evolution during exercise and recovery. Then in order to reduce the effect of noise at the maximum exercise intensity, each set of 10 PR interval segments was replaced by the corresponding average [5,6].

Estimation method

The PR intervals were estimated using the Generalized Woody method presented in [1,7]. This method consists in modelling the T wave, cancelling its influence, and finally estimating the PR intervals. Different modellings of T wave have been proposed and compared. In this paper, the decreasing part of the T wave was modelled by a piecewise linear function defined by 3 segments. Combining this modelling with the proposed time delay estimation method led to accurate PR intervals estimation. One representative example, for one subject from the ATH group, is shown in figure 1.

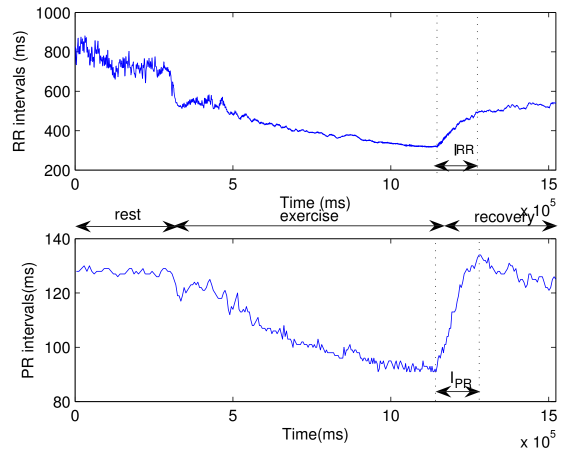

Figure 1. Representative example of RR and PR intervals evolutions for an athlete subject. The interval I is used for the calculation of the slope S, indicative of the “recovery rate”; the interval I is defined between the end of the exercise and the abrupt change of slope, and is delimited by the two dotted vertical lines.

3. Results

Using the proposed PR interval estimation method on the real ECG defined in section 2.1, we confirmed previous results founded on a few data set [1,3,7]:

- the times of abrupt change of slope in the early recovery

phase on RR and PR intervals are correlated,
• the slopes of PR interval series in the early recovery phase are dependant of the training status of the subject,
• an hysteresis phenomenon exists in the relation PR-RR intervals when data from exercise and recovery are compared.

3.1. Observation during the early recovery phase

Consistent with our previous observations [7, 8], we show an abrupt change of PR interval slope during the early recovery phase, which is significantly correlated with the RR interval slope. It exists a relationship between the PR and RR time of the abrupt change of slope during recovery (I_{PR} and I_{RR}). The time occurrence of abrupt change of slope I for all subjects is computed through a least-squares line method. For all the subjects of our data set, except for transplanted people, the times I_{PR} and I_{RR} are significantly correlated (r=0.70 ; p-value p<0.001). The location of this change of slope is related to each subject. Additionally, for all subjects, we calculate the slope S_{PR} of the evolution of the PR intervals, and S_{RR} for the RR one, on the time interval delimited by the two dotted vertical lines on figure 1 between the end of the exercise and the abrupt change of slope. This slope should be indicative of the "recovery rate" of the subject.

Figure 2 shows the relationship between S_{PR} and S_{RR}. Note that the values of slopes are weaker for transplanted subjects who certainly recover slower. Besides, the values of S_{PR} are higher for ATH group than for other subjects. A k-means clustering algorithm have been applied on the data set assuming a cluster for the ATH and one for the others. While exploiting the slopes data both of PR and RR intervals we obtained 30% of misclassification, 29% considering the data of the S_{RR} only, and 0% considering the S_{PR} only. This clustering was confirmed by a positive Welch's test with a p-value<0.001.

The mean value and standard deviation of S_{PR} for each group are reported in table 1. According to these values, we observe that the slopes S_{PR} are significantly higher for the ATH than for the others (p<0.001). Besides, note difference of mean value between the ATH group, the "healthy but no ATH" subjects, and the "Isc or transplanted subjects" in the bottom of the table. More precisely, the transplanted people exhibit a very weak "recovery rate" because of the slow values of the S_{PR} slope.

Group	Mean±SD of S_{PR} [ms/s]
ATH	0.258±0.023 ⋆
Others	0.101±0.043 ⋆
W	0.115±0.035
M	0.108±0.030
S	0.114±0.055
MM	0.129±0.017
Isc	0.115±0.030
TrL3	0.034±0.016
TrM3	0.070±0.056
Healthy but no ATH	0.113±0.035 •
Isc and All Transplanted	0.069±0.047
All Transplanted	0.050±0.040 •

Table 1. Mean ± standard deviation of S_{PR} for each group of the data set ($\star p < 0.001$, $\bullet p < 0.05$).

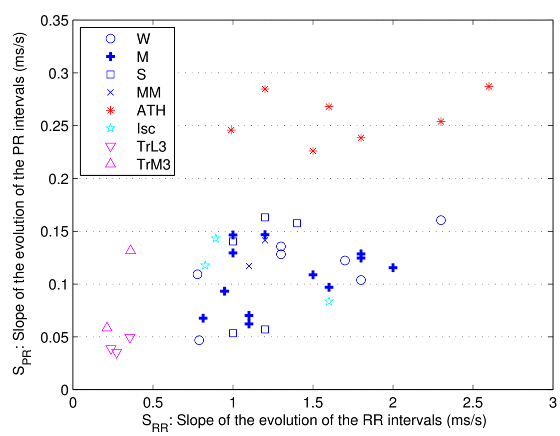

Figure 2. Relationship between the slope of the evolutions of the PR (S_{PR}) and RR (S_{RR}) intervals for all subjects.

3.2. PR-RR hysteresis phenomenon

For a same value of RR interval in exercise and recovery, the PR interval is extended during the recovery phase: this is called the PR-RR hysteresis phenomenon (see example on figure 3). To quantify the presence of the hysteresis phenomenon, an hysteresis criterion is defined as the difference of areas between the recovery curve and the exercise curve, normalized by the range of RR intervals of the subject. This criterion was calculated for each subject and reveals the presence of the hysteresis phenomenon for all subject.

The mean and standard deviation of the hysteresis criterion for each group of our data collection are shown in figure 4. Then, we observe that all the healthy subjects (W, M, S, MM, ATH) and the ischemic subjects exhibit a significant PR-RR hysteresis. Besides, we observe that the criterion is significantly higher for the ATH than for the others (p<0.005). The PR-RR hysteresis more pronounced for ATH subjects could be due to a higher return of parasympathetic tone on AV node than on the sinusal node at exercise end. At a physiological point of view, it is known that transplanted subjects do not have vagal nerve connection (and reinnervation is not yet proven). The humoral activity permit to them to do exercise but, of course, it does not amount to the sympathetic activity for healthy people and then, the maximal range of RR (between the rest and the maximal exercise) is not comparable for transplanted or healthy people. Note that the number of data for each group stay not enough to make strong physiological assumptions and statistics for the moment. But we can hypothesize that during recovery the parasympathetic tone increases a lot and then the conduction velocity at AV node decreases, leading to the PR-RR hysteresis.

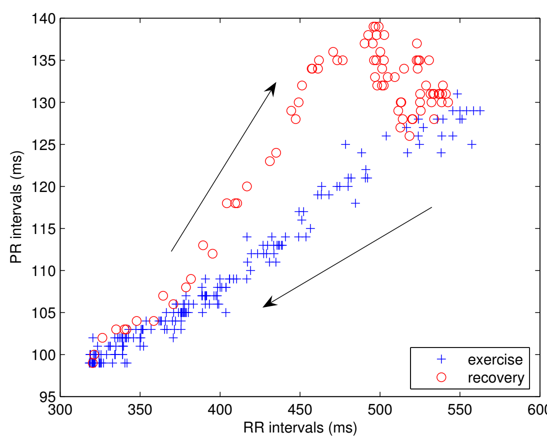

Figure 3. Representative example of PR-RR hysteresis phenomenon for an athlete subject. Evolution of PR intervals in function of RR intervals during exercise (+) and recovery (○). We note a clockwise hysteresis phenomenon.

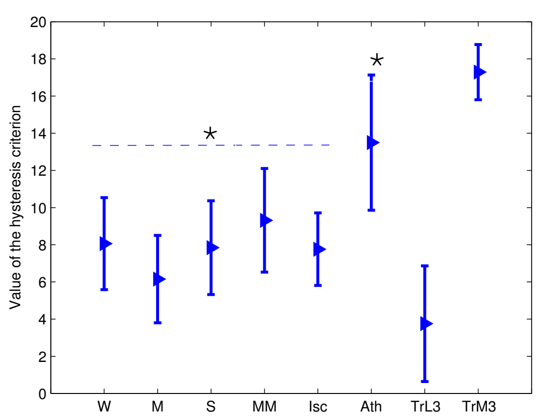

Figure 4. Values of the hysteresis criterion for the different group of the studied population. Stars $\star$ for $p < 0.005$.

4. Conclusion

The PR-RR hysteresis phenomenon has been evaluated on healthy people but also on ischemic subjects. Besides, consistent with the previous findings, the characterization of the subjects according to their training level studying the PR interval slope in the early recovery phase is possible. Further study should be done on the transplanted people in order to understand the physiological effects linked to the PR-RR hysteresis. The analysis of the PR interval pattern could be performed in order to evaluate the sympathetic-parasympathetic balance, but also to reveal the atrioventricular conduction properties [9].

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