Sequence Analysis of Pulse Transit Time and Systolic Blood Pressure during Dynamic Exercise

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Abstract

The pulse transit time (PTT), i.e. the time necessary to the arterial pulse to reach the periphery, and systolic arterial pressure (SAP) are inversely related (i.e. PTT decreases when increasing SAP). This relationship, although significant, is very weak at the level of PTT and SAP beat-to-beat variabilities. The study searches for sequences of PTT and SAP values characterized by a PTT increase (decrease) and SAP decrease (increase) in SAP and PTT variability series (i.e. SAP-/PTT+ and SAP+/PTT- sequences) derived from 13 healthy subjects during mild supine incremental bicycle exercise. The presence of these sequences on real data should guarantee that the SAP-PTT relationship might be sufficiently strong to encourage its exploitation in continuous non-invasive beat-to-beat SAP monitoring.

1. Introduction

The measurement of pulse wave velocity (PWV) may permit to face the issue of long-term beat-to-beat non-invasive AP monitoring. Indeed, the formula [1]

$$PWV^2 = \frac{\Delta AP \cdot V}{\rho \cdot \Delta V}$$

relates PWV to the AP change, ΔAP, (i.e. the stress) in an infinitely long thin-walled elastic isotropic tube filled with an incompressible fluid, where ΔV/V is the fractional deformation of luminal volume per unit length of artery (i.e. the strain) and ρ is the density of the blood. Usually the ratio of stress (i.e. ΔAP) to strain (i.e. ΔV/V) is referred to as elastic modulus. After assuming the strain constant and providing an initial calibration indicating the absolute AP value, the AP evaluation might be carried out by calculating PWV.

Usually PWV is estimated by evaluating the pulse transit time (PTT), i.e. the time necessary to the arterial pulse to reach periphery, and an inverse relationship is expected between PTT and ΔAP. The AP-PTT relationship was actually found by many groups when systolic AP (SAP) was considered (see e.g. [2]). However, this relationship, although significant, is very weak, thus questioning the presence of sequences of PTT and SAP values characterized by a PTT increase (decrease) and SAP decrease (increase) in the SAP and PTT variability series (i.e. SAP-/PTT+ and SAP+/PTT- sequences). The presence of these sequences on real data indicates that the SAP-PTT relationship is locally present in the series and stronger than indicated by a global correlation analysis.

The aim of the study is to verify the SAP-PTT relationship and search for SAP+/PTT- and SAP-/PTT+ sequences during dynamic incremental exercise inducing a stepwise increase of the mean SAP. A similar sequence analysis applied to SAP and RR beat-to-beat variabilities allowed the detection of sequences that have been soundly related to baroreflex [3].

2. Methods

2.1. Sequence analysis

Given the two series, PTT={PTT(i), i=1,…,N} and SAP={SAP(i), i=1,…,N} where i indicate the i-th cardiac beat, let us consider PTT(i) and SAP(i) as the independent and dependent variables respectively. Sequences characterized by the contemporaneous increase of SAP and decrease of PTT and viceversa are sorted out and referred to as SAP+/PTT- and SAP-/PTT+ sequences. The sequences appears in the (PTT(i),SAP(i)) plane as ramps: the SAP+/PTT- ramps are covered in ascending mode, while in the opposite direction the SAP-/PTT+ ones. Patterns of pairs (PTT(i),SAP(i)) are defined to be SAP+/PTT- and SAP-/PTT+ sequences if they fulfilled the following prerequisites: 1) the length of the sequence, L, is equal to 4 beats (i.e. 3 SAP and PTT variations); 2) SAP(i+1)>SAP(i) for SAP+/PTT- and SAP(i+1)<SAP(i) for SAP-/PTT+; 3) maximum absolute value of SAP variation >1 mmHg; 4) PTT(i+1)> PTT(i) for SAP-/PTT+ and PTT(i+1)<PTT(i) for SAP+/PTT-; 5) maximum absolute value of PTT variation >1 ms; 6)

absolute value of correlation coefficient r>=0.5. The small values of the PTT and SAP variations are related to the small PTT and SAP variabilities. The small r is in relation to the weak correlation usually found between PTT and SAP [2]. SAP+/PTT- and SAP-/PTT sequences were grouped together and termed as SAP/PTT sequences and the average value of their slope, b_{seq}, was calculated. As a consequence of the fixed length of the SAP/PTT sequences, the maximum number of sequences was fixed and equal to N-L+1 and their percentages were calculated as well.

2.2. Significance of the sequence analysis

To exclude that the SAP/PTT sequences are present by chance, a surrogate data approach was utilized. Surrogate series sharing the same distribution as the original ones but destroying any temporal pattern were generated by randomly shuffling the temporal order of the samples. Since shuffling was carried out according to two independent noise realizations, PTT and SAP surrogate series were uncorrelated as well. We generated 100 surrogate PTT and SAP pairs and we calculated the percentage of SAP/PTT sequences for each pair. The value defining the 5 percent most extreme percentages was taken as a critical value. If the percentage calculated over the original PTT and SAP pair was larger than the critical value, then the null hypothesis (i.e. no SAP/PTT sequence) was rejected and a significant number of SAP/PTT sequences was detected with a $p<0.05$.

2.3. Linear correlation analysis

According to the least-squares procedure we estimated the slope and the intercept of the best regression line and the correlation coefficient r. We utilized the t statistic

$$t = \frac{b}{se[b]}$$

to test the null hypothesis of flat or positive slope where b is the estimated slope and se[b] is the standard error of the slope. If the value of t was smaller than the critical value $t_{0.05}$ defining the 5 percent most extreme values in a one-tailed t distribution (i.e. about -1.65 with N=300), the null hypothesis (i.e. no or positive linear trend) was rejected and a significant negative drift was detected with a $p<0.05$ (one-tailed t test).

3. Experimental protocol and data analysis

In 13 healthy humans (age from 22 to 58, 44±1.4, mean±sd)) ECG (lead II), arterial pressure (AP) via a plethysmographic device (Finapres) and respiration via thoracic belt were recorded at rest and during mild supine bicycle exercise. The signals were sampled at 300 Hz.

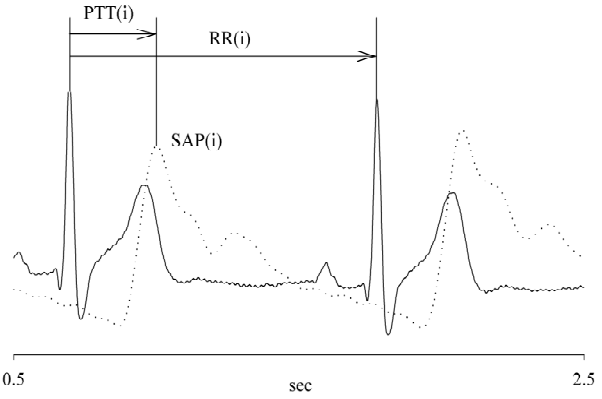

Figure 1. Convention for the i-th RR, SAP and PTT measures. PTT is approximated with the time interval between the QRS complex and systolic peak as detected from the periphery.

After 10 minutes at rest (R), the session involved three periods at 10%, 20% and 30% of the nominal maximum (EXE1, EXE2 and EXE3). The i-th SAP value, SAP(i), was detected as the maximum AP inside the i-th RR interval. The time between the first R peak defining RR(i) and the arrival of the i-th AP pulse at the finger as identified by the occurrence of SAP(i) was taken as PTT(i) (Fig.1). The sequence and linear correlation analyses were carried out on series of about 300 cardiac beats undergoing a smooth filtering (i.e. the average over 3 samples, one before and after the current sample) to reduce the effect of the low sampling rate on the detection of the SAP/PTT ramps (i.e. two consecutive PTT values could be found to be equal due to the low temporal resolution). The analysis was carried out without filtering as well by allowing the possibility that inside the SAP/PTT sequences one or two PTT variations are null provided that the total PTT absolute change is larger than 1 ms. Results were given as mean±sd.

4. Results

An example of typical RR, SAP and PTT series at rest and during EXE1, EXE2 and EXE3 is depicted in Fig.2 As expected mean RR interval and PTT progressively diminish, while mean SAP increases. Over the entire population mean RR was 875±164, 673±82, 609±63, 548±60, mean PTT was 295±23, 267±29, 250±26, 233±24, mean SAP was 125±17, 144±18, 152±18, 163±19 at R and during EXE1, EXE2, EXE3 respectively.

Fig.3a shows an example of linear correlation analysis. SAP(i) is plotted against PTT(i) and (PTT(i),SAP(i) points are represented as solid circles. The best linear fitting is superposed (solid line) with its 95 percent confidence interval (dotted lines). A significant negative

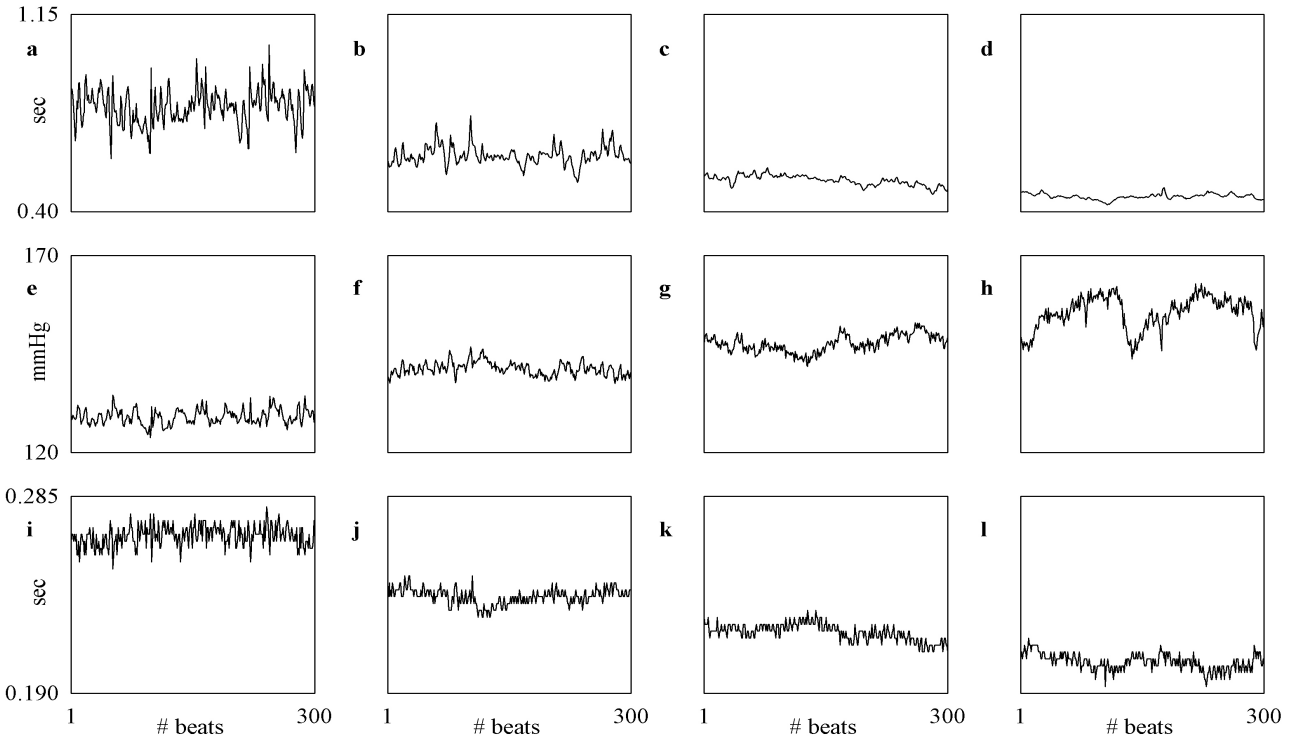

Figure 2. Example of RR, SAP and PTT series (upper, middle and lower rows) in a subject at R (a,e,i), EXE1 (b,f,j), EXE2 (c,g,k), and EXE3 (d,h,l).

trend is detected (r=-0.4, b=-182 mmHg/s). As expected, this trend is lost if a pair of uncorrelated surrogates is considered (Fig.3b).

Over the entire population we found that PTT and SAP were significantly linearly correlated in 9, 9, 12, 10 subjects at R and during EXE1, EXE2, EXE3 respectively. The correlation coefficient r was –0.34±0.19, -0.49±0.17, -0.46±0.19, -0.56±0.16 and the slope b was -377±276, -502±249, -475±256, -598±202. mmHg/s.

Without filtering PTT and SAP series were significantly linearly correlated in 10, 9, 11, 10 subjects (r=-0.32±0.17, -0.44±0.16, -0.43±0.17, -0.50±0.14 and b=-287±211, -347±118, -388±162, -465±153 mmHg/s).

Fig.4 shows an example of sequence analysis over the same data depicted in Fig.3. Fig.4a depicts the SAP/PTT

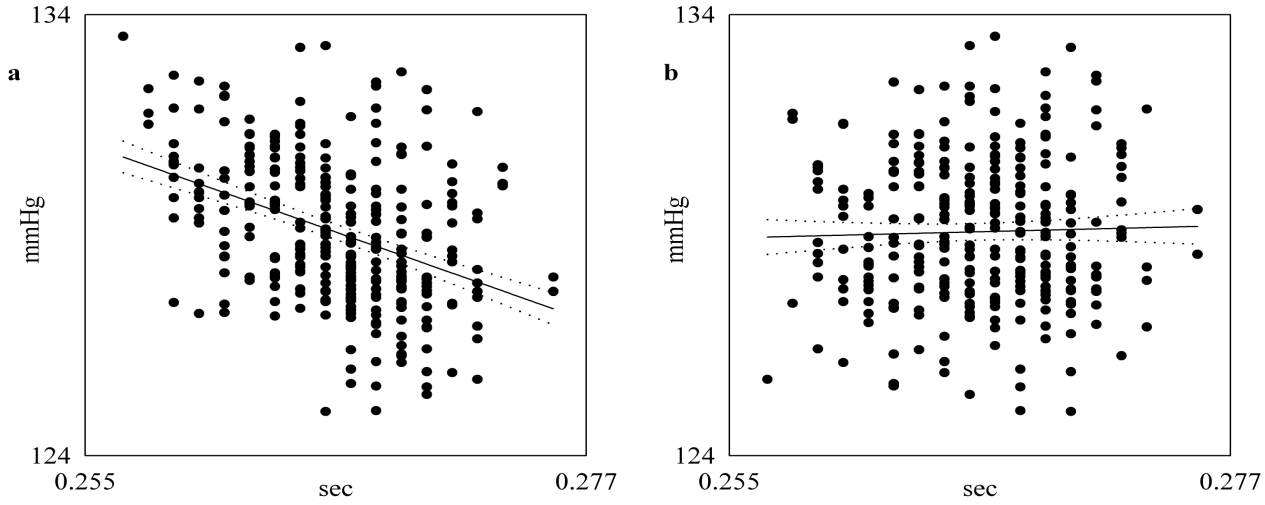

Figure 3. Linear correlation analysis in the plane (PTT(i),SAP(i)) on original data (a) and on a pair of shuffled uncorrelated surrogates (b) in a subject at rest. Points are represented as solid circles. Regression line is shown (solid line) with its 95 percent confidence interval (dotted lines). A significant negative linear trend is detected only in (a).

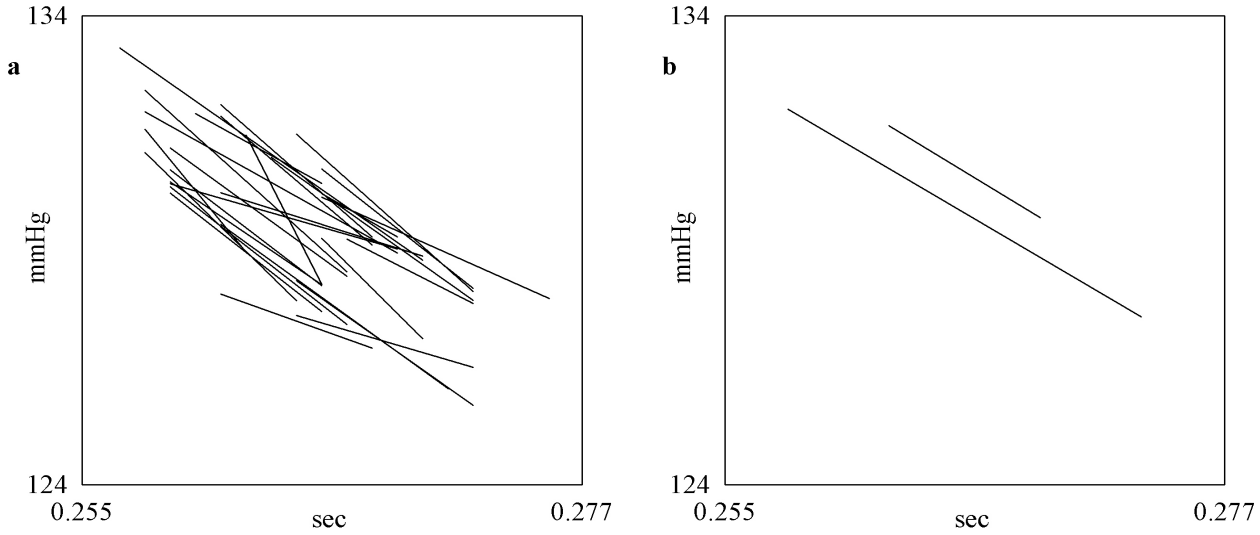

Figure 4. Sequence analysis on the same data depicted on Fig.3. The analyses on original data (a) and on shuffled uncorrelated surrogates are shown in (a) and (b) respectively.

sequences found in the original data (SAP/PTT sequences are 9% of the possible sequences, mean b=-357 mmHg/s). The number of SAP/PTT sequences dramatically decreases (0.67%) in a pair of uncorrelated surrogates (Fig.4b).

We detected a significant number of SAP/PTT sequences in all subjects during all the experimental conditions. The percentages of SAP/PTT sequences and b were 7.05±5.62, 4.88±1.96, 5.76±2.40, 5.56±2.26 and -600±242, -649±168, -680±153, -791±222 mmHg/s at R and during EXE1, EXE2 and EXE3 respectively. Without filtering SAP/PTT sequences were significantly found in 13, 11, 11, 11 and their percentages were 4.96±3.72, 2.13±1.08, 2.38±1.57, 2.94±1.61 with b=-594±339, -619±218, -642±218, -796±278 mmHg/s respectively.

5. Discussion

We confirm the presence of a significant inverse SAP-PTT relationship [2] at the level of SAP and PTT beat-to-beat variability series during mild incremental supine bicycle exercise (an AP decreases is accompanied by a PTT increase). Although significant in the majority of subjects, this relationship is weak (the mean absolute value of the correlation coefficient is quite small and not significant in a few subjects regardless of the experimental conditions).

On the contrary, the detection of a significant presence of SAP-PTT sequences suggests that the SAP-PTT relationship is stronger than detected by a global linear correlation analysis. This result is more striking after using a smooth filter (all the subjects exhibit a significant percentages of SAP-PTT sequences) but, even without applying it, the percentage of subjects exhibiting a significant number of SAP/PTT sequences is larger (or in the worst case equal to) than that showing a significant global linear relationship in the plane (PTT(i),SAP(i)). It can be hypothesised that the casual fast (within the same beat) link between AP changes and PTT could be detected locally along the series.

6. Conclusions

The detection of SAP/PTT sequences in all the subjects during incremental bicycle exercise suggests that the SAP-PTT relationship is more reliably represented in real data than previously thought based on a global linear correlation analysis, thus stimulating its exploitation in non-invasive beat-to-beat AP monitoring.

References

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