The Magnitude of the Postural Challenge Impacts on the Exponential Decay of the Baroreflex Impulse Response

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Abstract

We hypothesize that a postural challenge can affect the bandwidth of the cardiac baroreflex. The study estimated the impulse response function (IRF) of cardiac baroreflex via a model-based approach applied to spontaneous fluctuations of heart period (HP) and systolic arterial pressure (SAP). The exponential decay constant of the IRF was taken as an estimate of the bandwidth of the HP-SAP relationship: the higher the exponential decay constant, the wider the bandwidth. The IRF of the HP-SAP link was estimated in 17 healthy humans (age: 21–36 yrs, median = 29 yrs; 8 males) during graded head-up tilt with tilt table inclination at 0, 15, 30, 45, 60, 75 and 90 degrees. Each tilt session was preceded by a supine resting period and followed by a recovery. A bivariate autoregressive model with exogenous input was utilized to describe the dependence of HP variations on SAP changes. The exponential decay constant was calculated by fitting the IRF absolute value with a mono-exponential function. We found that the exponential decay constant gradually decreased with tilt table angles. This finding is compatible with a reduced bandwidth of the cardiac baroreflex, likely linked to the gradual vagal withdrawal associated with the magnitude of the challenge.

1. Introduction

The cardiac arm of the baroreflex is responsible for adjusting heart period (HP) in response to arterial pressure (AP) changes [1]. The relationship linking AP changes to HP variations can be observed from spontaneous fluctuations of HP and systolic AP (SAP) [2], it is positive [3-5] and its gain is higher when SAP rises [6]. The characterization of the cardiac baroreflex is commonly carried out in the frequency domain via the estimation of the transfer function from SAP to HP [7-9]. Although there is a straight link between transfer function and impulse response function (IRF) via the Fourier transform [10], the frequency domain representation of the HP-SAP dynamic relationship is rarely reverted into time domain [11-14]. However, IRF might provide information that cannot be easily extracted from the transfer function. Bandwidth is one of these key indexes that can be easily derived from IRF but hardly estimated from complex shapes of the transfer function gain. Bandwidth might contain important physiological information given that it is related to the rapidity with which baroreflex can respond to SAP variations: the wider is the bandwidth, the faster the response.

The aim of this study is to estimate the IRF of the dynamic relationship of HP to SAP changes during a graded head-up tilt (T). The HP-SAP dynamic link was estimated via a linear bivariate model-based approach directly from spontaneous beat-to-beat HP and SAP series [15,16] and its IRF was derived from the estimated HP-SAP transfer function.

2. Method

After the application of a linear detrending procedure to both HP and SAP series and their normalization to have unit variance, the dependence of HP on SAP values was modelled via an autoregressive (AR) model with exogenous (X) input (ARX) [15,16]. More specifically, the current HP was described as a linear combination of its p past values, present and past p values of SAP and a residual W [15,16] as

$$HP_n = A(z)\cdot HP_n + B(z)\cdot SAP_n + W_n\,, \qquad (1)$$

where $A(z)\cdot = \sum_{i=1}^{p} a_i \cdot z^{-i}$ and $B(z)\cdot = \sum_{i=0}^{p} b_i \cdot z^{-i}$ are polynomials in the Z-domain, z^{-1} is the one-step delay operator, w_n is a sample of the white Gaussian noise W and p is the model order. Immediate actions (i.e. within HP_n where SAP_n is detected) are allowed in agreement with the fastness of the vagal action [17,18]. The transfer function from SAP to HP is given by

$$H(z)=\frac{B(z)}{1-A(z)}\,. \qquad (2)$$

The long division of $B(z)$ to $1–A(z)$ provides the IRF coefficients, $h(n)$, as a function of cardiac beat progressive counter n. The IRF was truncated to 31 values (i.e. $0\leq n\leq 30$). IRF was multiplied by the ratio of the standard deviation of HP to SAP to achieve the usual units of HP-SAP relationship (i.e. ms·mmHg^{-1}).

3. Protocol and preprocessing

3.1. Experimental protocol

The database was exploited to assess modifications of the causal relationship along the baroreflex as a function of the magnitude of the orthostatic stimulus [19]. Therefore, we refer to [19] for the full description of the protocol. The study adheres to the principles of the Declaration of Helsinki for medical research involving human subjects. The human research and ethical review boards of the 'Luigi Sacco' Hospital, Milan, Italy approved the protocol. All participants gave written informed consent. Briefly, 17 healthy nonsmoking humans (aged from 21 to 36 yrs, median = 29 yrs; 8 males) participated in the study. We acquired electrocardiogram (Biosignal Conditioning Device, Marazza, Monza, Italy) from lead II and continuous plethysmographic arterial pressure (Finometer MIDI; Finapres Medical Systems, Amsterdam, The Netherlands). Signals were sampled at 300 Hz. We recorded signals for 7 min at rest in supine position with a tilt table angle of 0° (T0) and for 10 min during T with tilt table angles randomly chosen within the set {15°, 30°, 45°, 60°, 75°,90°} (T15, T30, T45, T60, T75, T90). Each T session was preceded by a T0 phase and followed by a recovery phase lasting 8 min. The full sequence of tilt inclinations was completed by all subjects without experiencing any sign of presyncope. During the protocol the subjects breathed spontaneously but they were not allowed to talk.

3.2. Beat-to-beat series extraction

HP was computed from the electrocardiogram as the time interval between two consecutive R-wave peaks. The *k*th SAP was defined as the maximum AP value within the *k*th HP. If isolated ectopic beats were detected, the abnormal values were substituted with their linear interpolation using the closest values unaffected by ectopic beats. IRF was computed over sequences of 256 consecutive values selected in a random position within the considered sessions.

3.3. Model identification and IRF analysis

The ARX model coefficients were estimated via traditional least squares approach solved via Choleski decomposition and the model order was optimized via Akaike figure of merit for multivariate processes in the range from 4 to 14 [20]. After computing the IRF directly from (2) via long division procedure, a mono-exponential fitting $y_n=y_0+a\cdot e^{-b\cdot n}$ was applied to the absolute values of the IRF to derive the exponential decay constant b. The parameter b was expressed in beats^{-1} and in s^{-1} by

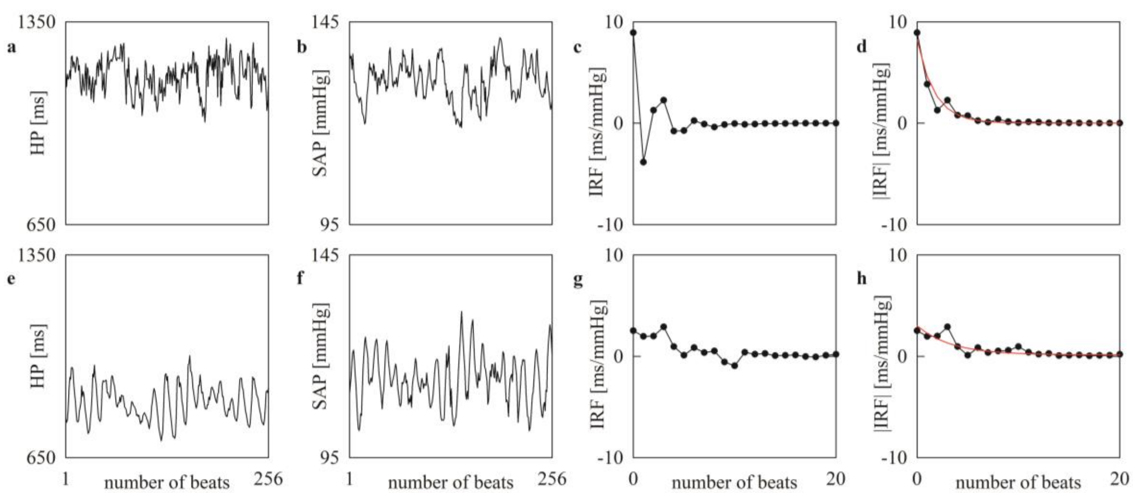

Figure 1. The line plots show the HP and SAP series recorded in a representative subject during T0 (a,b) and T75 (e,f). The correspondent IRF (black line with solid circles) is reported in (c,g), while the absolute value of the IRF (|IRF| black line with solid circles) and the mono-exponential fitting (red line) is given in (g,h). The exponential decay constant b is 0.56 beats^{-1} and 0.48 s^{-1} during T0 and 0.30 beats^{-1} and 0.35 s^{-1}during T75.

dividing it by the HP mean. It is worth noting that b is linked to the time constant τ of the exponential function by the relationship $\tau=b^{-1}$. The positive maximum of the IRF, h_{max}, was extracted as well and it was taken as a marker of baroreflex sensitivity (BRS) [11].

3.4. Statistical analysis

We performed one-way repeated-measures analysis of variance (Dunnett's test for multiple comparisons) to compare indexes derived from the IRF at any angle versus T0. If the normality test (Kolmogorov-Smirnov test) was not fulfilled, the Friedman one-way repeated-measures analysis of variance on ranks was utilized (Dunnett's test for multiple comparisons). Linear regression analysis of any IRF marker on tilt angles was carried out. Pearson product-moment correlation coefficient and type I error probability p were calculated. Statistical analysis was performed with a commercial statistical software (Sigmaplot v.14.0, Systat Software, San Jose, CA, USA). A $p<0.05$ was always deemed as significant.

4. Results

Figure 1 shows an example of HP and SAP series recorded at T0 (Figs.1a,b) and T75 (Figs.1e,f) in a representative subject. The corresponding IRF (black line with solid circles), absolute value of the IRF (black line with solid circles) and mono-exponential fitting (red line) are depicted as well (Figs.1c,d and Figs.1g,h). Exponential regressions clearly indicates that the decay is faster during T0 than T75 (Figs.1g,h).

The bar graphs in Fig.2 show the results relevant to the indexes derived from IRF as a function of the experimental condition. The h_{max}, b expressed in beats^{-1} and b expressed in s^{-1} are shown in Figs.2a,b,c respectively. All the indexes decreased toward 0 with the magnitude of the orthostatic challenge. Modifications of values compared to T0 were evident for h_{max} and b expressed in beats^{-1} (Figs.2a,b). The decrease of b expressed in beats^{-1} was only partially compensated by the increase of heart rate with tilt table angle in Fig.2c.

The parameters h_{max}, b expressed in beats^{-1} and b expressed in s^{-1} were significantly associated with tilt table angles (r=–0.540, p=2.39×10^{-10}; r=–0.426, p=2.85×10^{-8} and r=–0.256, p=4.97×10^{-3} respectively).

5. Discussion

The main findings of this study can be summarized as follows: i) IRF was computed via a model-based parametric approach using the ARX class; ii) h_{max} was able to detect the well-known gradual decrease of BRS with the magnitude of the postural challenge; iii) the parameter b expressed in beats^{-1} decreased with tilt table angle, thus indicating that bandwidth is reduced in relation to the challenge.

The IRF of the baroreflex is frequently estimated via a nonparametric approach computing the inverse of the Fourier transform [11]. In this study the IRF was calculated via a model-based parametric method rooted in the ARX class [15,16]. This approach avoids the strict relation between the series length and the frequency resolution that is inherent to the computation of Fourier transform [10]. It is well known that IRF can provide a marker of BRS, namely h_{max} [11]. In this study we suggest the possibility of using IRF to estimate the bandwidth of the HP-SAP dynamic relationship. This proposal is the consequence of the link of the cut-off of a low-pass filter, as it is the case of the HP-SAP transfer function according to the model proposed in [7], with the rapidity of the IRF of a low-pass filter to decline to 0: the higher the exponential decay constant, the faster the IRF goes to 0, the wider the bandwidth of the low pass filter.

The h_{max} is considered to be a marker of BRS: as a matter of fact, it was found to be correlated with BRS estimated via classical approach based on pressor and depressor responses to pharmacological agents [11]. In the present study we confirm that h_{max} is a measure of BRS because it exhibited the expected decrease in relation to the magnitude of the postural challenge [5,6].

The parameter b expressed in beats^{-1} decreased with the magnitude of the postural challenge. This finding suggests that T has a remarkable impact on the bandwidth of the HP-SAP dynamic relationship by shrinking it. This

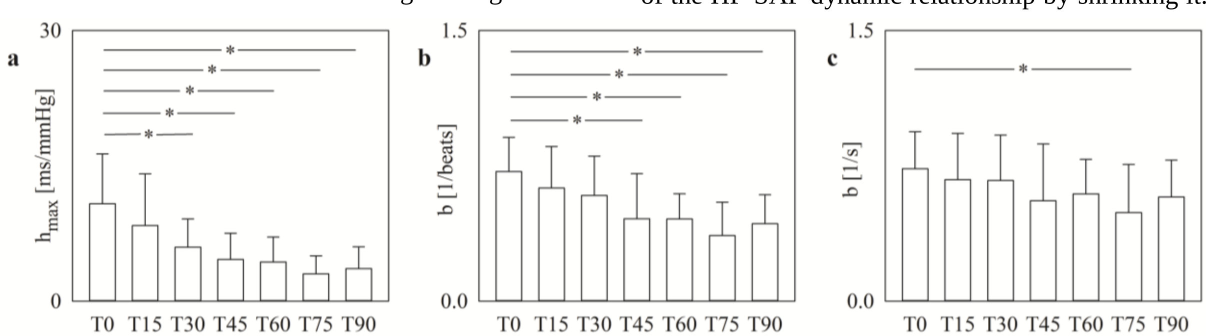

Figure 2. The bar graphs show h_{max} (a), b expressed in beats^{-1} (b) and b expressed in s^{-1} (c) derived from IRF from SAP to HP as a function of tilt table angle. The symbol * indicates a significant difference compared to T0 with p<0.05.

shrinkage occurred as a likely consequence of the vagal withdrawal associated to the gravitational stimulus that led to a reduction of the power of HP at higher frequencies [8,21]. We recommend to assessment of IRF and the computation of the time constant of the exponential decay in any experimental protocol devoted to the characterization of baroreflex function in healthy and pathological individuals.

6. Conclusion

The study proves the usefulness of typifying baroreflex from HP and SAP variabilities via the assessment of the IRF of the HP-SAP dynamic relationship above and beyond the computation of its peak value [11]. Indeed, the characterization of the rapidity of the exponential decay might provide additional information linked to the bandwidth of cardiac baroreflex. Postural challenge was found to gradually reduce the baroreflex bandwidth in relation to the magnitude of the stimulus. Future studies should account for respiration [18,22] as an additional factor capable of perturbing the HP-SAP dynamic link.

Acknowledgments

This work was partially supported the Piano Sostegno della Ricerca 2020.

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