

Spectral Decomposition of RR-Variability Obtained by an Open Loop Parametric Model for the Diagnosis of Neuromediate Syncope

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Abstract

The role of the cardiovascular regulatory mechanism in patients with neuromediate syncope (NS) is poorly understood. Aim of this study was to accomplish continuous non-invasive analysis of the baroreflex mechanism in patients during head-up tilt-table test (HTT) using an open loop autoregressive model with exogenous input. The model describes the causal dependence of the RR interval on the systolic arterial pressure (SAP) variability. Thus, RR variability results as the linear composition of SAP-dependent (Pdep) and SAP-independent parts. Further, the model allows the estimation of the baroreflex gain using the modulus of the transfer function (G) from SAP to RR in the low frequency band. Results showed a significant decrease of both Pdep and G immediately before syncope. Thus, a reduced functionality of the baroreflex and of the sympathetic tone seemed to be the mechanism responsible for the NS event.

1. Introduction

Syncope is defined as an abrupt but transient loss of consciousness associated with absence of postural tone, followed by rapid, usually complete recovery without the need for intervention to stop the episode.

The wide variety of possible causes and the yet partial comprehension of physiologic mechanisms involved required an expensive and time consuming diagnosis. Despite of this, the rate of syncopes without causal diagnosis remains high and varies from 10 to 50% [1,2]. The lack of an optimal diagnostic test seems to be the main cause of the diversity of approaches and the difficulties to get a correct diagnosis of neuromediate syncope (NS) [3]. In this context it is clear the demand of increasing knowledge on the etiological mechanisms of this pathology.

Reproduction of spontaneous symptoms by head-up tilt table test (HTT) represents a useful and widely recognized option for diagnosis and selection of therapy [4,5]. Heart rate variability and baroreflex sensitivity

analyses were extensively applied to investigate on the control mechanisms in tilt-induced syncope [6,7] hypothesising a potential diagnostic role of spectral analysis of RR interval during first minutes of tilting test [8]. However, the complexity and the dynamic response to the tilt position requests a continuous estimation of spectral and cross-spectral indices [9,10] and make mandatory the introduction of causal approaches in the study of baroreflex mechanism [11,12].

In this study a bivariate causal model was introduced to evaluate the open loop baroreflex gain and the contributing of systolic arterial pressure (SAP) variability on RR power spectrum in patients with previous episodes of NS and in healthy subjects.

2. Methods

2.1. Patients and experimental protocol

The study population consisted of 12 patients (Pts, 7 male; mean age 33±7 yrs) referred to the Syncope Unit for the evaluation of recurrent unexplained syncope and in whom a diagnosis of NS was established. Moreover, 16 healthy young subjects (9 male; mean age 25±3 yrs) were included in the study as control group (Ctrl).

HTT was performed in a quiet room after at least 5 hours of fasting. After 15 minutes of rest in the supine position (S), patients were positioned in the head-up position (H, 60 degrees) for a maximum of 30 minutes. If syncope occurred, the table was rapidly lowered to the supine position and the test was labelled as positive.

2.2. Data acquisition and pre-processing

The lead II of the surface ECG and noninvasive arterial pressure (Finapres, model 2300, Ohmeda) were acquired during the test with 1 kHz sampling rate and 12 bit precision. Beat-to-beat RR and SAP variability series were offline calculated and synchronised with the assumption that the *i*-th SAP is contained inside the *i*-th cardiac cycle.

Because of the dynamic response of variability of heart rate and blood pressure during HTT successive windows corresponding to peculiar epochs of the test

have been analyzed. Four windows of 300 samples were chosen, one during S and three during H (at 4 min (t1), 12 min (t2), and 20 min (t3) from tilt manoeuvre).

2.3. Open loop parametric model of RR-SAP interactions

After reducing the RR and SAP series to zero-mean processes (rr and sap), their interactions were modelled by an open loop causal parametric model (ARXAR) as follows [13]:

$$rr(n) = -\sum_{k=1}^p a_k rr(n-k) + \sum_{k=1}^p b_k sap(n-k) + u(n)$$

According to the ARXAR model, the rr series is affected by p samples of its own past (by a_k coefficients) and by p values of the sap sequence (by b_k coefficients). As outlined in figure 1, sap and u signals are described as autoregressive processes with w_{sap} and w_{rr} zero-mean input white noises. The blocks C and D are formed by the autoregressive parameters of sap and u , respectively. In the open loop ARXAR model the variability of SAP around its mean value is considered as an exogenous input, i.e. it may affect the RR interval variability without being affected. The effects on RR variability of other sources independent from SAP, considered as noise in this context, are accounted for means of the u series. The coefficient estimation followed an iterative identification task based on the generalized least squares method. The model order p was chosen, in the set {6,8,10,12}, minimizing the Akaike figure of merit for the bivariate joint process $|rr\ sap|$ [14].

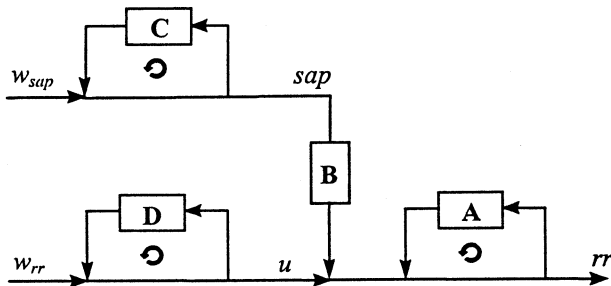


Figure 1. Bivariate autoregressive model with exogenous input (ARXAR model) for the description of the causal effects of SAP on RR. In the open loop scheme, rr values are separately determined by the exogenous input sap and by sap -unrelated variations described by the series u .

The ARXAR model allows computing the power spectral density of RR interval variability, $P_{rr}(f)$, as a sum of two partial spectra [13]:

$$P_{rr}(f) = P_{rr/sap}(f) + P_{rr/u}(f)$$

which represent respectively the variability of RR dependent on SAP ($P_{rr/sap}(f)$) and independent of it ($P_{rr/u}(f)$). A measure of the dependency of the RR variability on SAP changes (Pdep) was obtained as the percentage ratio between the SAP-related RR power and the total RR power. The autoregressive moving average spectral decomposition method [15] applied to the global RR spectrum was used to calculate the power content in the two bands of physiological interest (LF: around 0.1 Hz; HF: 0.14-0.4 Hz). The ratio between the RR power in LF band and the total RR power ($P_{LF}\%$) was then estimated in percentage units.

The gain of the RR-SAP transfer function $G(f)$ was estimated directly from the coefficients of A_{12} and A_{11} blocks. The value of the gain in LF band (GLF) was considered by sampling $G(f)$ on the LF peak of the spectrum of the driving series sap . Gain values were considered reliable when Pdep was larger than 40%.

The significance of the differences between Ctrl and Pts was evaluated by Student's t test, and a value of $P < 0.05$ was considered statistically significant.

3. Results

The tilting test was positive for all Pts, with syncope occurring at 23 ± 4 minutes from tilt table manoeuvre.

As expected, we verified in both Pts and Ctrl an increase of LF relative power (from 45% to about 70%) after the reaching of passive orthostatic postural position, documenting the sympathetic activation. Moreover, a significant decrease ($< 52\%$, $p < 0.05$) was observed in Pts about three minutes before syncope (Figure 2). Excepting for SAP in the last analysed window, no significant differences in the mean values of the cardiovascular series during the tilting test between the two populations were found (Table 1).

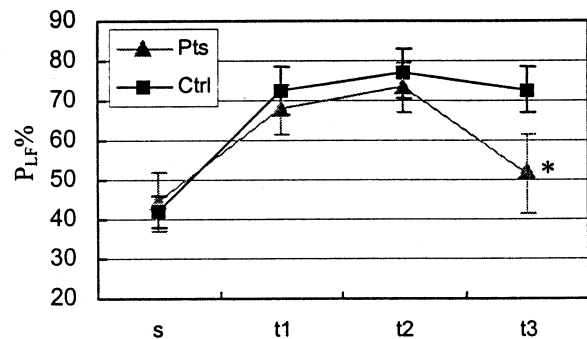


Figure 2. Evolution of the power content in LF band of RR variability expressed in normalised percentage units. Values are mean \pm std.err. evaluated for the two groups in the four epochs selected during HTT. * $P < 0.05$ vs Ctrl.

Mean values of the baroreflex gain obtained by the ARXAR model are shown in Figure 3. The difference

between GLF in Pts and Ctrl became more and more significant (t2: $p < 0.05$; t3: $p < 0.005$) with the maintenance of the posture.

Table 1. Mean RR and SAP values in the two groups during four epochs of HTT.

	RR [ms]		SAP [mmHg]	
	Pts	Ctrl	Pts	Ctrl
s	782±52	844±23	129±6	122±5
t1	683±49	695±17	128±6	120±4
t2	629±45	684±17	121±7	118±4
t3	667±57	683±15	105±7*	118±3

Values are mean±std.err. * $P < 0.05$ vs Ctrl.

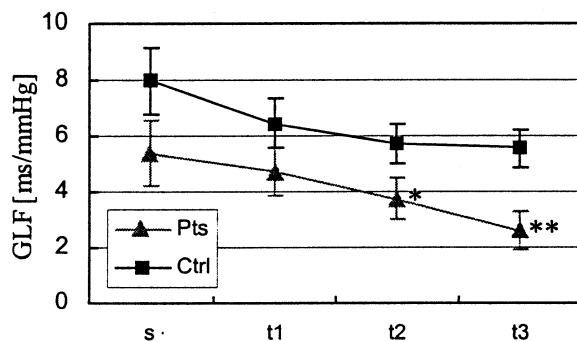


Figure 3. Evolution of baroreflex gain estimated in LF band by the ARXAR model. Values are mean±std.err. evaluated for the two groups in the four epochs selected during HTT. * $P < 0.05$, ** $P < 0.005$ vs Ctrl.

As shown in Figure 4, the spectral decomposition of the heart rate variability pointed out that the percentage of RR power dependent on SAP changes increased after tilt posture up to about 60% in both Ctrl and Pts. Moreover, in Pts this percentage fall down to 17% immediately before syncope.

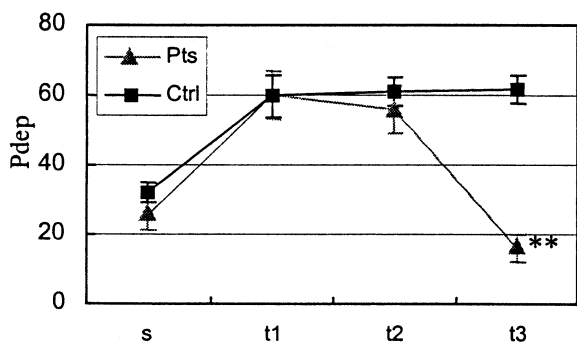


Figure 4. Evolution of the percentage of RR variability dependent on SAP variability as estimated by the ARXAR model. Values are mean±std.err. evaluated for the two groups in the four epochs selected during HTT. ** $P < 0.005$ vs Ctrl.

4. Discussion

The significant increase of LF power in the RR series observed in the upright position confirms the activation of the sympathetic tone due to the tilt manoeuvre. Moreover, the decrease of the LF component noticed 2-3 minutes before syncope suggests that this activation or the coupling between nerve activity and vessels is missing immediately before the loss of consciousness.

The developed causal model allowed us to observe that slow RR fluctuations, beside their increase with tilt, become highly dependent on SAP variability. A possible explanation of this strengthened “causal coupling” could lie in the vagal deactivation, with consequent stronger sympathetic impulse, that characterise the assumption of the orthostatic position. Therefore, the reduced ability of the arterial pressure to drive the duration of the cardiac period observed in the minutes just before syncope can be attributable to a marked vagal re-activation.

These findings could be interpreted hypothesising the contemporary presence of two trigger in the cardiovascular regulation, one of baroreflex and the other of sympathetic-central origin [16]. Indeed, in supine position the considerable vagal and the poor sympathetic activation bring about an uncoupling between the two triggers, and the different origin of the LF peak in the SAP and RR series make them uncoupled. By Tilt manoeuvre, the sympathetic-central trigger become predominant both in SAP and RR series with the same LF peak, thus explaining the stronger dependence of RR changes on SAP changes. Again, the markedly decreasing dependence of RR on SAP noticed prior the loss of consciousness could lead the loss of synchronisation between central and baroreflex trigger to be considered as a major determinant of the syncope event.

The baroreflex gain index elaborated by ARXAR model showed itself to be a good predictive parameter, pointing out a difference between patients and healthy subjects control group which is significant already 10±2 minutes before syncope (t2 window). This result agrees with a previous work showing decreasing baroreflex modulus, calculated with cross-spectral technique, at increasing tilt angles [17].

5. Conclusion

Our study suggests that an important role in provoking syncope is played, beside the weakening of the low-frequency fluctuations of the cardiac period, by the impairment of their modulation through the systolic pressure. Thus, the introduction of causal models able to characterise the regulation of the heart rate in response to pressure changes could be useful in the comprehension of the mechanisms leading to syncope and in the well-timed prediction of the event.

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