

# The Synchrony between Baroreflex Sequences and Cardio-Respiratory Activity

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## Abstract

The bias observed between methods developed to assess the baroreflex control of Heart Rate (HR) lead to gain further insight into those methods. In two groups of subjects were studied: a group of young adults, and a group of middle-aged adults, cardiovascular (CV) and respiratory parameters were continuously recorded during a graded bicycle exercise. This study focused on the sequence method, and its particular time sequence pattern (up and down sequences). Features of respectively the up and down sequences were analysed through comparative analysis and sequence pattern analysis. No significant changes were noticed between the up and down sequences for both the number of sequences and the baroreflex gain. A synchrony was present according to the phase of respiration and also with the diastolic arterial pressure (dap). It may suggest a relation between the baroreflex function and the Bainbridge reflex in governing CV oscillations.

## 1. Introduction

The baroreflex response to arterial pressure changes acts through several effector mechanisms (heart rate (HR), cardiac output (CO), peripheral resistance (PR)). The response of HR is the most studied, since the study of other baroreflex effector mechanisms should face to the difficulty of getting reliable beat-to-beat quantifiable measures.

The baroreflex control of heart rate (HR) is assessed by an index named BRG (Baroreflex Gain, ms/mmHg) through numerous methods in order to evaluate the state of the baroreflex function. Those indexes estimate the overall ability of the baroreflex function; but they do not permit the characterization of specific attributes of the baroreflex system. Thus, the presence of confounding effects relative to each method may introduce a bias in the value. However, their clinical relevance has been demonstrated, showing decreased values to be an independent risk factor after myocardial infarction [1]. A

single measure does not allow to disentangle the part of the cardiovascular variability and oscillations to be ascribed to the baroreflex system from that reflecting the cardio-respiratory interactions. This study focused on the pioneer method used to compute the BRG: the sequence method [2], which can be derived from spontaneous variations from systolic arterial pressure (sap) and RR intervals (rr) [3]. This method allow to separate the feedforward pathway (rr→sap) from the baroreflex feedback pathway (sap→rr). However, this method do not untangle confounding effects of the respiration and of rhythmic source affecting RR intervals independently from the baroreflex feedback mechanisms [4].

Local pattern analysis in the time domain is fostered in order to extract further information and the possible relationship and synchronism with the baroreflex sequences.

## 2. Methods

Two groups of subject were studied: a young adult (n = 7) and a middle-aged group (n= 9) during an incremental workload bicycle ergometer test, including successively a phase of rest (REST), following by three epochs of exercise respectively at 10% (EXE1), 20% (EXE2), and 30% (EXE3) of the nominal maximal effort, and ending by a phase of recovery (REC).

Throughout the protocol, arterial blood pressure via photoplethysmography, EKG, and the respiration via a thoracic belt were continuously recorded. All signal were sampled at a frequency of 300 Hz.

The up and down baroreflex sequences were identified as follows: detection of parallel changes in three or more consecutive beats simultaneously in sap and rri either an increase (+rri/+sap) or a decrease (-rri/-sap) with a minimum change between beats of 4 ms for rri and of 1 mmHg for sap values. The baroreflex gain was derived for both the up and down sequences (BRG, ms/mmHg), for the up sequences (BRG+, ms/mmHg), and for the down sequences (BRG-, ms/mmHg).

At the time of occurrence of either up and down sequences, detection of patterns was performed on the

respiratory and diastolic arterial pressure (dap) signals. A syntactic pattern recognition algorithm was applied to both signals, a complete description can be found in [5]. This algorithm allows to transform the signal to a string of symbols representing an up ramp (u), down ramp (d), a nadir (n), an apex (a), or invariant (o) changes observed in the signal. For each baroreflex sequence, the corresponding string sequence in the respiratory and dap signals was analyzed to detect specific sequence pattern described in Fig. 1 in order to observe if template matching occurs between signals and baroreflex sequences.

The ANOVA test for repeated measures (Tukey's test) was used to determine if significant differences were observed among conditions. A p-value < 0.05 was considered as statistically significant.

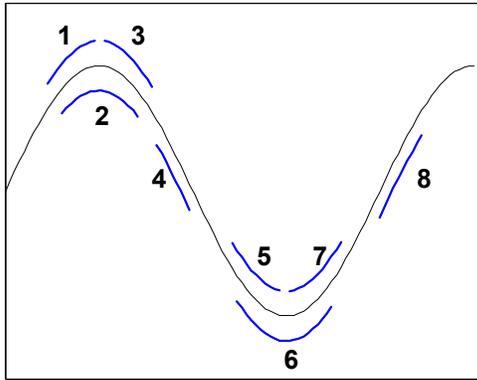


Figure 1: Representation of the eight pattern class representing features of interest for short sequences in periodic oscillations: pattern 1 and 3: respectively upstroke and downstroke sequences containing the apex; pattern 2: upstroke followed by downstroke containing the peak; pattern 3: downstroke sequence containing the apex; pattern 4 and 8: respectively downstroke and upstroke sequences without the apex and nadir point; pattern 5 and 7: respectively downstroke and upstroke sequences containing the nadir point; pattern 6: downstroke followed by an upstroke sequence containing the nadir point.

### 3. Results

The cardiovascular variables are summarized in Table 1. Both group showed a significant decrease of rr intervals with exercise, with a parallel non significant increase in hemodynamic variables. The middle-aged group exhibited lower values for rr intervals and a higher hemodynamic profile.

Table 1: Summary of cardiovascular and haemodynamics variables. (Values are expressed as mean  $\pm$  SD. The symbol <sup>a</sup> indicates a significant decrease from Rest,  $P < 0.05$ ; <sup>b</sup> a significant decrease from Rec,  $P < 0.05$ ; <sup>c</sup> a significant decrease from Exe1,  $P < 0.05$ . RR, RR intervals; SAP, Systolic Arterial Pressure; DAP, Diastolic Arterial Pressure.)

Group	RR (ms)	SAP (mmHg)	DAP (mmHg)
<b>Young</b>			
Rest	932 $\pm$ 86	115 $\pm$ 14	76 $\pm$ 5
Exe1	731 $\pm$ 75 <sup>ab</sup>	130 $\pm$ 18	80 $\pm$ 6
Exe2	657 $\pm$ 47 <sup>ab</sup>	135 $\pm$ 19	80 $\pm$ 5
Exe3	589 $\pm$ 48 <sup>abc</sup>	141 $\pm$ 21	82 $\pm$ 5
Rec	875 $\pm$ 79	119 $\pm$ 14	77 $\pm$ 3
<b>Middle-Aged</b>			
Rest	794 $\pm$ 101	122 $\pm$ 22	80 $\pm$ 10
Exe1	630 $\pm$ 54 <sup>a</sup>	142 $\pm$ 30	87 $\pm$ 10
Exe2	583 $\pm$ 56 <sup>ab</sup>	146 $\pm$ 34	87 $\pm$ 10
Exe3	531 $\pm$ 53 <sup>ab</sup>	154 $\pm$ 36	90 $\pm$ 10
Rec	727 $\pm$ 105	120 $\pm$ 19	79 $\pm$ 10

Fig. 2 showed the baroreflex gain and the relative number of sequences in the young adult group (A) and the middle-aged group (B). Both groups displayed a significant BRG decrease (BRG, BRG+, BRG-), as well as a decrease in the number of sequences with exercise. No significant changes were noticed between BRG+ and BRG- in both group. The middle-aged group exhibited lower baroreflex gain value among epochs.

The sequences represented in average about 30% (REST, REC), 20% (EXE1), 15% (EXE2), 11% (EXE3) of all beats for the young adults; while the sequences counted for about 20% (REST, REC), 10% (EXE1), 6% (EXE2), 1% (EXE3) of all beats for the middle-aged group.

Fig. 3, 4 showed typical sequence patterns found at REST (Fig. 3) and EXE1 (Fig. 4) in both the respiratory and dap signals during the occurrence of respectively up and down baroreflex sequences. The up sequences (+rr/+sap) occurred during the phase of expiration around the maximum effort, while similar behavior is observed to the dap signal (around the peak of oscillations). Conversely, the down sequences (-rr/-sap) occurred around the maximum effort encountered during the inspiration, while they occurred around the nadir point in the dap oscillations.

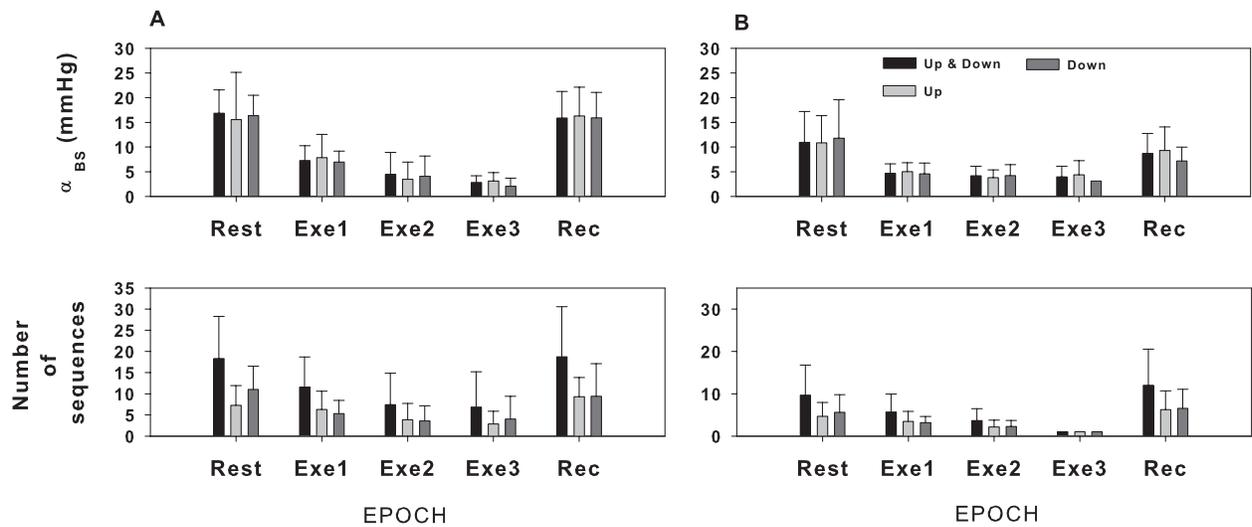


Figure 2 : Baroreflex gain (top) and number of sequences (bottom) during the five epoch for all sequences (up and down), for the up sequences (up), and for the down sequences (down) in the young adult group (A), and in the middle-aged group(B).

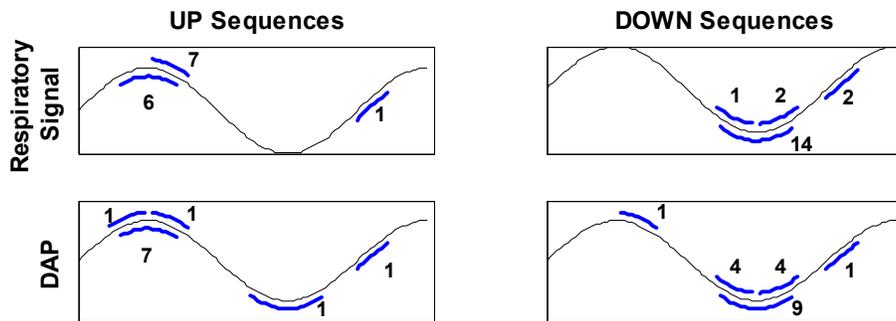


Figure 3 : Typical pattern observed in the respiratory (top) and dap (bottom) signal during the occurrence of the UP and DOWN sequences for a young adult at REST. Up sequences and down sequences were detected with the sequence method.

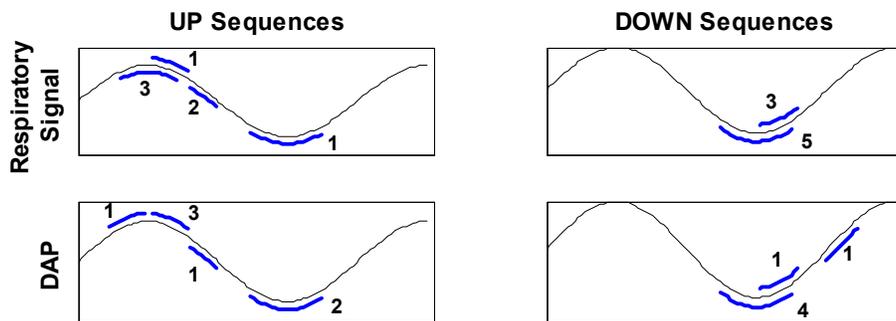


Figure 4 : Typical pattern observed in the respiratory (top) and dap (bottom) signal during the occurrence of the UP and DOWN sequences for a young adult during exercise (EXE2). Up sequences and down sequences were detected with the sequence method.

#### 4. Discussion and conclusions

The features of the sequence method (BRS-, BRG+, number of sequences) displayed a significant decrease with exercise and its intensity, that is in accordance with other studies [6]. The middle-aged group exhibited lower values for those features whatever the conditions with comparison to the young adult group confirming previous works [7]. The baroreflex gain and the number of sequences did not differ between the up and down sequences meaning that the baroreceptor activity might respond identically to the pressor and the depressor effect.

The sequence pattern analysis exhibited synchronism between the cardiovascular and respiratory parameters at the time of occurrence of the up and down sequences. This result underlined the strong influence of the respiration on the CV variables, and particularly the influence of the respiration on HR (respiratory sinus arrhythmia (RSA)). The synchrony between the sequence and respiration was already stressed by previous works [2,9]. The synchronism with dap signal might afford further insight inside the closed relation of CV and respiratory parameters on CV oscillations since the sequences represent about 30% of all the beats contained in the signal. This further confirmation of the close relationship between baroreflex function and Bainbridge or CP reflexes may suggest a different interpretation of this and other BRG indexes and a more solid use of their indubitable clinical value.

#### Acknowledgements

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#### References

- [1] La Rovere MT, Bigger JT, Jr, Marcus FI, Mortara A, Schwartz PJ. Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators. *Lancet* 1998 Feb 14;351(9101):478-484.
- [2] Smyth HS, Sleight P, Pickering GW. Reflex regulation of arterial pressure during sleep in man. A quantitative method of assessing baroreflex sensitivity. *Circ.Res.* 1969 Jan;24(1):109-121.
- [3] Bertinieri G, di Rienzo M, Cavallazzi A, Ferrari AU, Pedotti A, Mancia G. A new approach to analysis of the arterial baroreflex. *J.Hypertens.Suppl.* 1985 Dec;3(3):S79-81.
- [4] Porta A, Baselli G, Rimoldi O, Malliani A, Pagani M. Assessing baroreflex gain from spontaneous variability in conscious dogs: role of causality and respiration. *Am.J.Physiol.Heart Circ.Physiol.* 2000 Nov;279(5):H2558-67.
- [5] Wang TP, Vagnucci AH, Li CC. Peak detection of the plasma cortisol time series by syntactic pattern recognition. *Systems, Man, and Cybernetics*, 1991. 'Decision Aiding for Complex Systems, Conference Proceedings., 1991 IEEE International Conference on 1991:135-140 vol.1.
- [6] Raven PB, Fadel PJ, Ogoh S. Arterial baroreflex resetting during exercise: a current perspective. *Exp.Physiol.* 2006 Jan;91(1):37-49.
- [7] Laitinen T, Hartikainen J, Vanninen E, Niskanen L, Geelen G, Lansimies E. Age and gender dependency of baroreflex sensitivity in healthy subjects. *J.Appl.Physiol.* 1998 Feb;84(2):576-583.
- [8] Rothlisberger BW, Badra LJ, Hoag JB, Cooke WH, Kuusela TA, Tahvanainen KU, et al. Spontaneous 'baroreflex sequences' occur as deterministic functions of breathing phase. *Clin.Physiol.Funct.Imaging* 2003 Nov;23(6):307-313.

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