

# Physiological Regularity of Cardiovascular and Spontaneous Respiration Series in Healthy Humans

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## Abstract

*All cardiovascular and respiratory series are characterized by a variable regular dynamics in human beings, underlying the complexity of the interaction among the control system, the target organs and external/endogenous stimuli. Conditional corrected entropy (CCE) provides information about the regularity of dynamic signal variations: the technique has been applied to RR interval, non invasive systolic arterial pressure, diastolic arterial pressure and spontaneous respiratory signals, from 15 healthy subjects monitored during quiet supine resting. As a regularity index (RI, ranging from 0 to 1), the difference between 1 and the minimum of CCE has been calculated (mean value  $\pm$  SD,) RI resulting  $0.263 \pm 0.090$  for respiration,  $0.500 \pm 0.080$  for systolic arterial pressure, and  $0.459 \pm 0.09$  for diastolic arterial pressure. Heart rate and respiratory dynamics appear more complex than arterial pressure dynamics.*

## 1. Introduction

The analysis of heart rate variability (HRV), investigated in the time and frequency domain is widely used as a tool for the investigation of the neural influence on heart activity: spectral indexes are currently considered as independent markers of either sympathetic or vagal modulation of sinus node [1]. The spontaneous variability of other biological signals than heart rate, such as blood pressure and respiration is determined by the physiological autonomic influence on cardiovascular and respiratory systems. Recently, a novel approach has been introduced,

adding informative content to conventional analysis of biological signals variability, consisting in computation of conditional corrected entropy of a signal (CCE) [2]. CCE provides information about signal entropy, its regularity (and its opposite, complexity), and predictability of its dynamic variations. In other terms, signal predictability is described by CCE analysis, without any *a priori* hypothesis, or any constraint on stationarity of the series under investigation, or its length (as it is the case of Lyapunov coefficients analysis, and Grassberger-Procaccia approach application). This method has been tested over multiparametric signal recordings, collected during short-term sessions, and in long-term circadian RR interval series from healthy volunteers.

## 2. Methods

The regularity of the signals has been investigated in the information domain, exploiting the algorithm proposed by Porta [2]. The recurrence of specific patterns along a time series, as an index of regularity, is quantified by the Shannon entropy [3], characterising the complexity of a given signal. The main drawback of this technique consists in the need of long time series, resulting not suitable for the study of short term dynamics. CCE has been proposed to solve this constraint, being defined as:

$$CCE(L) = CE(L) + \text{perc}(L) \cdot E(1) \quad (1)$$

Where  $E(1)$  is the estimate of Shannon entropy of the process,  $CE$  is its Conditional Entropy [4],  $L$  is the length of the pattern and  $\text{perc}(L)$  is the percentage of length  $L$  patterns found only one time in the data set.

In this study, CCE has been computed on various biological signals simultaneously collected in healthy volunteers, over 256 sample consecutive windows. The technique has been applied to RR interval, non invasive (Finapres, Ohmeda) systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and spontaneous respiratory signal (RESP) from 15 healthy subjects (25 ± years, 10 males), during a 50 minute long quiet supine resting recording session.

The computation has been performed using 6 quantization levels, reconstructing a 12-dimensional phase space.

The series have been normalized to obtain processes with zero mean and unitary variance, by subtracting the average value and dividing by the standard deviation. As a regularity index (RI, ranging from 0 to 1), the difference between 1 and the minimum of CCE has been calculated (mean value ± SD). Paired samples two-sided t-test has been performed to verify the hypotheses about difference between couples of means. Kolmogorov-Smirnov test has been performed to check the normal distribution of data.

Furthermore, the method has been applied to RR interval series, derived from seven 24 hour recordings of ECG by a bipolar lead FM Holter recorder system (Remco-Italia, Cardioline, Milan) collected in healthy volunteers (32 ± 3 years, 5 males) during free-living conditions, analysed over consecutive 256-beat long windows by autoregressive spectral analysis (Levinson-Durbin algorithm, model order 12), as described elsewhere [5]. The following conventional indexes were computed: RR interval, total power, very low (VLF, 0,003-0.030 Hz) power and frequency, absolute and normalized values of low (LF, 0,030-0.150 Hz) and high frequency (HF, 0,150-0.500 Hz) components, as their central frequency, and LF/HF ratio.

Variance analysis was used to assess the interdependence between RI of RR interval and the time and frequency domain indexes; the correlation between the variables has been assessed by Pearson coefficient computation and 2-tailed significance. A p value of 0.05 has been accepted as statistically significant.

Statistical analysis has been performed by SPSS (software package for Windows, 1995).

### 3. Regularity index in short-term recordings

The regularity index resulted  $0.263 \pm 0.090$  for RR (0.209 reported by Porta) interval series,  $0.228 \pm 0.090$  for

respiratory series,  $0.520 \pm 0.080$  for systolic arterial pressure (0.406 by Porta), and  $0.459 \pm 0.090$  for diastolic arterial pressure, as shown in the figure below:

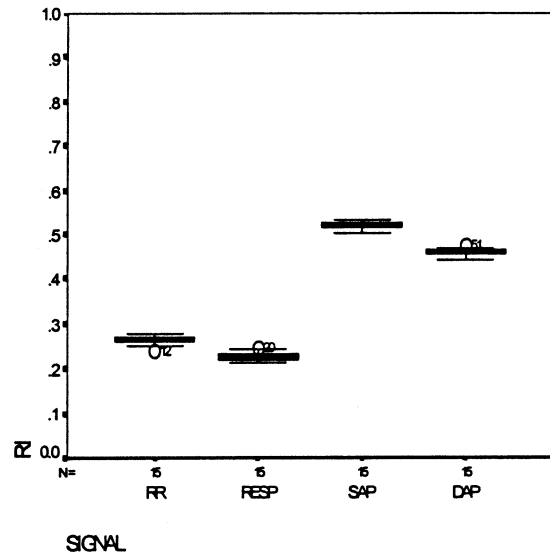


Fig. 1.: Average RI values in controls referred to RR, respiratory, systolic and diastolic arterial pressure series.

RI computed from RR interval is linearly correlated only with SAP RI, as shown in Table 1:

		RR_RI	RES_RI	SAP_RI	DAP_RI
Pearson Correlation	RR_RI	1.000	.060	.579*	.412
	RES_RI	.060	1.000	.218	.053
	SAP_RI	.579*	.218	1.000	.477
	DAP_RI	.412	.053	.477	1.000
Sig. (2-tailed)	RR_RI	.	.832	.024	.127
	RES_RI	.832	.	.435	.850
	SAP_RI	.024	.435	.	.072
	DAP_RI	.127	.850	.072	.
N	RR_RI	15	15	15	15
	RES_RI	15	15	15	15
	SAP_RI	15	15	15	15
	DAP_RI	15	15	15	15

\*. Correlation is significant at the 0.05 level (2-tailed).

Table 1.: Correlations among RR, respiratory, SAP, and DAP RI values.

Correlations

		RI	RR	SD	SDANN	POW	VLF	LF	HF	LF-HF
Pearson Correlation	RI	1.000	-.486	-.640	-.534	-.474	-.702	-.547	-.247	-.069
	RR	-.486	1.000	.664	.504	.643	.573	.636	.544	.542
	SD	-.640	.664	1.000	.959**	.629	.876**	.770*	.248	.427
	SDANN	-.534	.504	.959**	1.000	.443	.747	.601	.067	.413
	POW	-.474	.643	.629	.443	1.000	.776*	.967**	.874*	.542
	VLF	-.702	.573	.876**	.747	.776*	1.000	.900**	.394	.158
	LF	-.547	.636	.770*	.601	.967**	.900**	1.000	.720	.455
	HF	-.247	.544	.248	.067	.874*	.394	.720	1.000	.615
LF-HF	-.069	.542	.427	.413	.542	.158	.455	.615	1.000	
Sig. (2-tailed)	RI	.	.268	.122	.217	.283	.079	.204	.594	.883
	RR	.268	.	.104	.249	.119	.178	.124	.207	.209
	SD	.122	.104	.	.001	.130	.010	.043	.592	.340
	SDANN	.217	.249	.001	.	.319	.054	.154	.886	.357
	POW	.283	.119	.130	.319	.	.040	.000	.010	.209
	VLF	.079	.178	.010	.054	.040	.	.006	.382	.735
	LF	.204	.124	.043	.154	.000	.006	.	.068	.305
	HF	.594	.207	.592	.886	.010	.382	.068	.	.142
LF-HF	.883	.209	.340	.357	.209	.735	.305	.142	.	
N	RI	7	7	7	7	7	7	7	7	7
	RR	7	7	7	7	7	7	7	7	7
	SD	7	7	7	7	7	7	7	7	7
	SDANN	7	7	7	7	7	7	7	7	7
	POW	7	7	7	7	7	7	7	7	7
	VLF	7	7	7	7	7	7	7	7	7
	LF	7	7	7	7	7	7	7	7	7
	HF	7	7	7	7	7	7	7	7	7
LF-HF	7	7	7	7	7	7	7	7	7	

\*\* Correlation is significant at the 0.01 level (2-tailed).

\* Correlation is significant at the 0.05 level (2-tailed).

Table 2. Correlation among RR interval RI, and time/frequency domain markers of HRV from long-term recordings.

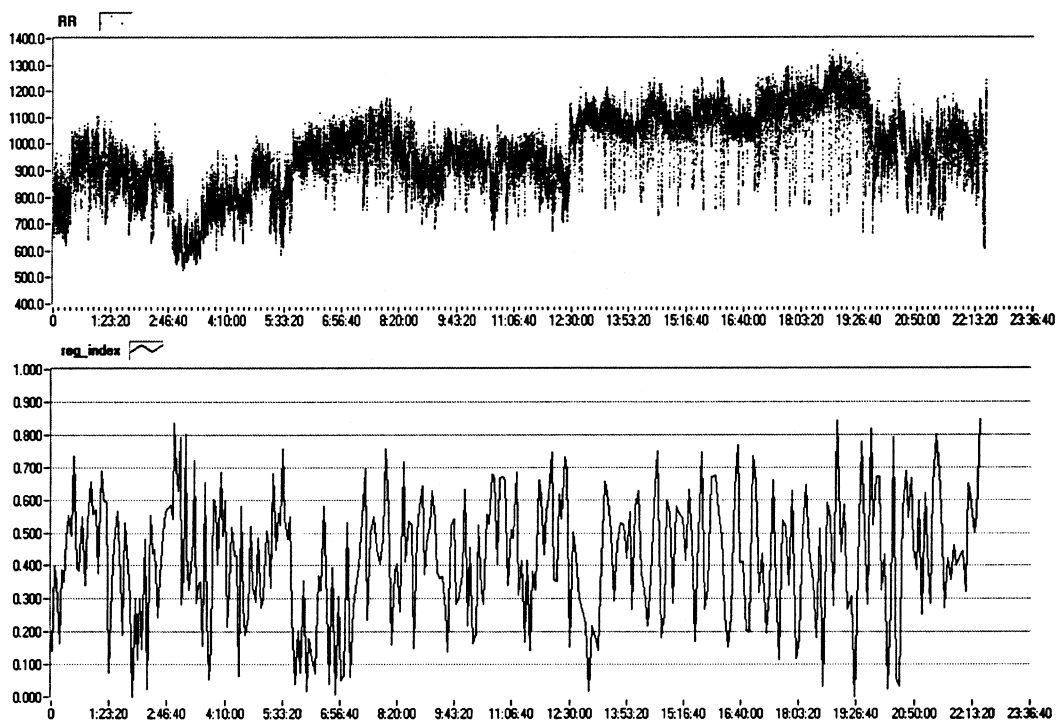


Figure 2. Top-to bottom: 24-hour behavior of RR interval and RR interval RI.

## 4. Long-term recordings

The regularity index was computed in seven patients over 24-hour RR interval time series: average value resulting  $0.675 \pm 0.105$ . The correlation among RI, time domain and frequency domain indexes (by computing the Pearson correlation coefficient) is shown in Table 2: RI was not correlated with any time or frequency domain indexes of HRV computed in the same recordings.

Time course of the RI computed over the 24-hour analysis period on 256-beat long consecutive RR series in a control subject is shown in Figure 2: greater values of RR interval RI, markedly variable, were found during free living recordings, than during steady state fixed protocol monitoring.

## 5. Conclusions

All cardiovascular and respiratory series are characterized by variable regular dynamics, underlying the complexity of the interaction among the control system, the target organs and the environment. Nevertheless, RR and respiratory behavior seems more complex than arterial pressure. In multiparametric short-time long clinostatic recordings, RI indicates a more evident complexity of RR interval and respiratory signal, in comparison with arterial pressure RI. These findings confirm in part, the original observations by Porta, adding the specific information upon respiration regularity [2].

As concerns the application of this analytical approach to RR interval dynamics, as derived from 24-hour ambulatory recordings, RI variability was quite evident, and, interestingly, RI values were higher than in controlled conditions. Various internal/external stimuli might exert a profound influence on the regularity of heart rate signal, which might be interpreted as the result of the beat-to-beat everchanging interplay between neural outflow activity and inherent sinus node function pattern.

Interestingly, no correlation was found among RR interval RI and time/frequency domain indexes of heart rate variability, underlying the specific complementary information provided by this parameter.

In conclusion, CCE is a novel analytical approach which, as in the desiderata of Porta, can be applied to "small amount of data", providing quantitative, reliable indexes of regularity in heart rate, hemodynamic, respiratory signals in controlled and free living conditions. Its independence from conventional statistic and spectral HRV markers, as to heart rate dynamics is important,

underlying the specific informative content of RI. Its application to pathophysiological conditions might provide a deeper insight into mechanisms underlying disease, potentially useful as clinical and prognostic indicators.

## References

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