Assessing complexity of the interactions among cardiovascular variables via multivariate linear model-based approach

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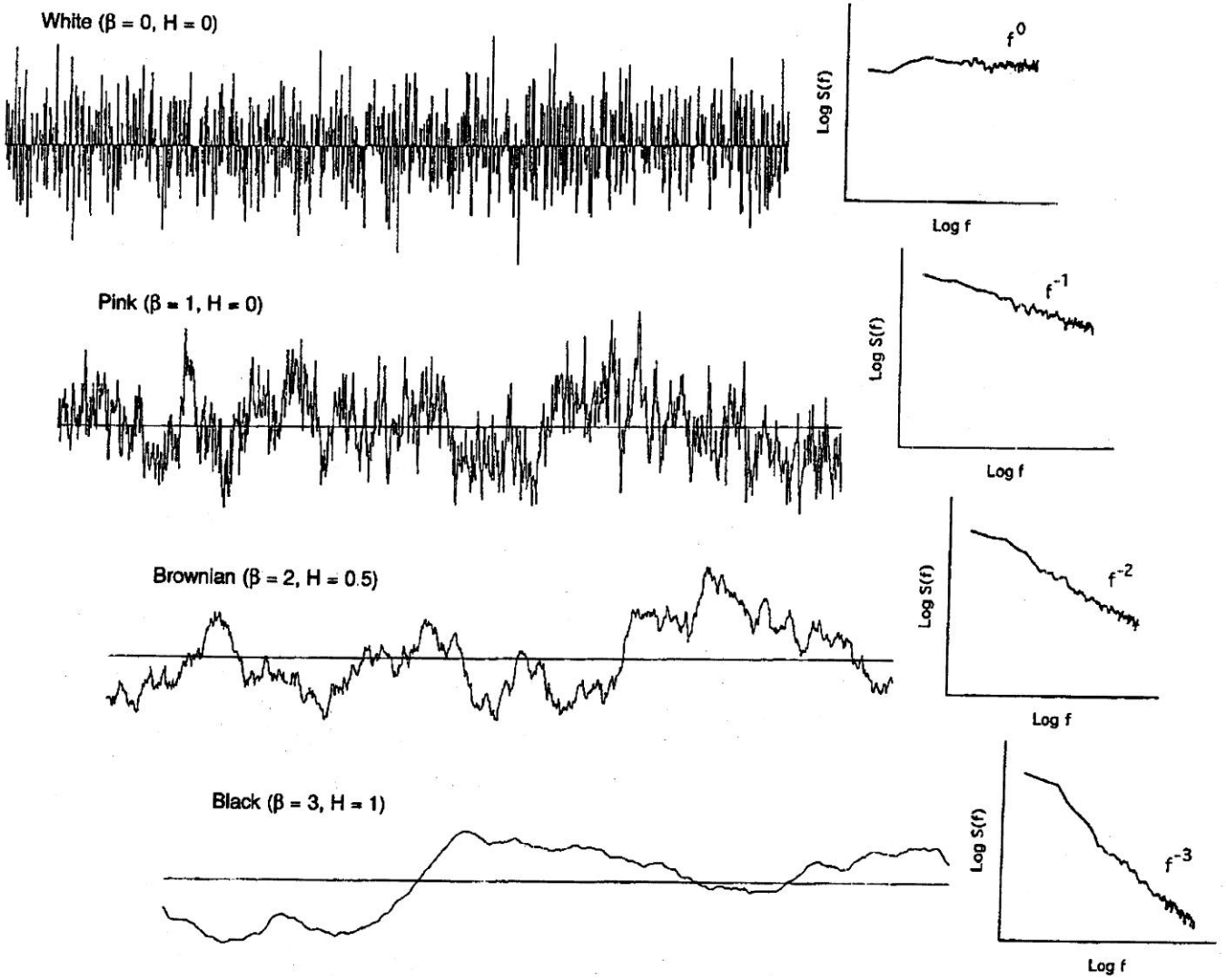
Introduction

Complexity analysis of cardiovascular control provides important physiological and clinical information

The assessment of complexity of cardiovascular control is mainly based on univariate approaches

Among these approaches fractal analysis is one of the most commonly utilized

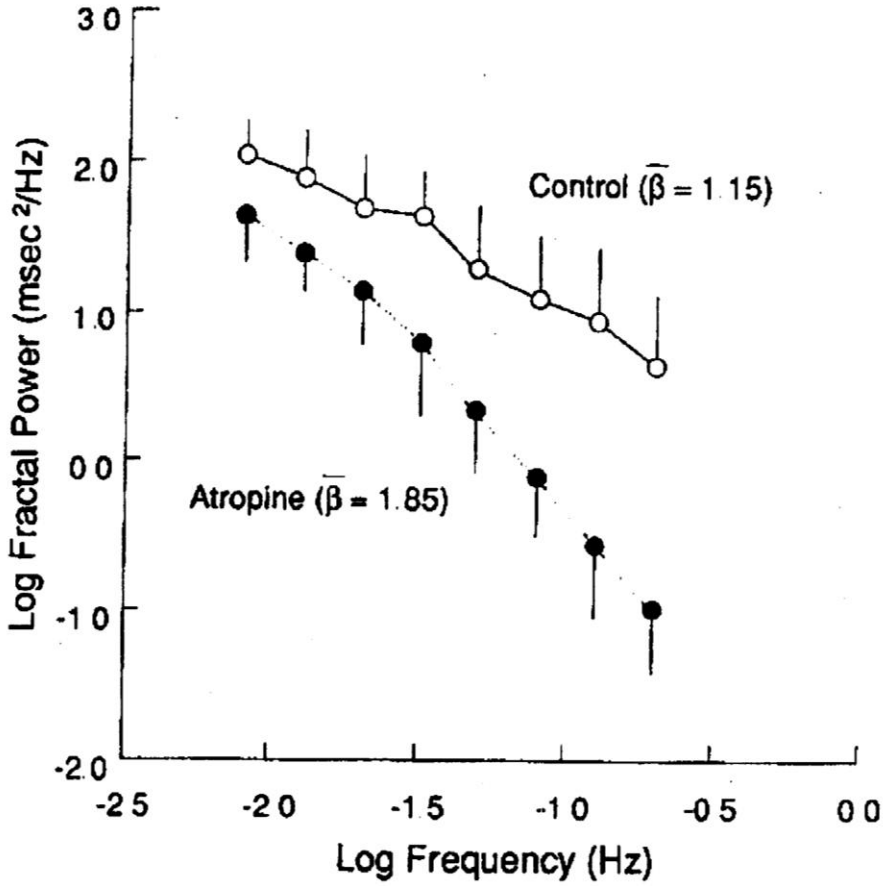
Computer-simulated fractal processes



Complexity decreases with scaling exponent β

Y. Yamamoto et al, Am J Physiol, 269, R830-R837, 1995

Fractal analysis of heart period variability during vagal blockade



Y. Yamamoto et al, Am J Physiol, 269, R830-R837, 1995

Fractal analysis of heart period variability during β-adrenergic blockade

Table 2. *The effects of propranolol on heart rate variability parameters: study 2*

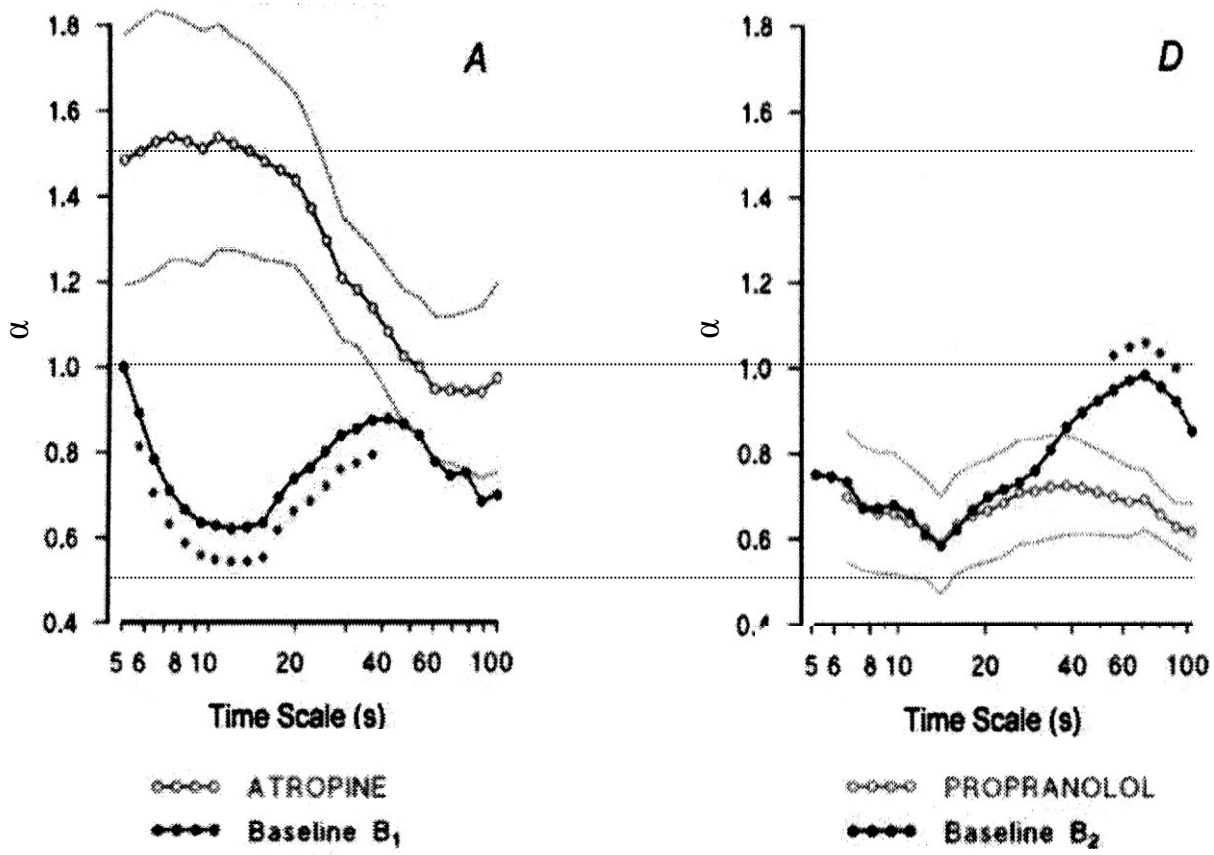
	Long-Term Data		Short-Term Data	
	Placebo	Propranolol	Placebo	Propranolol
$\overline{RR}$, ms	912 ± 111	1,134 ± 133*	914 ± 111	1,128 ± 138*
SD_{RR}, ms	82 ± 28	107 ± 20*	73 ± 23	96 ± 19*
%Fractal	83.0 ± 3 2	85.3 ± 3 8	69.6 ± 11.2†	59.4 ± 13.8†
β	1.15 ± 0.23	1.03 ± 0 22	1.17 ± 0 28	1.02 ± 0 22
H	0.077 ± 0 115	0 015 ± 0 114	0.083 ± 0.139	0.010 ± 0.111
%LF	11 9 ± 3 0	8 9 ± 1 9	22.5 ± 10.3†	25.5 ± 12.3†
%HF	5.2 ± 2.1	5.9 ± 2 8	8.0 ± 3.0	15.0 ± 3 0*
LF/HF	2 76 ± 1.57	1.82 ± 0 81*	3.07 ± 1 17	1 72 ± 0 79*

Values are means ± SD Short-term data were from the 512-beat study *$P < 0.05$ from placebo, and †$P < 0.05$ from the long-term data

Y. Yamamoto et al, Am J Physiol, 269, R830-R837, 1995

Overall spectrum of the scaling exponents of heart rate variability via detrended fluctuation analysis

Atropine **Propranolol**



Brownian motion

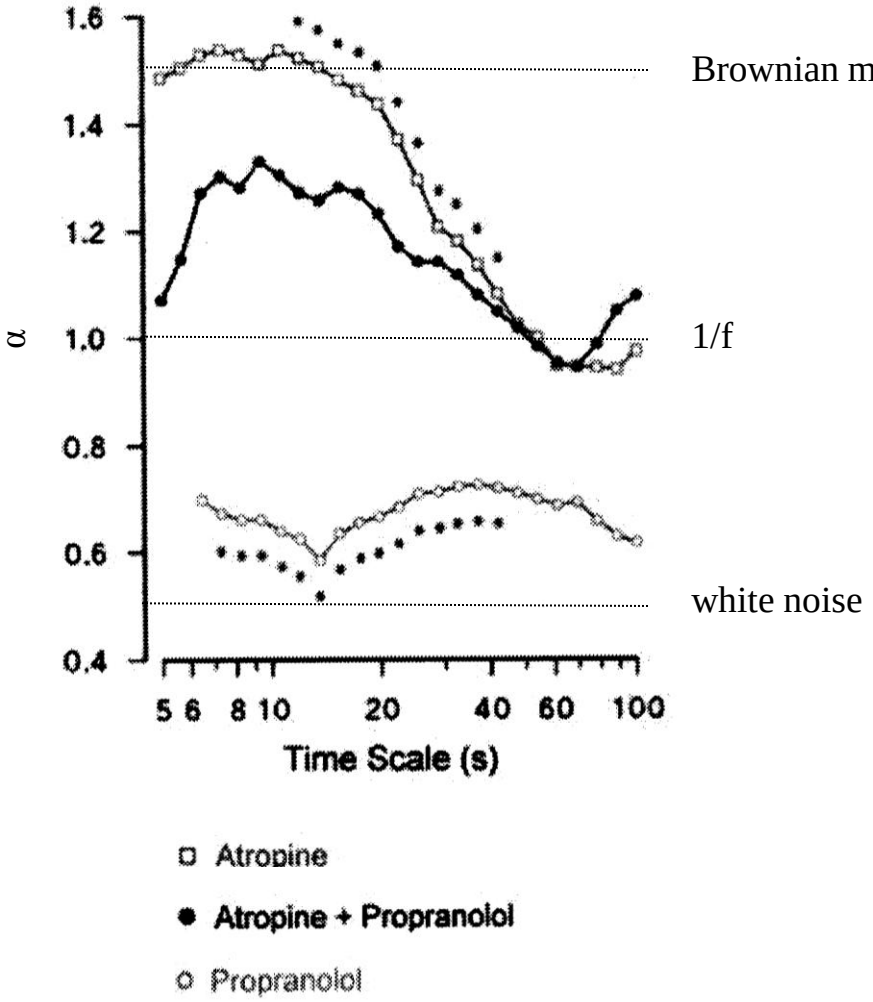
1/f

White noise .

with $\alpha = (\beta+1)/2$

P. Castiglioni et al, J Physiol, 589, 355-369, 2011

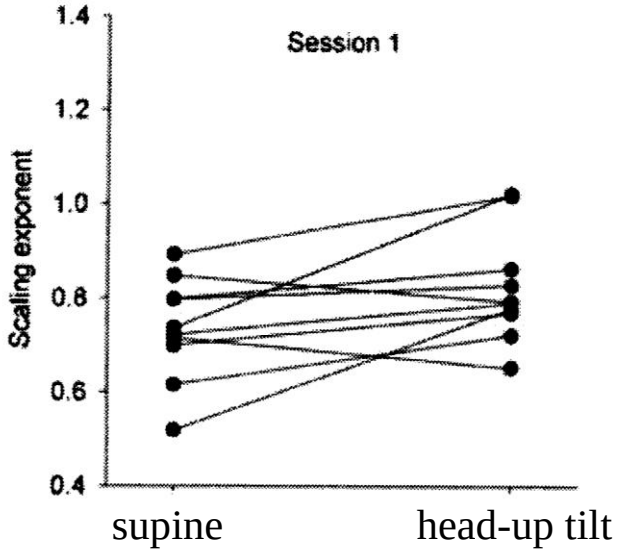
Overall spectrum of the scaling exponents of heart rate variability via detrended fluctuation analysis



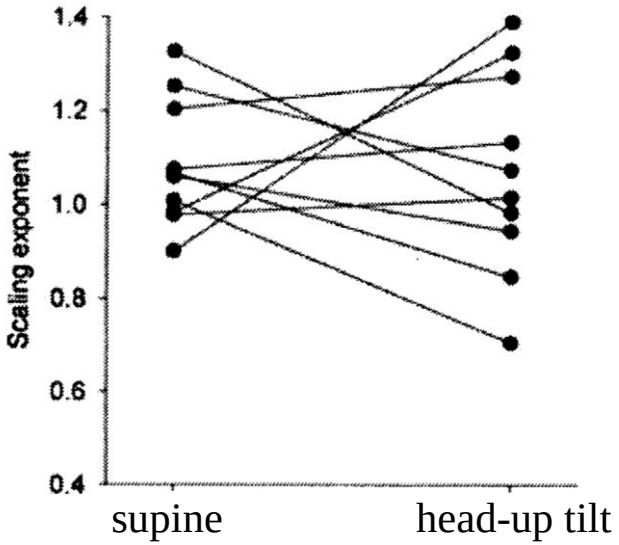
P. Castiglioni et al, J Physiol, 589:355-369, 2011

Fractal analysis of heart period variability during sympathetic activation

baseline



after double-blockade



C.O. Tan et al, J Physiol, 587, 3929-3941, 2009

Age-related alterations in fractal scaling of heart period variability

Table 1. *Heart rate and fluctuation measures for subjects*

	Young ($n = 10$)	Old ($n = 10$)
Mean heart rate	60.55 ± 8.77	57.22 ± 8.60
Range of heart rate	46–73	41–71
SD heart rate	6.12 ± 1.28	2.82 ± 0.99
Fluctuation measures		
α_s	0.90 ± 0.14	1.12 ± 0.19
α_l	0.99 ± 0.10	0.75 ± 0.17
β	1.14 ± 0.15	1.33 ± 0.29

Values are means ± SD; n = no. of subjects.

N. Iyengar et al, Am J Physiol, 271, R1078-R1084, 1996

Drawback of the univariate approaches for the assessment of complexity of the cardiovascular control

Univariate approaches for the evaluation of complexity of cardiovascular control has a major drawback

They cannot take into account the relations among cardiovascular variables and quantify the contribution of specific physiological mechanisms to the overall complexity

Aims

1) to propose a multivariate model-based approach to the assessment of complexity of cardiovascular control

2) to decompose the complexity of a signal into contributions due to the relations among variables

3) to introduce in the assessment of complexity the notion of causality to allow a deeper characterization of the interactions among variables

Outline

1) Multivariate model-based approach for the assessment of complexity of the cardiovascular system

2) Multivariate model-based approach for the assessment of the contribution of specific mechanisms to the overall complexity in the case of open loop interactions

3) Multivariate model-based approach for the assessment of the contribution of specific mechanisms to the overall complexity in the case of closed loop interactions

4) Granger-causality: a method for the quantification of the contribution of specific mechanisms to the overall complexity

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Multivariate AR model

$$y(n) = A(z) \cdot y(n) + w(n)$$

with

$$y(n) = \begin{vmatrix} rr(n) \\ sap(n) \\ r(n) \end{vmatrix} \quad w(n) = \begin{vmatrix} w_{rr}(n) \\ w_{sap}(n) \\ w_{r}(n) \end{vmatrix} \quad A(z) = \begin{vmatrix} A_{rr\text{-}rr}(z) & B_{rr\text{-}sap}(z) & B_{rr\text{-}r}(z) \\ B_{sap\text{-}rr}(z) & A_{sap\text{-}sap}(z) & B_{sap\text{-}r}(z) \\ B_{r\text{-}rr}(z) & B_{r\text{-}sap}(z) & A_{r\text{-}r}(z) \end{vmatrix}$$

where

w_{rr}, w_{sap}, w_r are WGN with zero mean and variance λ^2_{rr}, λ^2_{sap}, λ^2_r

$A_{rr\text{-}rr}(z)$, $A_{sap\text{-}sap}(z)$, $A_{r\text{-}r}(z)$, are causal FIR filters of order p describing the auto-link of a series on itself

$B_{sap\text{-}rr}(z)$, $B_{r\text{-}rr}(z)$, $B_{r\text{-}sap}(z)$ are causal FIR filters of order p describing the cross-link between series (immediate effects are not modeled)

$B_{rr\text{-}sap}(z)$, $B_{rr\text{-}r}(z)$, $B_{sap\text{-}r}(z)$ are causal FIR filters of order p+1 describing the cross-link between series (immediate effects are modeled)

The coefficients of A(z) are estimated via least squares approach and the model order p is optimized via Akaike criterion for multivariate processes

Goodness of fit of the multivariate AR model

The one-step-ahead prediction of y(n) is

$$\hat{y}(n/n-1) = \hat{A}(z)\cdot y(n)$$

Defined the prediction error as

$$e(n) = y(n) - \hat{y}(n/n-1)$$

the covariance matrix of the prediction error, Λ^2, is

$$\Lambda^2 = \frac{1}{N}\sum_{n=1}^{N} e(n)\cdot e^T(n)$$

where ^{T} stands for the transpose operator

$MSPE_{rr}$, $MSPE_{sap}$, and $MSPE_r$ lie on the main diagonal of Λ^2

$MSPE_{rr}$ = complexity of cardiac control
$MSPE_{sap}$ = complexity of vascular control

Experimental protocol

9 healthy males (age: 25-46, 9 men)

We recorded ECG (lead II) and noninvasive finger blood pressure (Finapress 2300) at 500 Hz. Respiratory series was obtained by assessing respiratory-related amplitude changes of the ECG

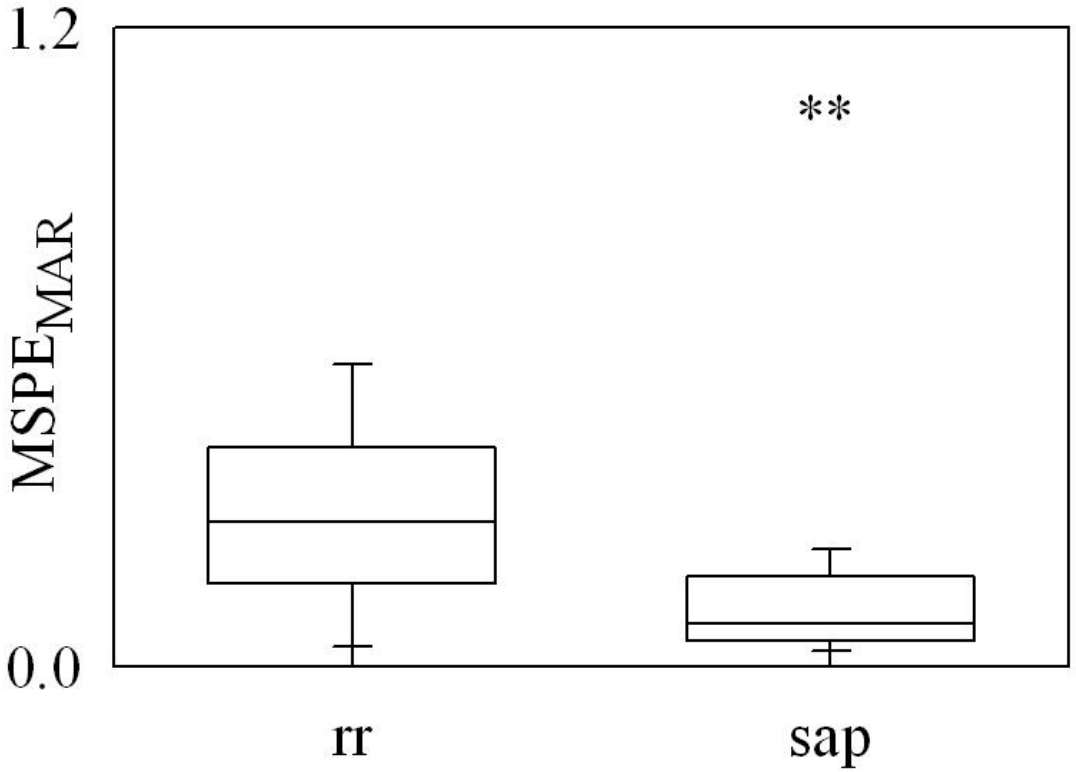
Experimental sessions were carried out in 3 days

AT: parasympathetic blockade with 40 $\mu g \cdot kg^{-1}$ i.v. atropine sulfate
PR: β-adrenergic blockade with 200 $\mu g \cdot kg^{-1}$ i.v. propranolol
AT+PR: β-adrenergic blockade with PR after parasympathetic blockade with AT
CL: 120 minutes after 6 $\mu g \cdot kg^{-1}$ per os clonidine hydrochloride to centrally block the sympathetic outflow to heart and vasculature

AT+PR session followed AT session
AT, PR and CL were always preceded by baseline (B) recording

Series of 256 beats were analyzed after linear detrending

MSPE of rr vs MSPE of sap during pharmacological challenges

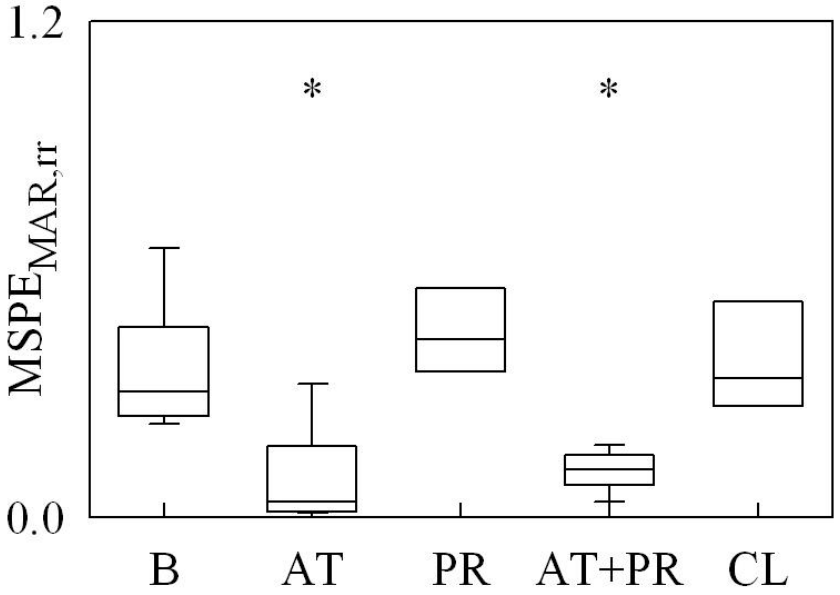


** p<0.001

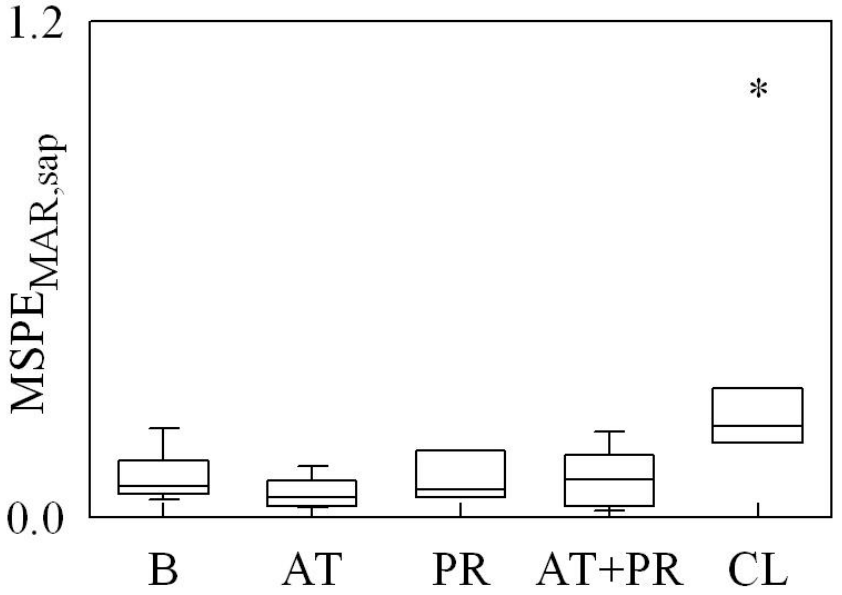
A. Porta et al, J Appl Physiol, 113, 1810-1820, 2012

MSPE of rr vs MSPE of sap during pharmacological challenges

MSPE of rr



MSPE of sap



* $p<0.05$ vs B

A. Porta et al, J Appl Physiol, 113, 1810-1820, 2012

Experimental protocol

19 nonsmoking healthy humans (age: 21-48, median=30, 8 men)

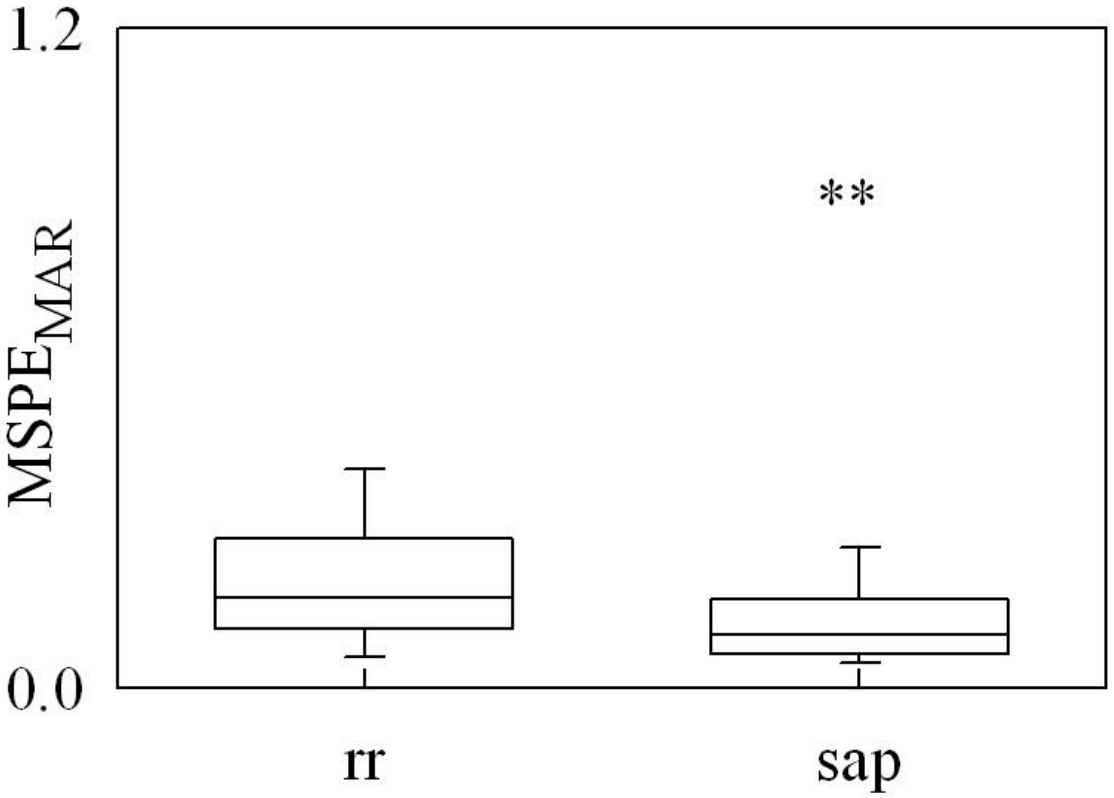
We recorded ECG (lead II), noninvasive finger arterial pressure (Finometer MIDI) and respiration (thoracic belt) at 300 Hz during head-up tilt (T)

Table angles were randomly chosen within the set {15,30,45,60,75,90}

Each T session (10 min) was always preceded by a session (7 min) at rest (R) and followed by a recovery period (3 min)

Series of 256 beats were analyzed after linear detrending

MSPE of rr vs MSPE of sap during graded head-up tilt



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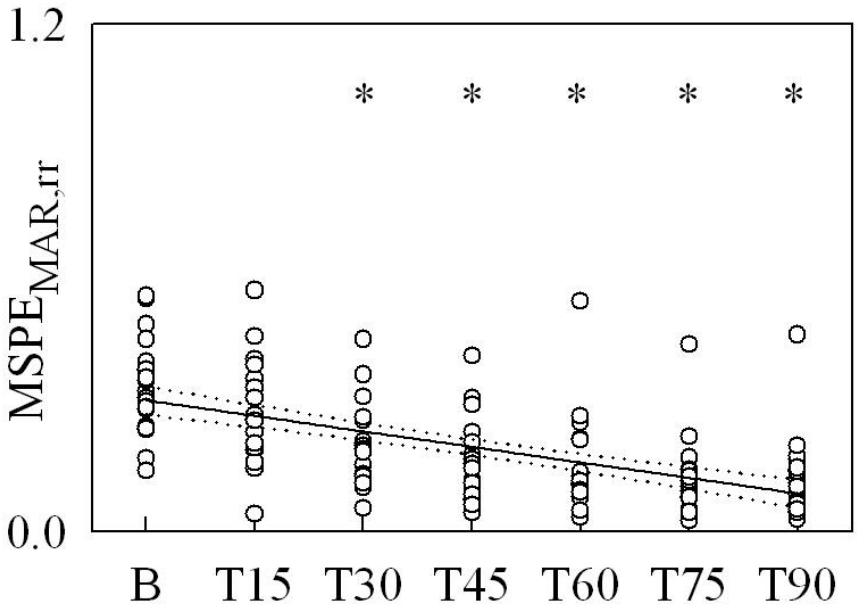
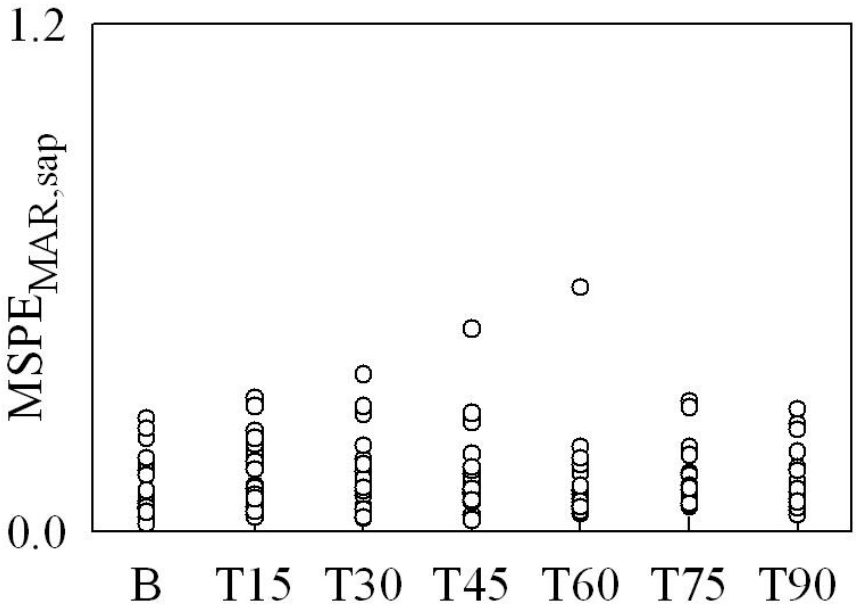
A. Porta et al, J Appl Physiol, 113, 1810-1820, 2012

MSPE of rr vs MSPE of sap during graded head-up tilt

MSPE of rr



MSPE of sap



* $p<0.05$ vs B

A. Porta et al, J Appl Physiol, 113, 1810-1820, 2012

Experimental protocol

- 12 Parkinson disease (PD) patients without orthostatic hypotension or symptoms of orthostatic intolerance (age: 55-79, median=65, 8 men, Hoehn and Yhar scale=2-4)

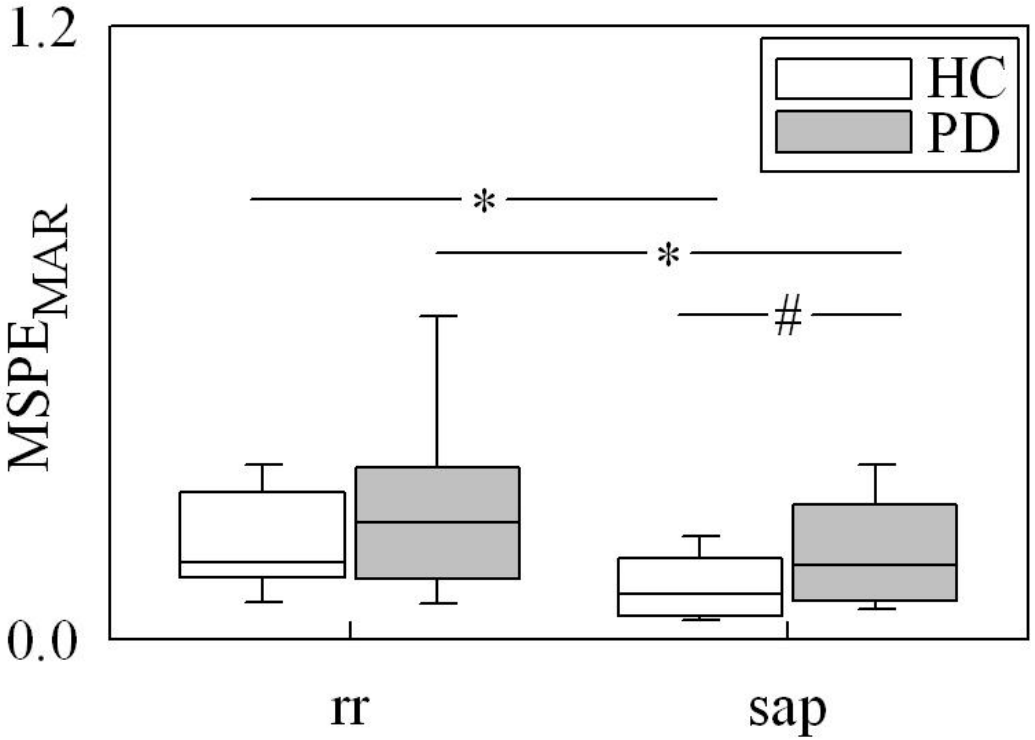
- 12 healthy control (HC) subjects (age: 58-72, median=67, 7 men)

We recorded ECG (lead II), noninvasive finger arterial pressure (Finapress 2300) and respiration (thoracic belt) at 300 Hz during 75° head-up tilt (T75)

Each T75 session (10 min) was always preceded by a baseline (B) session (10 min) at rest in supine position

Series of 256 beats were analyzed after linear detrending

MSPE of rr vs MSPE of sap in Parkinson disease patients

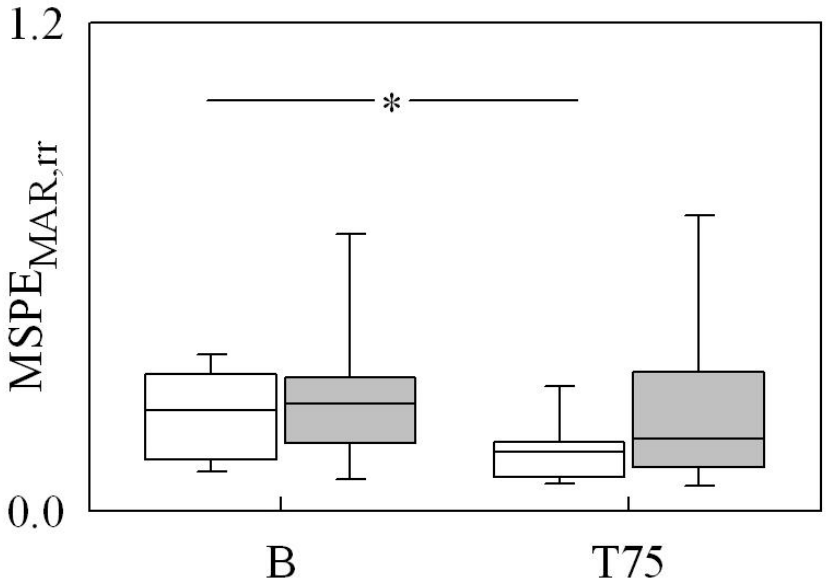


* p<0.05 within population
# p<0.05 within series

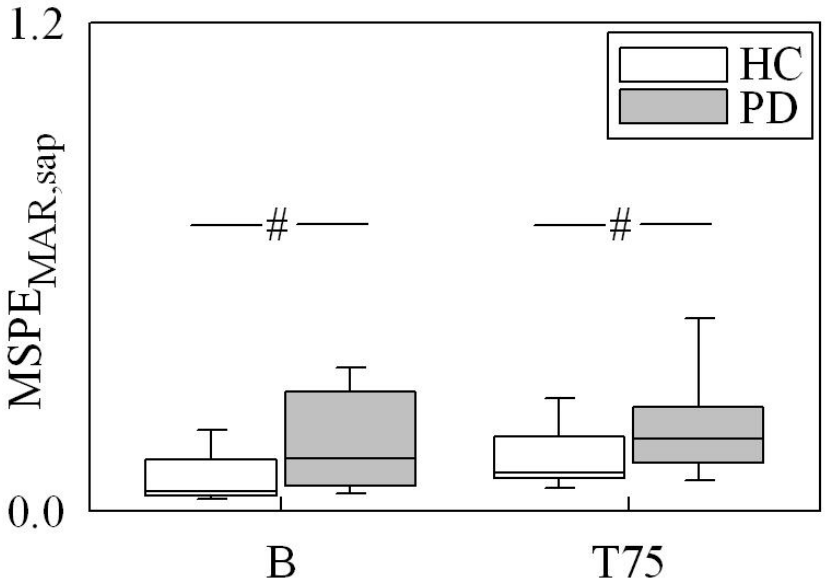
A. Porta et al, J Appl Physiol, 113, 1810-1820, 2012

MSPE of rr vs MSPE of sap in Parkinson disease patients

MSPE of rr



MSPE of sap



* p<0.05 within population
# p<0.05 within experimental condition

A. Porta et al, J Appl Physiol, 113, 1810-1820, 2012

Conclusions (healthy humans)

Complexity of vascular control is smaller than that of cardiac regulation

Vagal activity keeps high the complexity of the cardiac control

Sympathetic activity keeps low the complexity of vascular control

Complexity analyses of cardiac and vascular controls provide different information

Conclusions (Parkinson disease patients)

In Parkinson disease patients without orthostatic hypotension or symptoms of orthostatic intolerance the impairment of cardiac control becomes noticeable in response to an orthostatic challenge

In Parkinson disease patients without orthostatic hypotension or symptoms of orthostatic intolerance the impairment of vascular control is noticeable just in baseline condition

Outline

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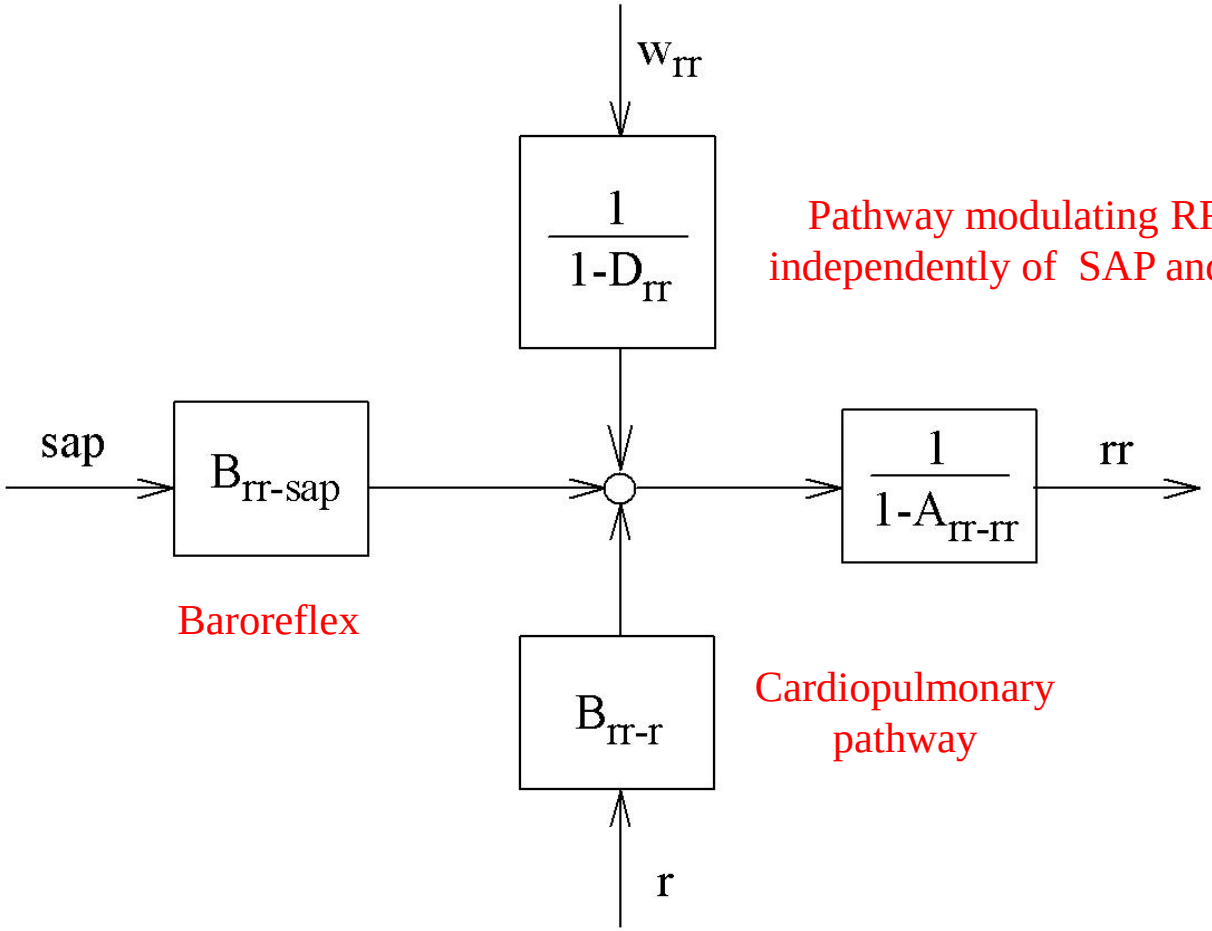
4) Granger-causality: a method for the quantification of the contribution of specific mechanisms to the overall complexity

Trivariate open loop model describing heart period variability



A. Porta et al, Am J Physiol, 279, H2558-H2567 , 2000

Trivariate open loop model describing heart period variability

$AR_{rr}X_{sap}X_rAR_w$ model on rr:

$$rr(i) = A_{rr\text{-}rr}(z)\cdot rr(i) + B_{rr\text{-}sap}(z)\cdot sap(i) + B_{rr\text{-}r}(z)\cdot r(i) + \frac{1}{1\text{-}D_{rr}(z)}\cdot w_{rr}(i)$$

AR_{sap} model on sap:

$$sap(i) = A_{sap\text{-}sap}(z)\cdot sap(i) + w_{sap}(i)$$

AR_r model on r:

$$r(i) = A_{r\text{-}r}(z)\cdot r(i) + w_r(i)$$

where

w_{rr}, w_{sap}, w_r are WGN with zero mean and variance λ^2_{rr}, λ^2_{sap}, λ^2_r

$A_{rr\text{-}rr}(z)$, $A_{sap\text{-}sap}(z)$, $A_{r\text{-}r}(z)$, $B_{rr\text{-}sap}(z)$, $B_{rr\text{-}r}(z)$, $D_{rr}(z)$, are FIR filters of order p in the z-domain

Trivariate open loop model: factorization of heart period variability into partial processes

Under the hypothesis of uncorrelation among w_{rr}, w_{sap} and w_r, the rr series can be factorized as

$$rr(i) = rr(i)|_{w_{sap}} + rr(i)|_{w_r} + rr(i)|_{w_{rr}}$$

where

$$rr(i)|_{w_{sap}} = \frac{B_{rr\text{-}sap}}{(1-A_{rr\text{-}rr})\cdot(1-A_{sap\text{-}sap})} \cdot w_{sap}(i)$$

baroreflex pathway

$$rr(i)|_{w_r} = \frac{B_{rr\text{-}r}}{(1-A_{rr\text{-}rr})\cdot(1-A_{r\text{-}r})} \cdot w_r(i)$$

cardiopulmonary pathway

$$rr(i)|_{w_{rr}} = \frac{1}{(1-A_{rr\text{-}rr})\cdot(1-D_{rr})} \cdot w_{rr}(i)$$

Trivariate open loop model: heart period variability decomposition

Under the hypothesis of uncorrelation among w_{rr}, w_{sap} and w_r, the variance of rr series can be factorized as

$$\sigma^2_{rr} = \sigma^2_{rr}|_{w_{sap}} + \sigma^2_{rr}|_{w_r} + \sigma^2_{rr}|_{w_{rr}}$$

where

$\sigma^2_{rr}|_{w_{sap}}$ is the variance of $rr(i)|_{w_{sap}}$

$\sigma^2_{rr}|_{w_r}$ is the variance of $rr(i)|_{w_r}$

$\sigma^2_{rr}|_{w_{rr}}$ is the variance of $rr(i)|_{w_{rr}}$

Assessing the contributions of baroreflex and cardiopulmonary pathways to the complexity of heart period variability

Contribution of baroreflex to RR complexity

$$\chi^2_{rr\text{-}sap} = \frac{\sigma^2_{rr}|_{w_{sap}}}{\sigma^2_{rr}}$$

$$0 \leq \chi^2_{rr\text{-}sap} \leq 1$$

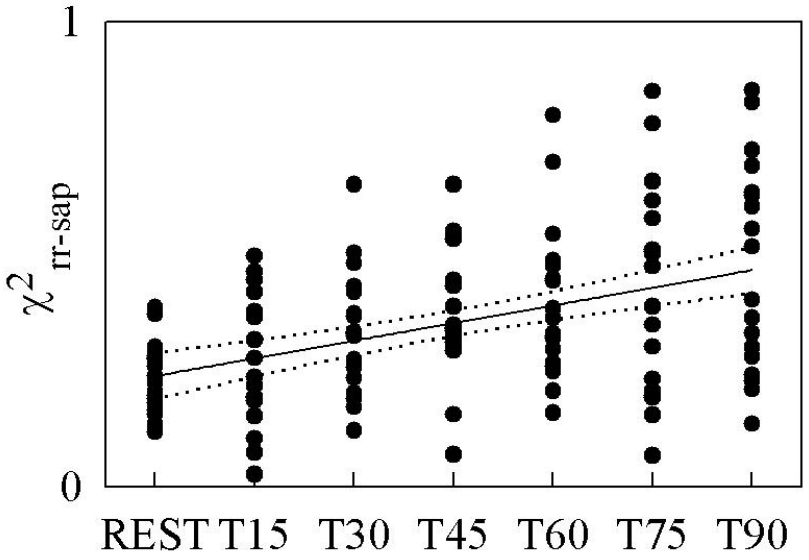
Contribution of cardiopulmonary pathway to RR complexity

$$\chi^2_{rr\text{-}r} = \frac{\sigma^2_{rr}|_{w_r}}{\sigma^2_{rr}}$$

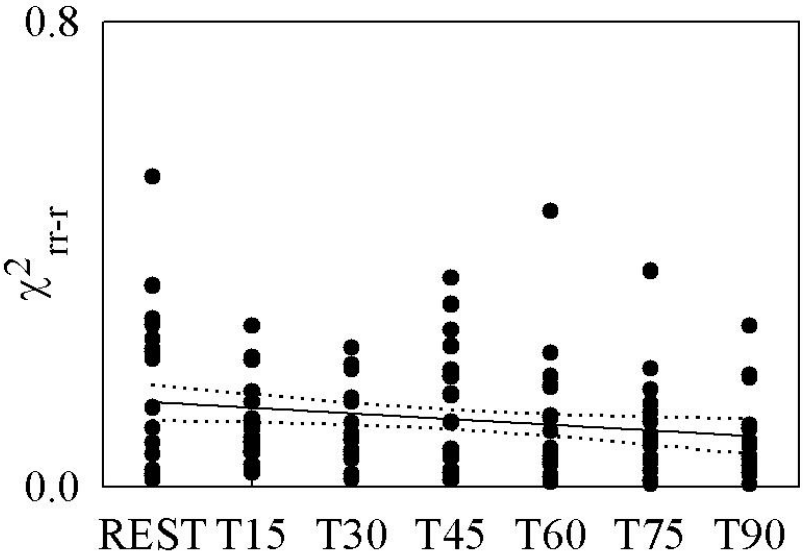
$$0 \leq \chi^2_{rr\text{-}r} \leq 1$$

Baroreflex and cardiopulmonary contributions to the complexity of heart period variability during graded head-up tilt: the open loop trivariate model approach

baroreflex contribution

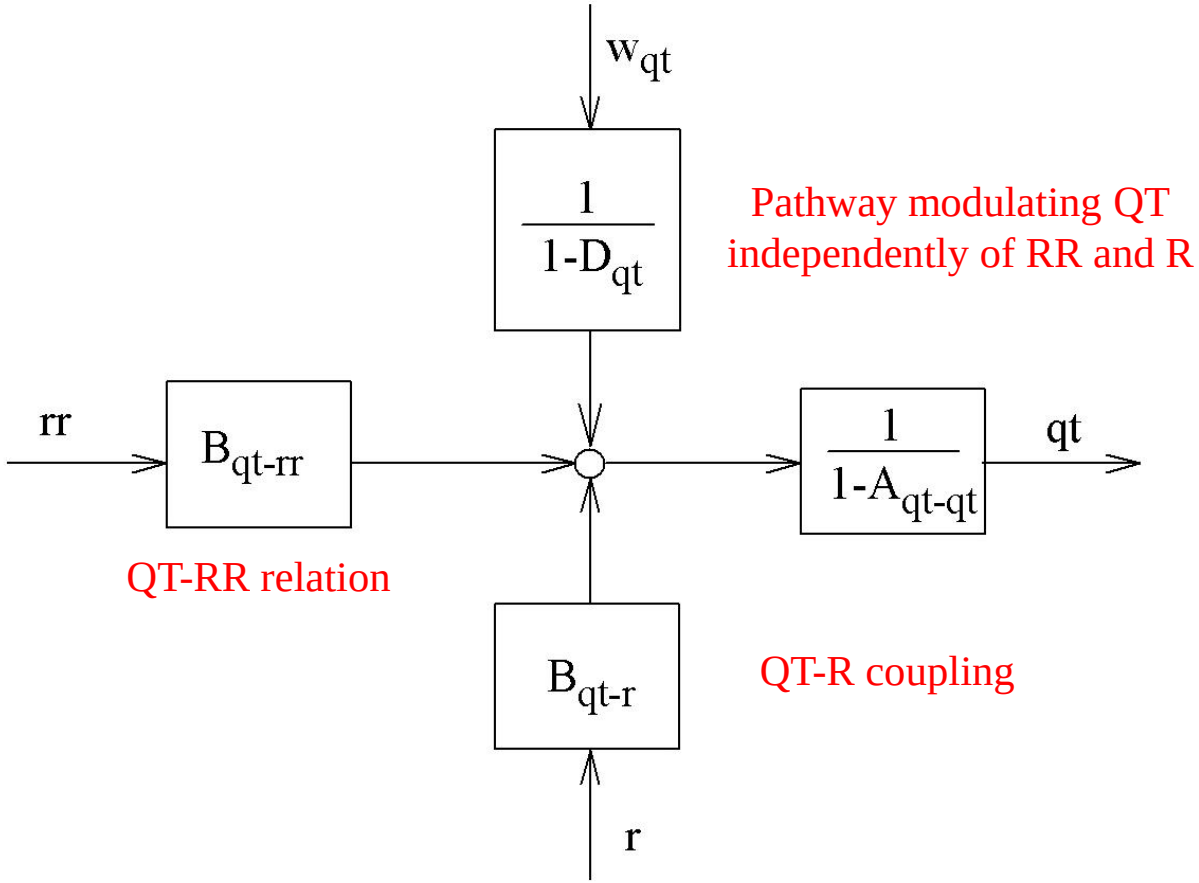


cardiopulmonary contribution



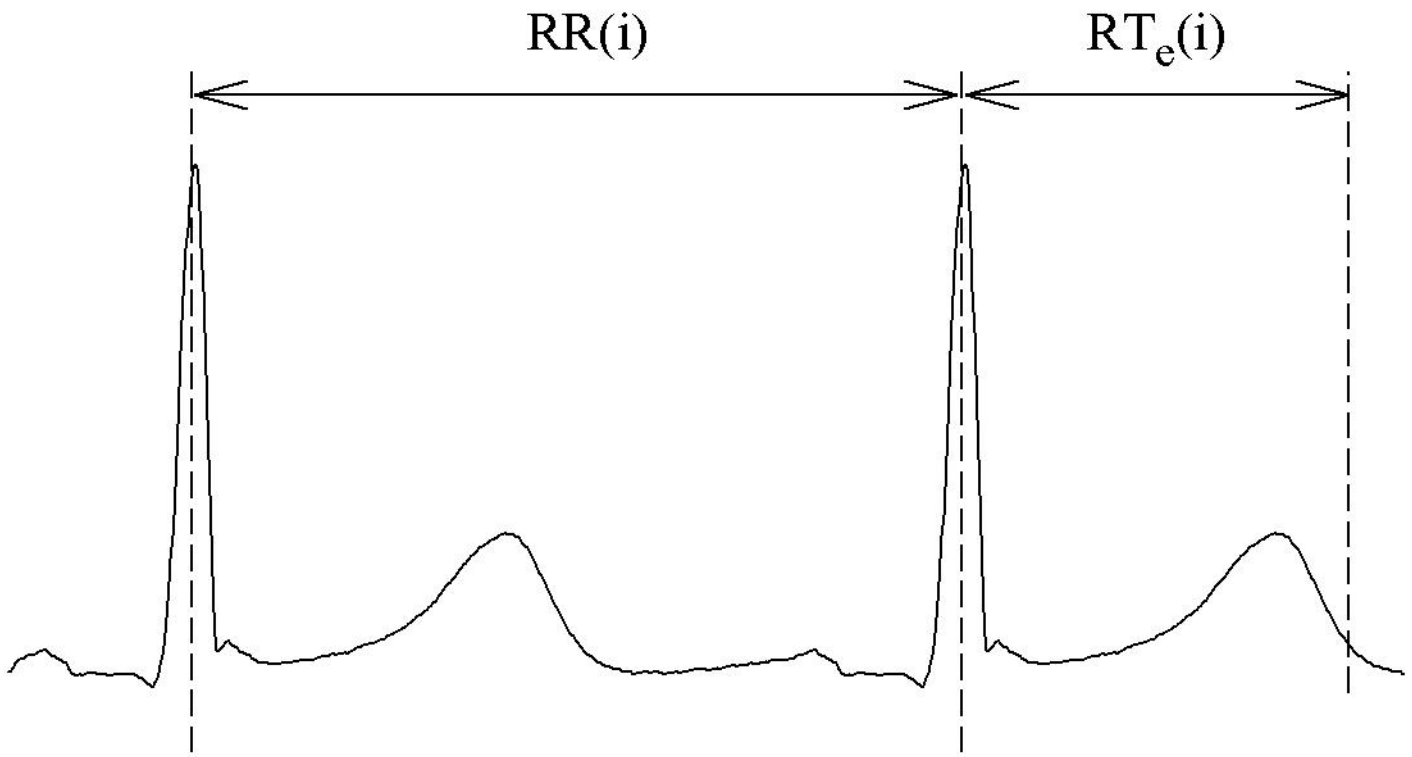
A. Porta et al, Comput Biol Med, 42, 298-305, 2012

Trivariate open loop model describing QT-RR relation



A. Porta et al, Am J Physiol, 298, H1406-H1414, 2010

Approximation of the QT interval and measurement conventions



The i-th RTe interval follows the i-th RR interval

Experimental protocol

17 healthy young humans (age from 21 to 54, median=28)

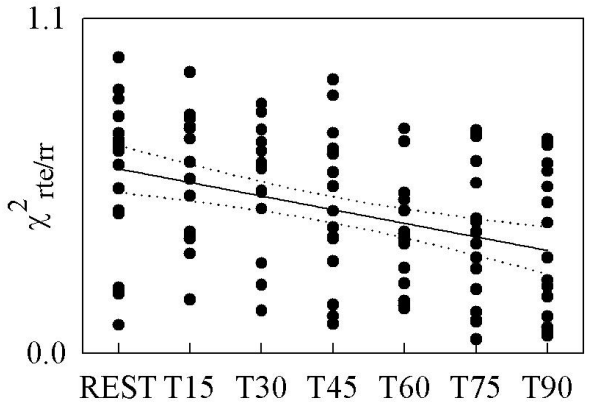
We recorded ECG (lead II) and respiration (thoracic belt) at 1 kHz during head-up tilt (T)

Table angles were randomly chosen within the set {15,30,45,60,75,90}

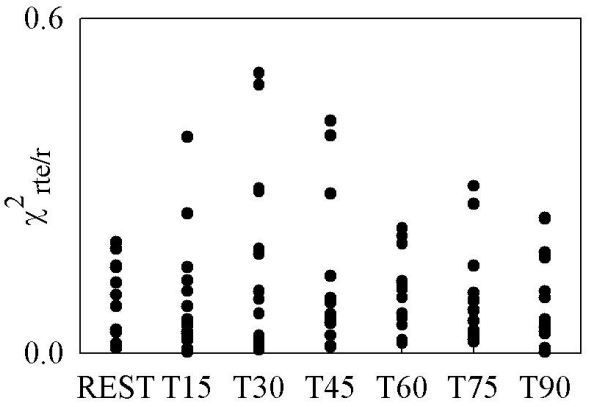
Each T session (10 min) was always preceded by a session (7 min) at rest (R) and followed by a recovery period (3 min)

Contributions to the complexity of RTe variability during graded head-up tilt: the open loop trivariate model approach

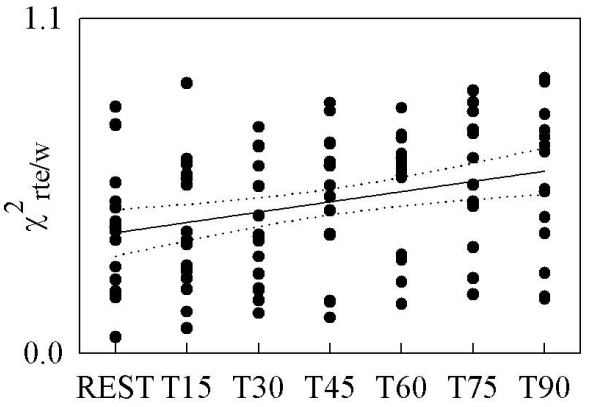
contribution of RR



contribution of R



contribution of influences unrelated to RR and R



A. Porta et al, Am J Physiol, 298, H1406-H1414, 2010

Conclusions (open loop model)

The contribution of baroreflex to the complexity of heart period variability gradually increases as a function tilt table angle

The contribution of cardiopulmonary pathway to the complexity of heart period variability gradually decreases as a function of tilt table angle

The contribution of the QT-RR relation to the complexity of QT variability gradually decreases as a function of tilt table angle

The contribution of inputs independent of heart period changes and respiration to the complexity of QT variability gradually increases as a function of tilt table angle

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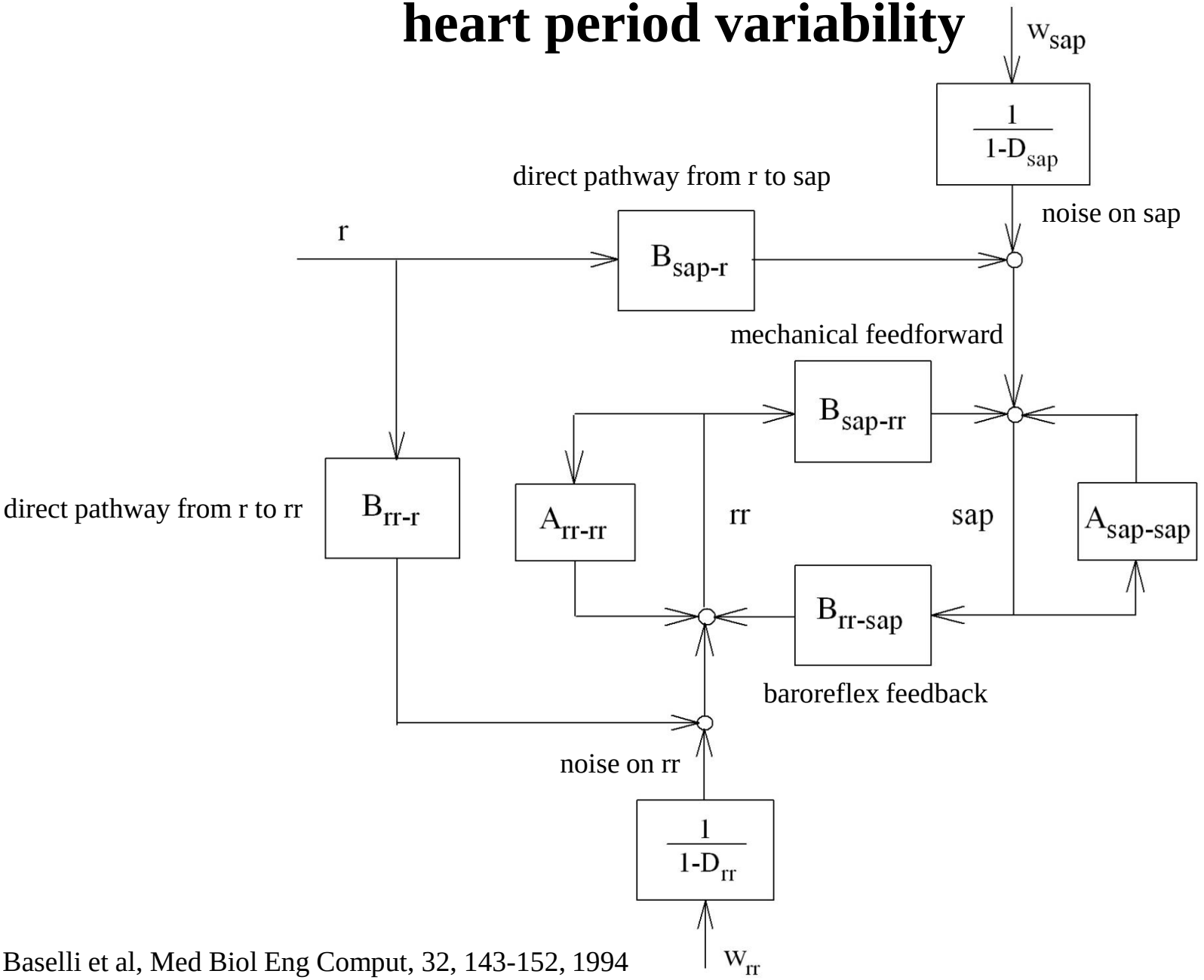


G. Baselli et al, Med Biol Eng Comput, 32, 143-152, 1994

Trivariate closed loop model describing heart period variability

$AR_{rr}X_{sap}X_rAR_w$ model on rr:

$$rr(i) = A_{rr\text{-}rr}(z)\cdot rr(i) + B_{rr\text{-}sap}(z)\cdot sap(i) + B_{rr\text{-}r}(z)\cdot r(i) + \frac{1}{1\text{-}D_{rr}(z)}\cdot w_{rr}(i)$$

$AR_{sap}X_{rr}X_rAR_w$ model on sap:

$$sap(i) = A_{sap\text{-}sap}(z)\cdot sap(i) + B_{sap\text{-}rr}(z)\cdot rr(i) + B_{sap\text{-}r}(z)\cdot r(i) + \frac{1}{1\text{-}D_{sap}(z)}\cdot w_{sap}(i)$$

AR_r model on r:

$$r(i) = A_{r\text{-}r}(z)\cdot r(i) + w_r(i)$$

where

w_{rr}, w_{sap}, w_r are WGN with zero mean and variance λ^2_{rr}, λ^2_{sap}, λ^2_r

$A_{rr\text{-}rr}(z)$, $A_{sap\text{-}sap}(z)$, $A_{r\text{-}r}(z)$, $B_{rr\text{-}sap}(z)$, $B_{rr\text{-}r}(z)$, $B_{sap\text{-}rr}(z)$, $B_{sap\text{-}r}(z)$, $D_{rr}(z)$, $D_{sap}(z)$ are FIR filter of order p in the z-domain

Trivariate closed loop model: factorization of heart period variability into partial processes

Under the hypothesis of uncorrelation among w_{rr}, w_{sap} and w_r, the rr series can be factorized as

$$rr(i) = rr(i)|_{w_{sap}} + rr(i)|_{w_r} + rr(i)|_{w_{rr}}$$

where

$$rr(i)|_{w_{sap}} = \frac{B_{rr\text{-}sap}}{\Delta_{loop}\cdot(1-D_{sap})} \cdot w_{sap}(i)$$

baroreflex pathway

$$rr(i)|_{w_r} = \frac{B_{rr\text{-}sap}\cdot B_{sap\text{-}r} + B_{rr\text{-}r}\cdot(1-A_{sap\text{-}sap})}{\Delta_{loop}\cdot(1-A_{r\text{-}r})} \cdot w_r(i)$$

cardiopulmonary pathway

$$rr(i)|_{w_{rr}} = \frac{1-A_{sap\text{-}sap}}{\Delta_{loop}\cdot(1-D_{rr})} \cdot w_{rr}(i)$$

with $\Delta_{loop}=(1-A_{rr\text{-}rr})\cdot(1-A_{sap\text{-}sap})-A_{rr\text{-}sap}\cdot A_{sap\text{-}rr}$

Trivariate closed loop model: heart period variability decomposition

Under the hypothesis of uncorrelation among w_{rr}, w_{sap} and w_r, the variance of rr series can be factorized as

$$\sigma^2_{rr} = \sigma^2_{rr}|_{w_{sap}} + \sigma^2_{rr}|_{w_r} + \sigma^2_{rr}|_{w_{rr}}$$

where

$\sigma^2_{rr}|_{w_{sap}}$ is the variance of $rr(i)|_{w_{sap}}$

$\sigma^2_{rr}|_{w_r}$ is the variance of $rr(i)|_{w_r}$

$\sigma^2_{rr}|_{w_{rr}}$ is the variance of $rr(i)|_{w_{rr}}$

Assessing the contributions of baroreflex and cardiopulmonary pathways to the complexity of heart period variability

Contribution of baroreflex to RR complexity

$$\chi^2_{rr\text{-}sap} = \frac{\sigma^2_{rr}|_{w_{sap}}}{\sigma^2_{rr}}$$

$$0 \leq \chi^2_{rr\text{-}sap} \leq 1$$

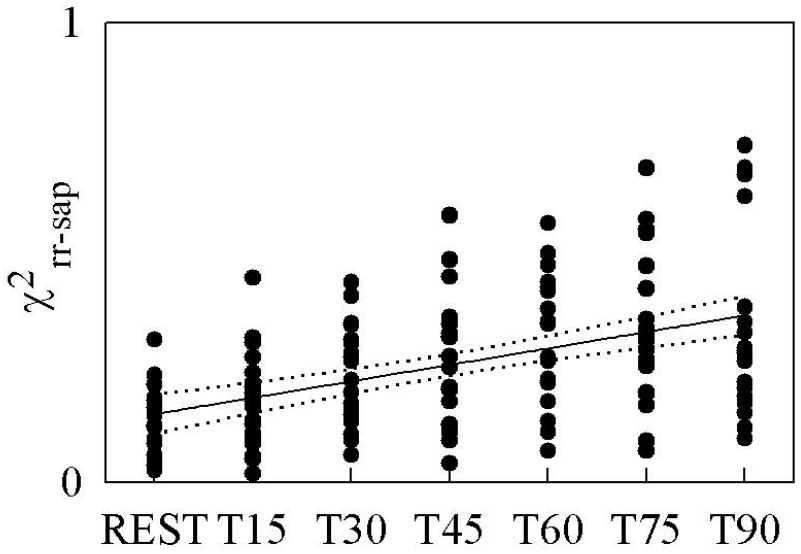
Contribution of cardiopulmonary pathway to RR complexity

$$\chi^2_{rr\text{-}r} = \frac{\sigma^2_{rr}|_{w_r}}{\sigma^2_{rr}}$$

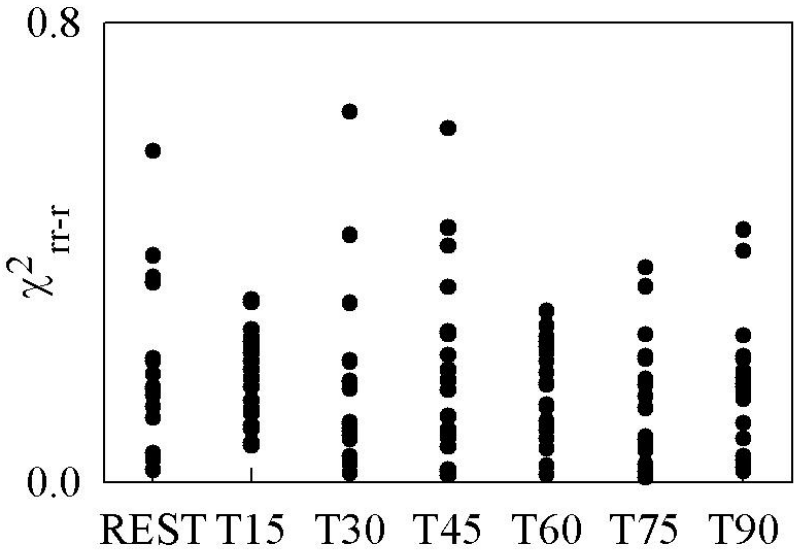
$$0 \leq \chi^2_{rr\text{-}r} \leq 1$$

Baroreflex and cardiopulmonary contributions to the complexity of heart period variability during graded head-up tilt: the closed loop trivariate model approach

baroreflex contribution



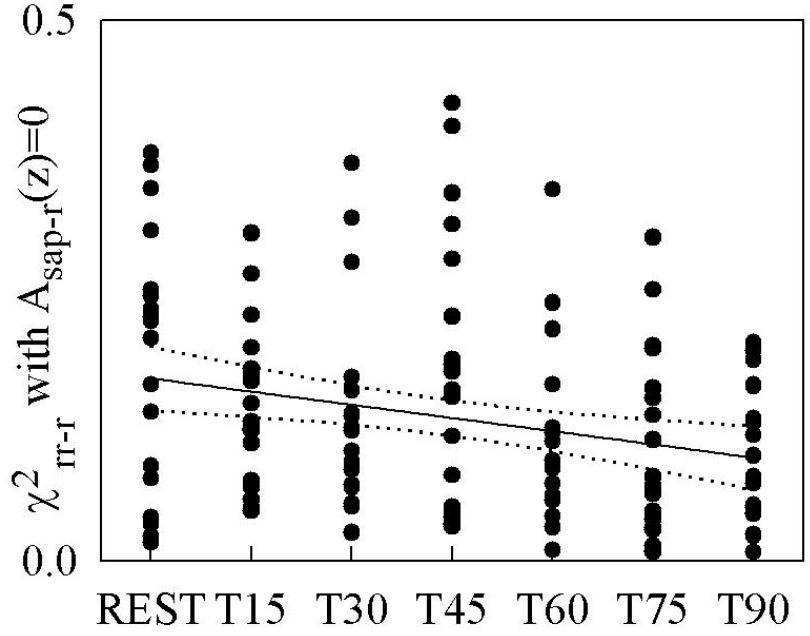
cardiopulmonary contribution



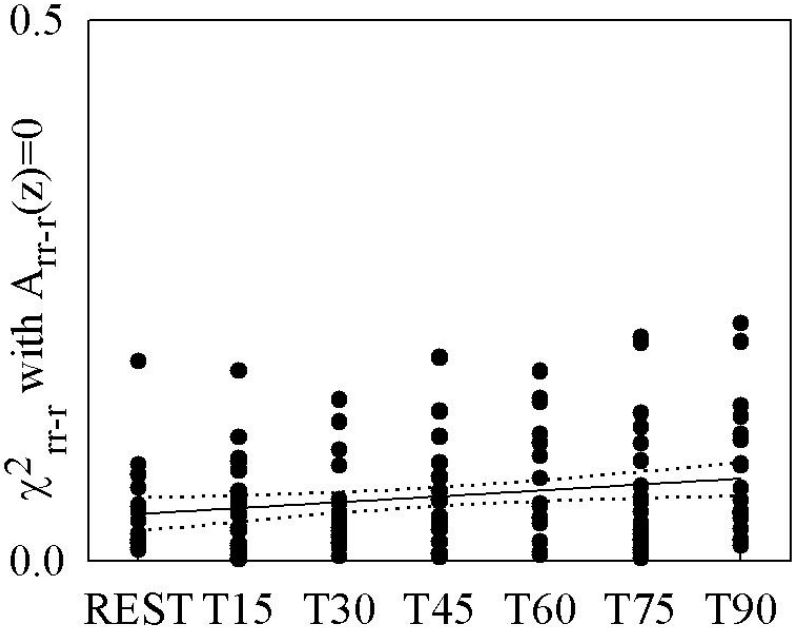
A. Porta et al, Comput Biol Med, 42, 298-305, 2012

Decomposition of cardiopulmonary contributions to the complexity of heart period variability during graded head-up tilt: the closed loop trivariate model approach

direct cardiopulmonary contribution



cardiopulmonary contribution mediated by SAP



A. Porta et al, Comput Biol Med, 42, 298-305, 2012

Conclusions (closed loop model)

The contribution of baroreflex to the complexity of heart period variability gradually increases as a function tilt table angle

The contribution of cardiopulmonary pathway to the complexity of heart period variability was unaffected by the orthostatic challenge

The contribution of cardiopulmonary pathway to the complexity of heart period variability can be decomposed into two terms, related to direct link from respiration to heart period and to indirect link mediated by systolic arterial pressure changes

The direct contribution of cardiopulmonary pathway to the complexity of heart period variability decreases, while the indirect one increases with tilt table angles

Outline

1) Multivariate model-based approach for the assessment of complexity of the cardiovascular system

2) Multivariate model-based approach for the assessment of the contribution of specific mechanisms to the overall complexity in the case of open loop interactions

3) Multivariate model-based approach for the assessment of the contribution of specific mechanisms to the overall complexity in the case of closed loop interactions

4) Granger-causality: a method for the quantification of the contribution of specific mechanisms to the overall complexity

Granger causality: definition

Given $\Omega = \{x_1, \ldots, x_i, \ldots, x_M\}$ the set formed by M signals with $x_i = \{x_i(n), n=1, \ldots, N\}$

x_j is said to Granger-cause x_i if x_i is better predicted in Ω than in Ω after excluding x_j (i.e. Ω-$\{x_j\}$)

Granger causality: modeling

$AR_{xi}X_{\Omega-\{xi\}}$ model in Ω:

$$x_i(n) = A_{xi\text{-}xi}(z)\cdot x_i(n) + \sum_{k=1,\, k\neq i}^{M} B_{xi\text{-}xk}(z)\cdot x_k(n) + w_{xi}(n)$$

$AR_{xi}X_{\Omega-\{xi,xj\}}$ model in $\Omega-\{x_j\}$:

$$x_i(n) = A_{xi\text{-}xi}(z)\cdot x_i(n) + \sum_{k=1,\, k\neq i,j}^{M} B_{xi\text{-}xk}(z)\cdot x_k(n) + w_{xi}(n)$$

Granger causality: assessment of the mean square prediction error

Given the predictors

$$\hat{x}_i(n)|_{\Omega} = \hat{A}_{xi\text{-}xi}(z)\cdot x_i(n) + \sum_{k=1,\, k\neq i}^{M} \hat{B}_{xi\text{-}xk}(z)\cdot x_k(n)$$

$$\hat{x}_i(n)|_{\Omega\text{-}\{xj\}} = \hat{A}_{xi\text{-}xi}(z)\cdot x_i(n) + \sum_{k=1,\, k\neq i,j}^{M} \hat{B}_{xi\text{-}xk}(z)\cdot x_k(n)$$

and defined the predictor errors as

$$e(n)|_{\Omega} = x_i(n) - \hat{x}_i(n)|_{\Omega} \quad \text{and} \quad e(n)|_{\Omega\text{-}\{xj\}} = x_i(n) - \hat{x}_i(n)|_{\Omega\text{-}\{xj\}}$$

the mean square prediction errors (MSPEs) can be assessed as

$$MSPE_{xi}|_{\Omega} = \frac{1}{N\text{-}1}\sum_{i=1}^{N} e^2(n)|_{\Omega} \quad \text{and} \quad MSPE_{xi}|_{\Omega\text{-}\{xj\}} = \frac{1}{N\text{-}1}\sum_{i=1}^{N} e^2(n)|_{\Omega\text{-}\{xj\}}$$

Granger causality: predictability improvement

$$F_{xj \to xi}|_{\Omega} = \frac{MSPE_{xi}|_{\Omega-\{xj\}} - MSPE_{xi}|_{\Omega}}{MSPE_{xi}|_{\Omega}} \cdot \frac{\nu_{den}}{\nu_{num}}$$

ν_{num} = degrees of freedom of the numerator
(i.e. number of coefficients of B_{xi-xj})

ν_{den} = degrees of freedom of the denominator
(i.e. N – number of coefficients of the model $AR_{xi}X|_{\Omega-\{xi\}}$)

If $F_{xj \to xi}|_{\Omega}$ is larger than the critical value of the F distribution for $p<0.01$, the null hypothesis of absence of causality from x_j to x_i is rejected and the alternative hypothesis, $x_j \to x_i$, is accepted

Granger causality: fractional contribution to complexity

$$F_{xj \to xi}|_{\Omega} = \frac{MSPE_{xi}|_{\Omega-\{xj\}} - MSPE_{xi}|_{\Omega}}{MSPE_{xi}|_{\Omega}} \cdot \frac{\nu_{den}}{\nu_{num}}$$

$F_{xj \to xi}|_{\Omega}$ represents the fractional contribution of the relation from x_j to x_i to the complexity of x_i in Ω

Experimental protocol

19 nonsmoking healthy humans (age: 21-48, median=30, 8 men)

We recorded ECG (lead II), noninvasive finger arterial pressure (Finometer MIDI) and respiration (thoracic belt) at 300 Hz during head-up tilt (T)

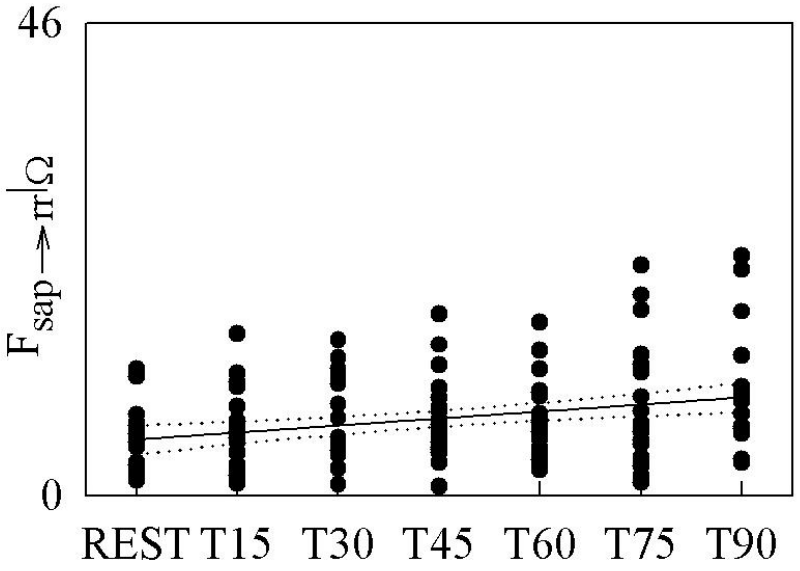
Table angles were randomly chosen within the set {15,30,45,60,75,90}

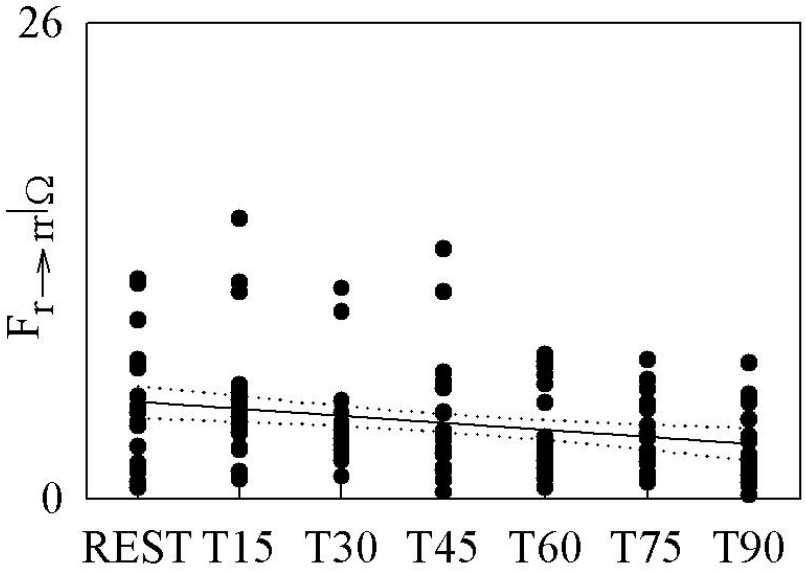
Each T session (10 min) was always preceded by a session (7 min) at rest (R) in supine position.

Series of 256 beats were analyzed after linear detrending

Granger causality: fractional contribution to complexity of heart period variability

Given Ω={rr, sap, r}





A. Porta et al, In: "Methods in brain connectivity inference through multivariate time series analysis", CRC Press, Chapter 15 , in press

Conclusions

Complexity of the cardiovascular control can be assessed through a multivariate model-based approach

This approach is particularly helpful to asses the contributions to complexity of physiological variables given the presence of causal relations with others

Since this approach assesses the interactions between variables in specific time directions (e.g. along baroreflex), it allows the characterization of specific relations among variables