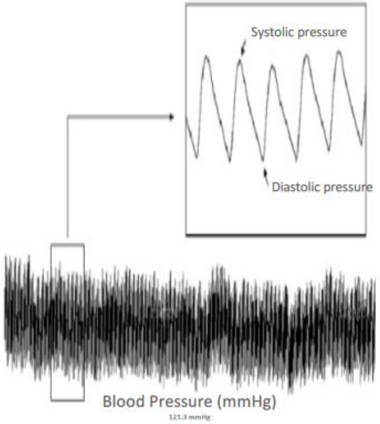
Universidade Federal Fluminense

Colóquio Interinstitucional Modelos Estocásticos e Aplicações

Dinâmica das séries temporais de sinais biológicos para a investigação dos mecanismos fisiológicos de controle cardiovascular



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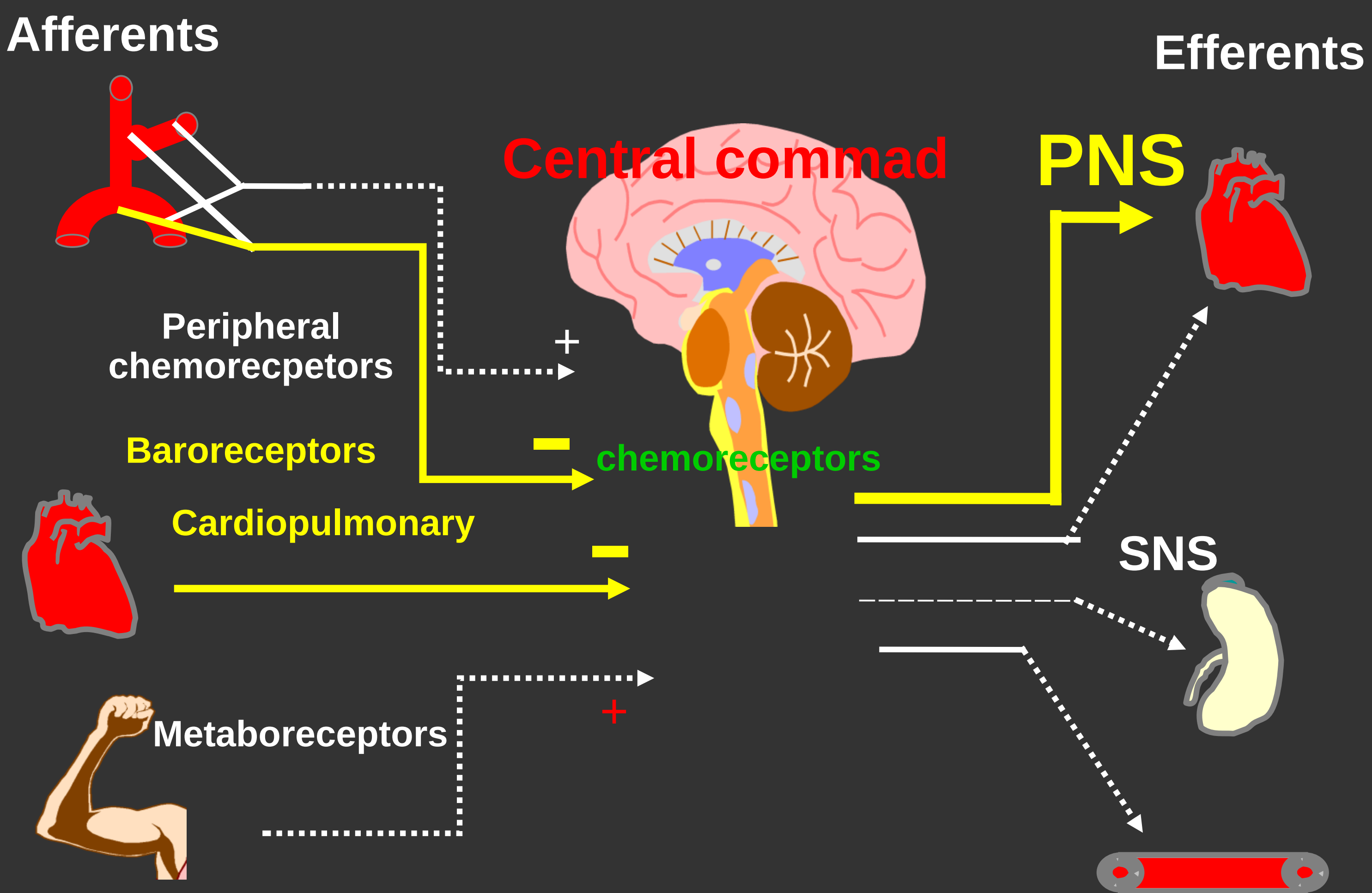
Laboratório de Fisiologia do Exercício Experimental e Aplicada

Instituto Biomédico
Universidade Federal Fluminense

Roteiro

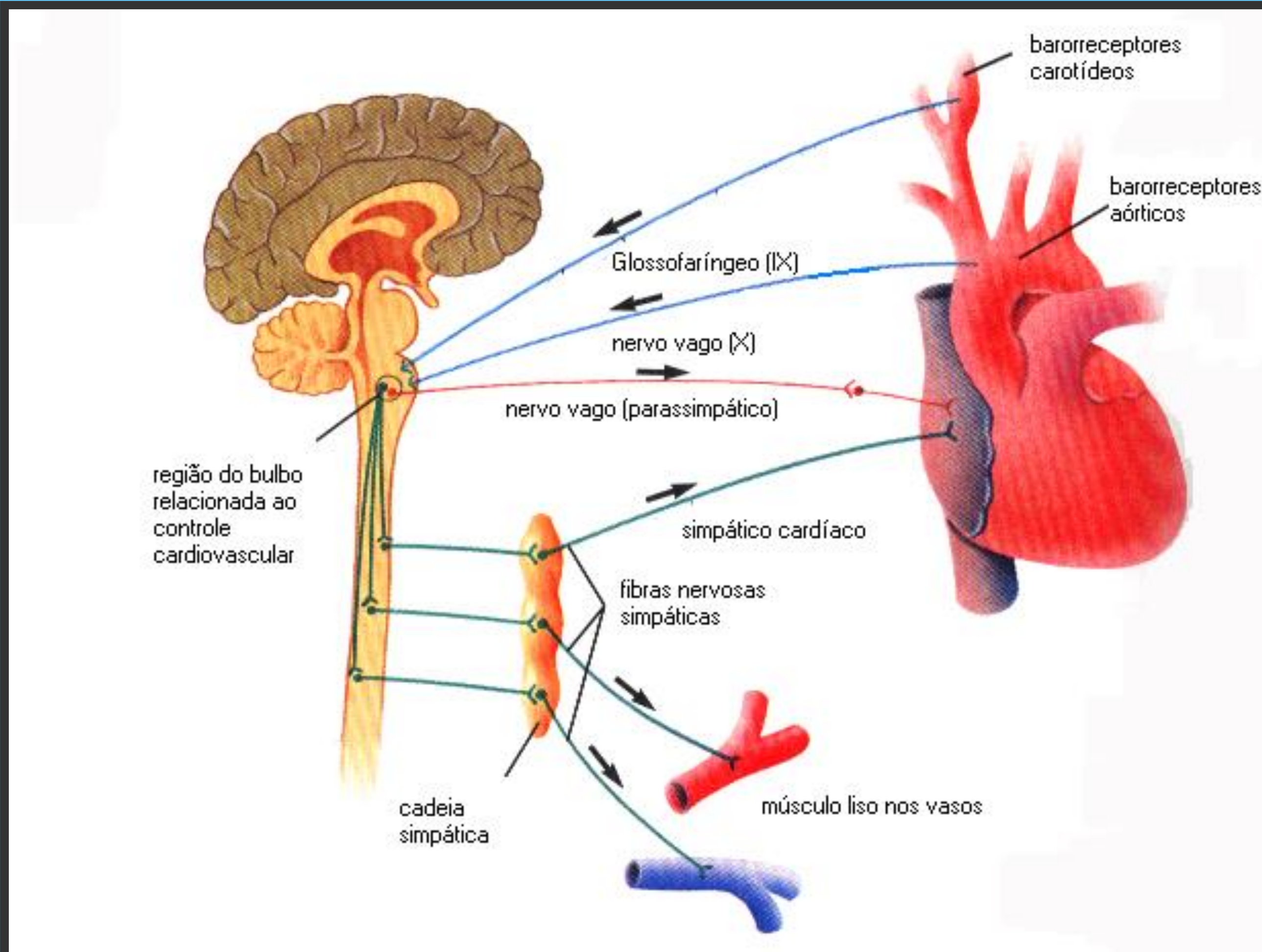
- Mecanismos de controle cardiovascular
- Variabilidade da frequência cardíaca - HRV
- Análise tempo *vs* frequência
- Relevância fisiológica e clínica
- Bases fisiológicas
- Métodos não-lineares
- Aplicações e perspectivas

Autonomic Control



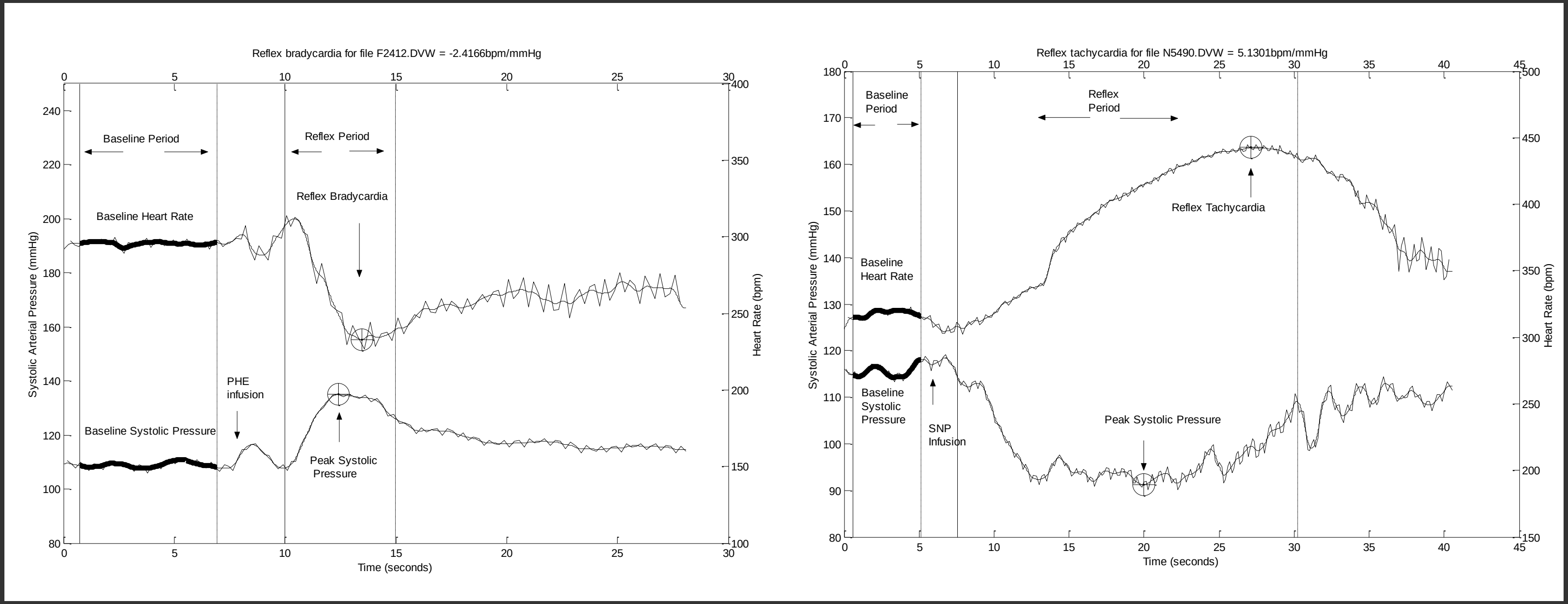
Floras et al JACC. 1993 ; 27:72A.

BAROREFLEX



barorreceptores carotídeos
barorreceptores aórticos
Glossofaríngeo (IX)
nervo vago (X)
nervo vago (parassimpático)
região do bulbo relacionada ao controle cardiovascular
simpático cardíaco
fibras nervosas simpáticas
cadeia simpática
músculo liso nos vasos

semi-automatic monitor BRS



PHENYLEFRINE

NITROPRUSIDE

Soares *et al*. 2005, Braz J Med Biol Res 38(6):949-57

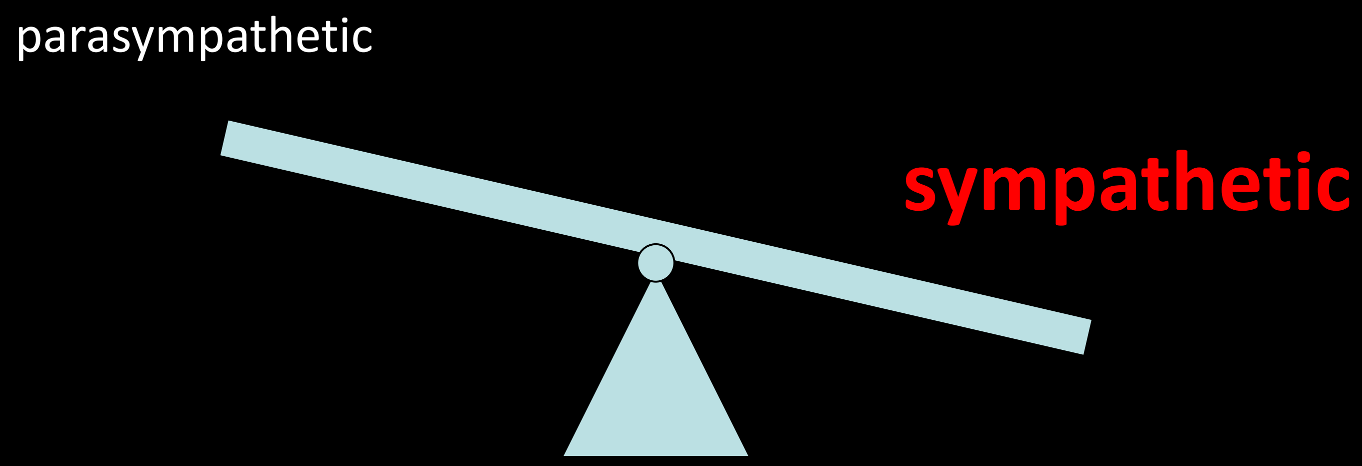
Parasympathetic

conservation

Sympathetic

'fight or flight'

Risk fator associated to cardiovascular diseases



What is HRV?

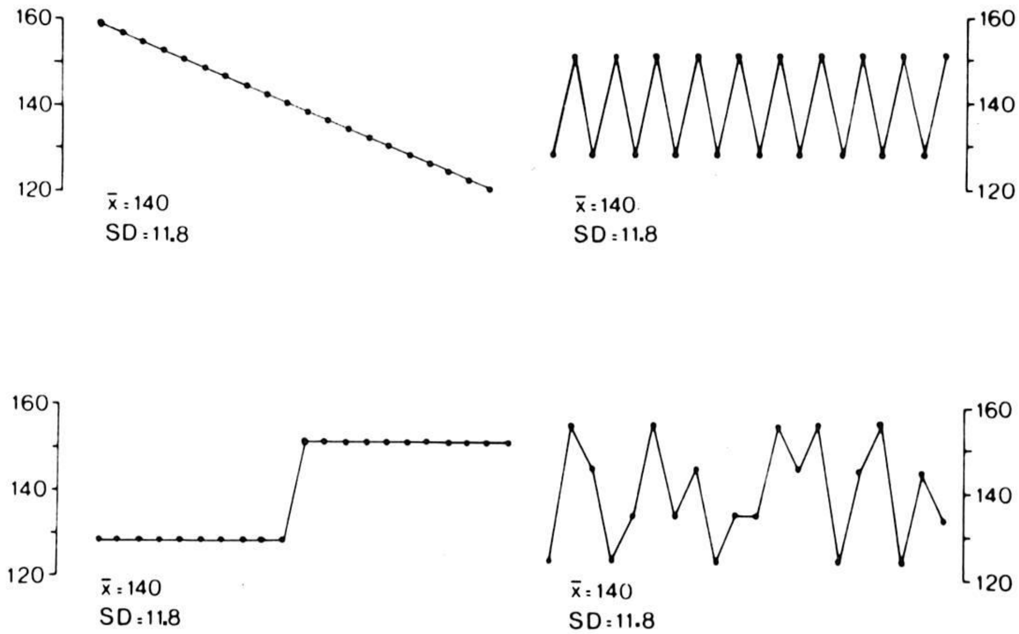
HRV definitions

- ***Time domain:*** description of the variability of biological signals over the time

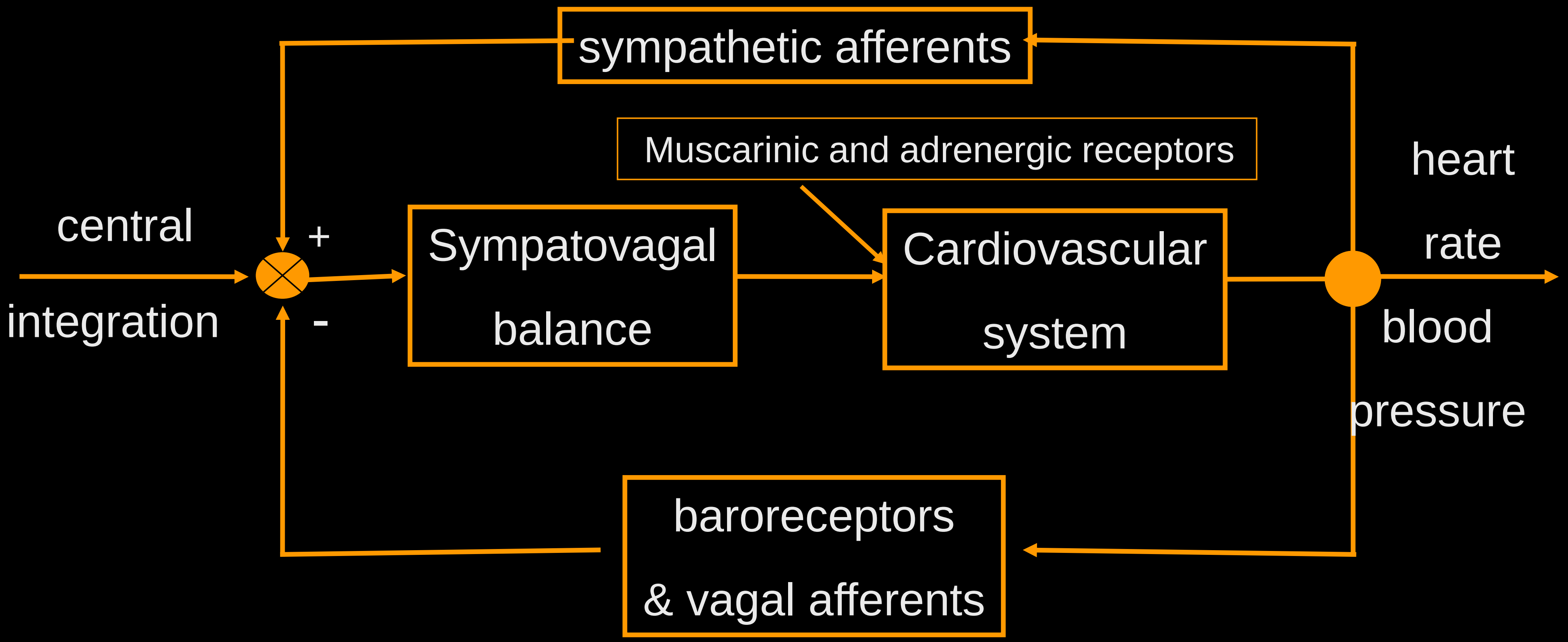
- ***Frequency domain:*** description of the variability of biological signals as the sum of elementary oscillatory components defined in terms of frequency, amplitude and phase

HRV Metodology

- Time domain
- Linear methods (frequency domain)
  - autoregressive algorithms
  - FFT
  - time-varying algorithms
- Non-linear methods

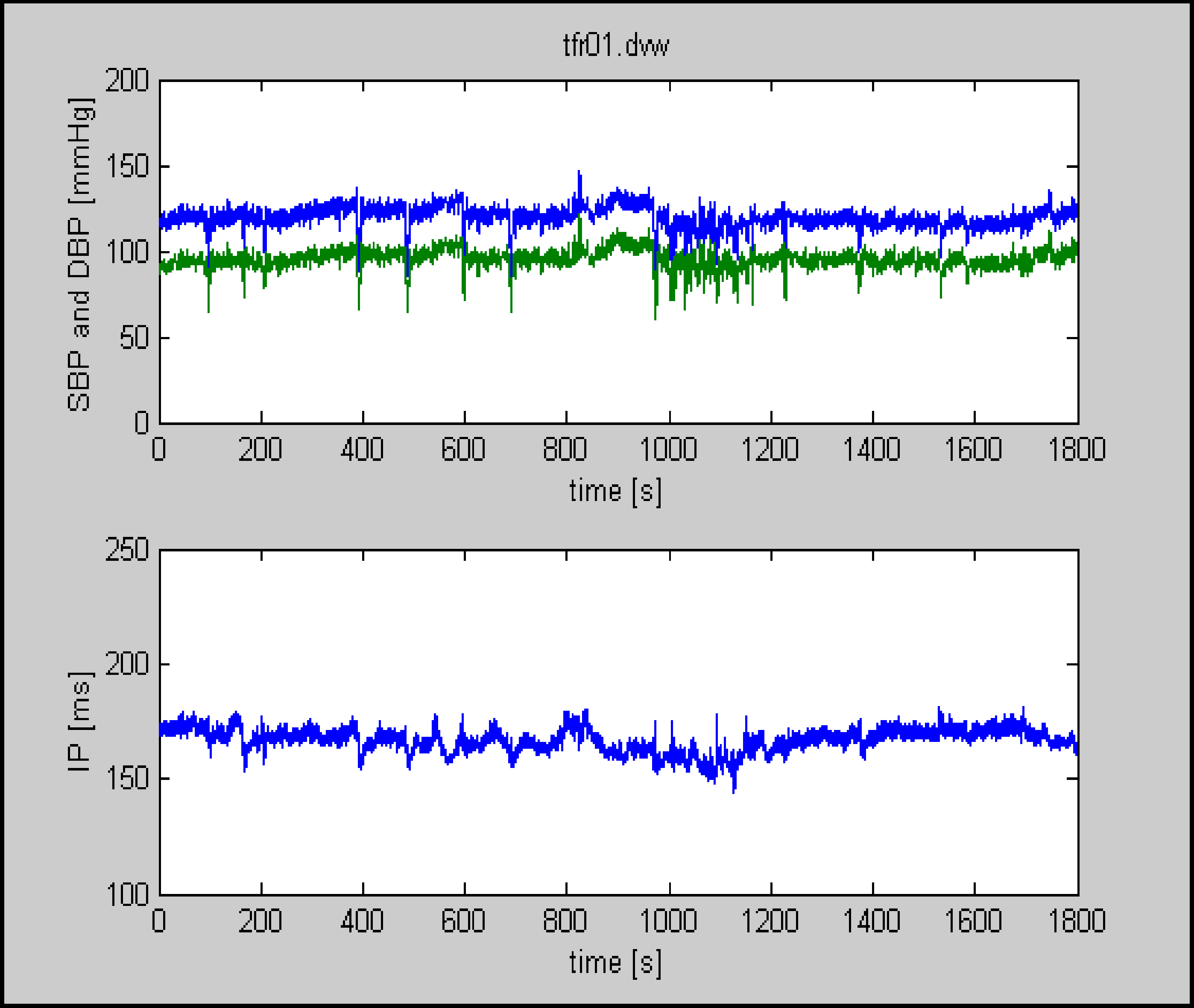


(From De Boer F, *PhD Thesis, 1975*)

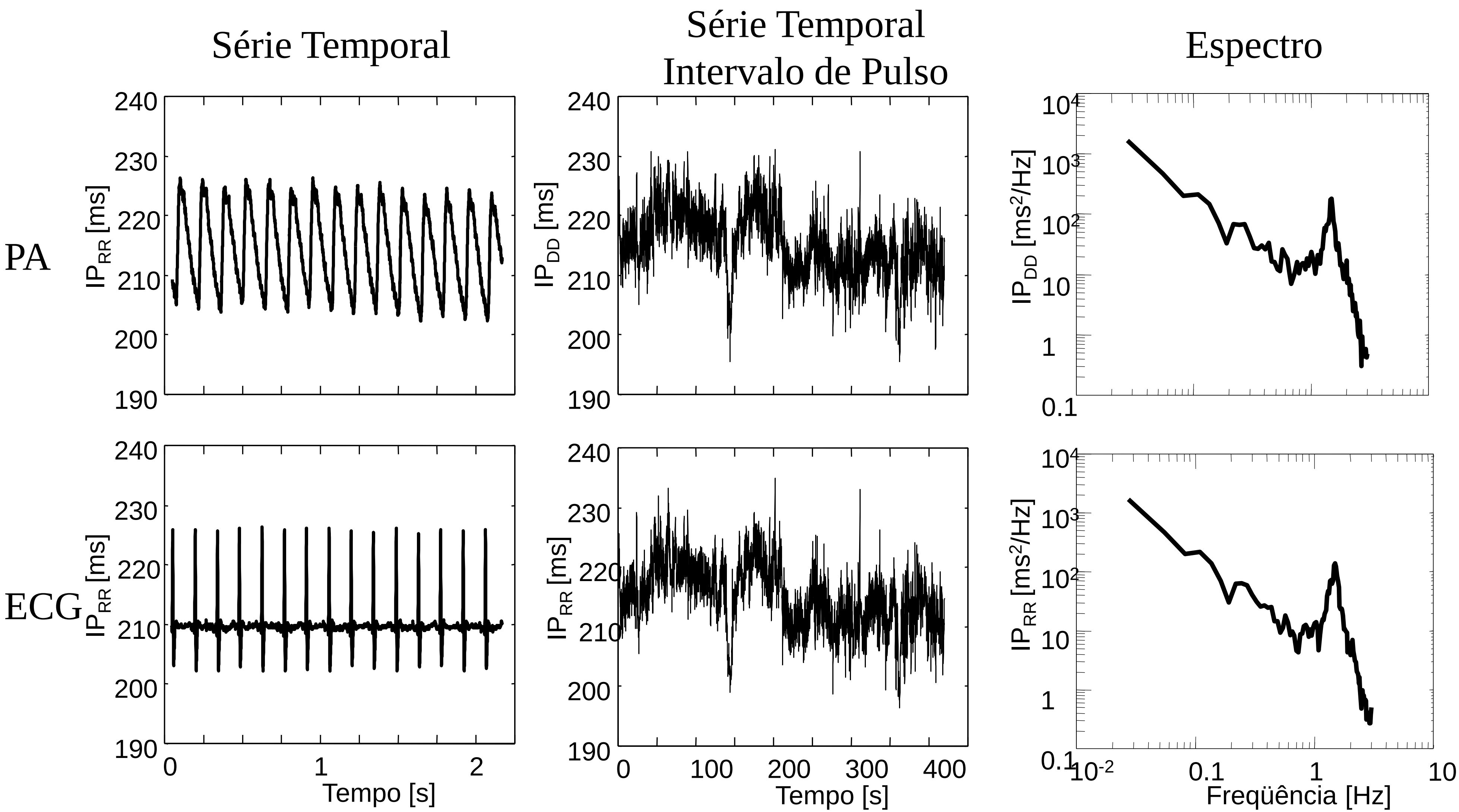


Adapted from Malliani et al. *Circulation*, 84: 482-492, 1991

Séries temporais sistólica, diastólica e de intervalos de pulso



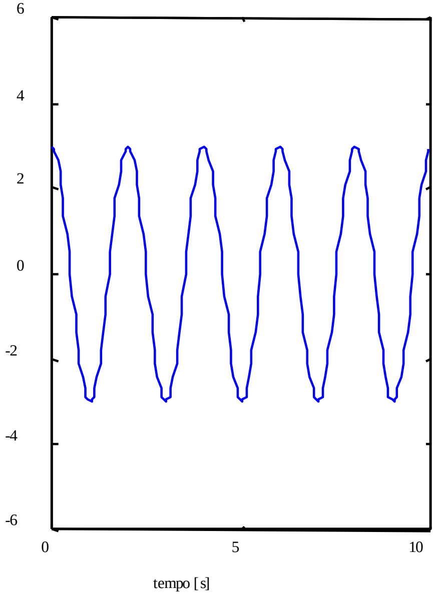
Comparação do Espectro do Intervalo entre Eventos Diastólicos e Intervalo RR



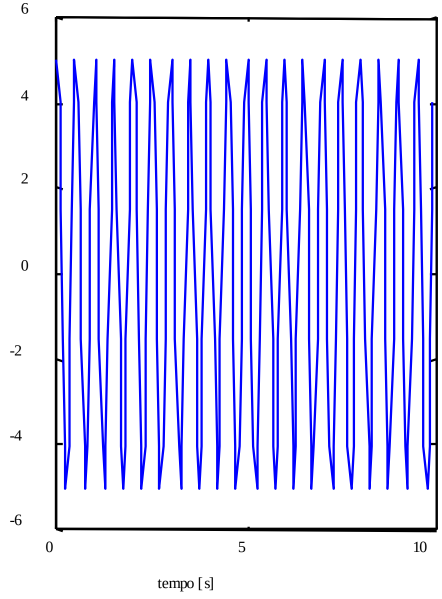
ANÁLISE ESPECTRAL

Transformada Rápida de Fourier

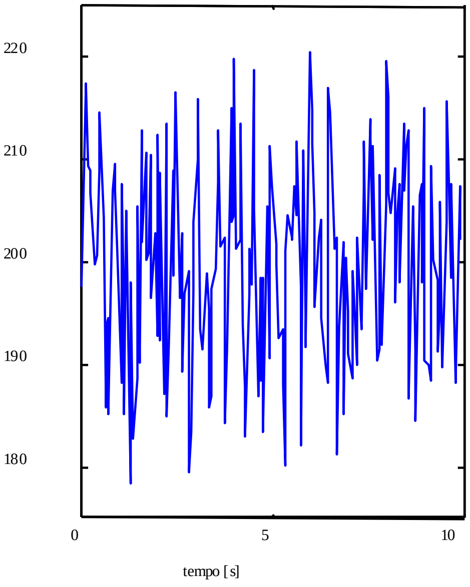
Mayer
0.5 Hz



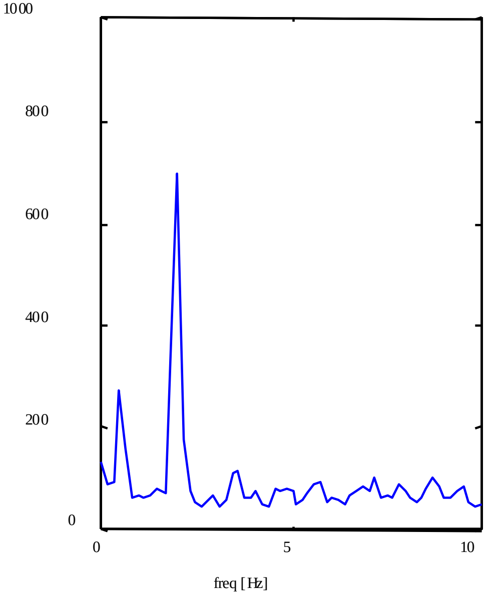
Hering
2 Hz

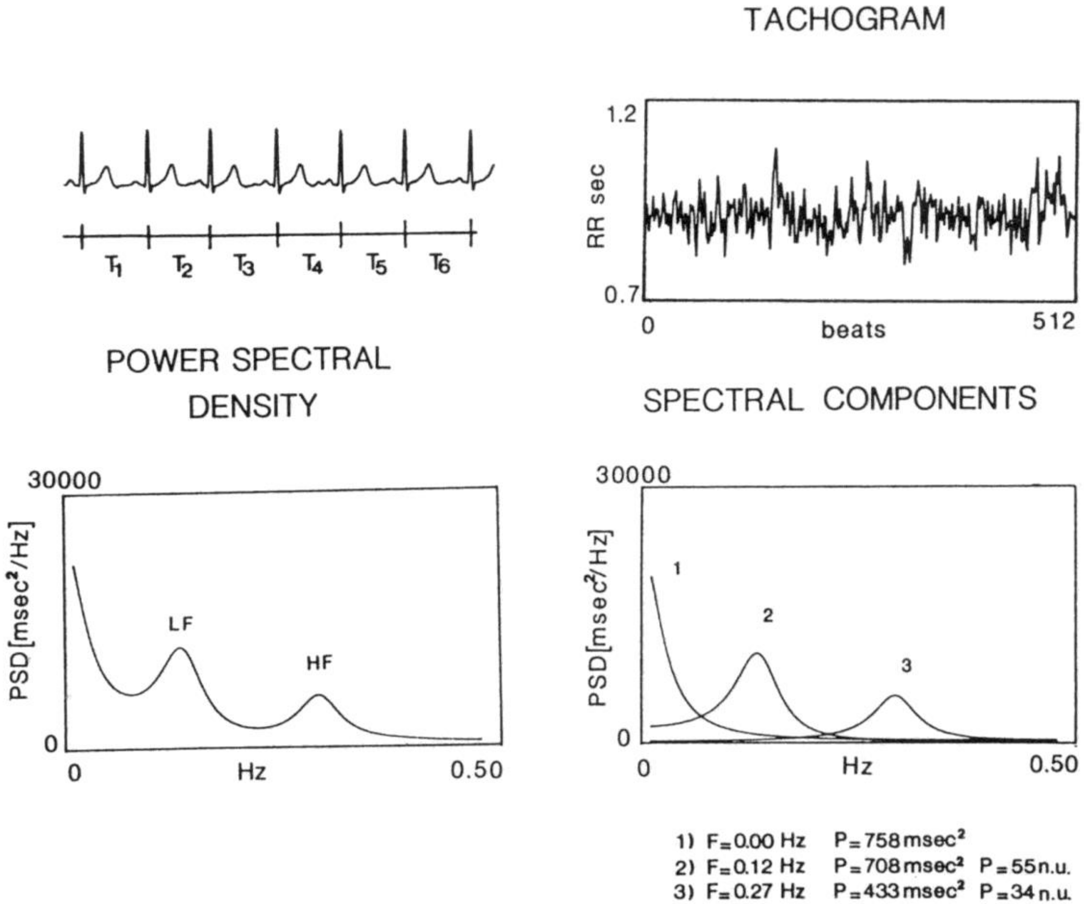


sinal



espectro





TACHOGRAM
1.2
RR sec
0.7
0
beats
512
T1
T2
T3
T4
T5
T6
POWER SPECTRAL DENSITY
30000
PSD [msec²/Hz]
LF
HF
0
0
Hz
0.50
SPECTRAL COMPONENTS
30000
PSD [msec²/Hz]
1
2
3
0
0
Hz
0.50
1) F=0.00 Hz P=758 msec²
2) F=0.12 Hz P=708 msec² P=55 n.u.
3) F=0.27 Hz P=433 msec² P=34 n.u.

ANÁLISE ESPECTRAL
Transformada Rápida de Fourier

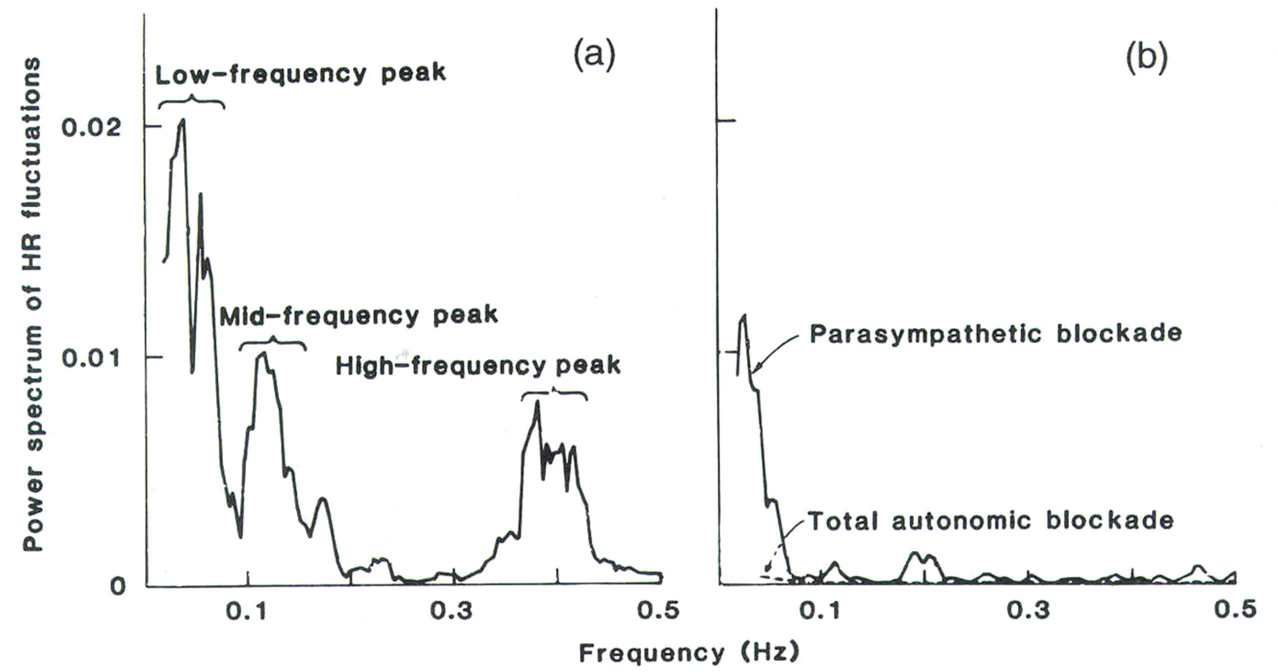


Figure III.1 (a) Power spectrum of heart rate in an adult conscious dog, demonstrating three discrete spectral peaks. The low- and mid-frequency peaks are often not distinct. The high-frequency peak is associated with respiration. (b) Power spectrum of heart rate fluctuations under parasympathetic blockade and combined parasympathetic and sympathetic (beta-adrenergic) blockade. (Reproduced with permission from reference 4: © American Association for the Advancement of Science)

Akselrod et al. Science 213(4504):220-22, 1981

ANÁLISE ESPECTRAL
Modelo Autorregressivo

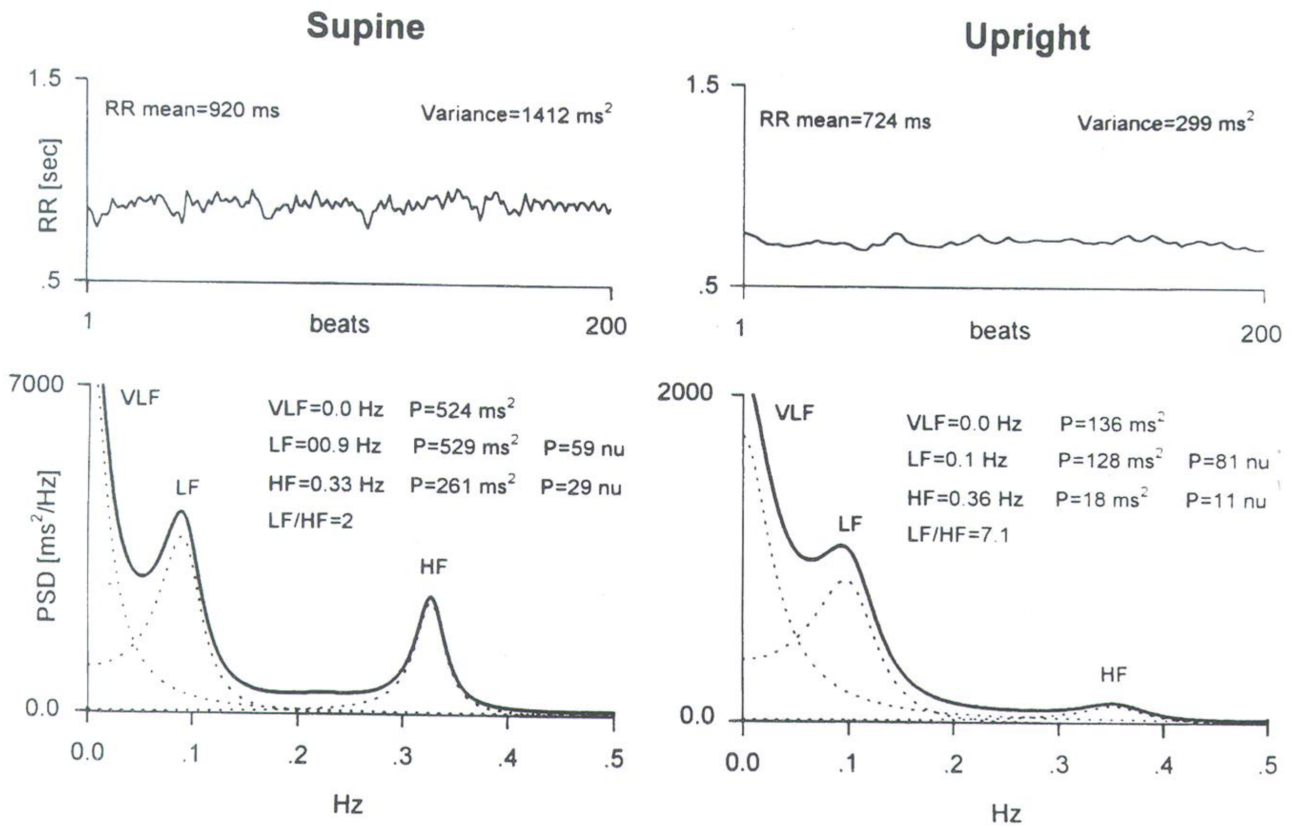


FIGURE 2. *Top*: R-R interval series (tachogram) of a healthy subject in supine and upright (passive 90° tilt) positions. *Bottom*: power spectrum autoregressive analysis (note 2 different scales). The power of each component (spectral decomposition) is indicated by dotted lines. PSD, power spectral density; VLF, very low frequency; LF, low frequency; HF, high frequency. For other details, see text. From Ref. 7 with permission.

Malliani et al. *Circulation* 96:4143-4145, 1997

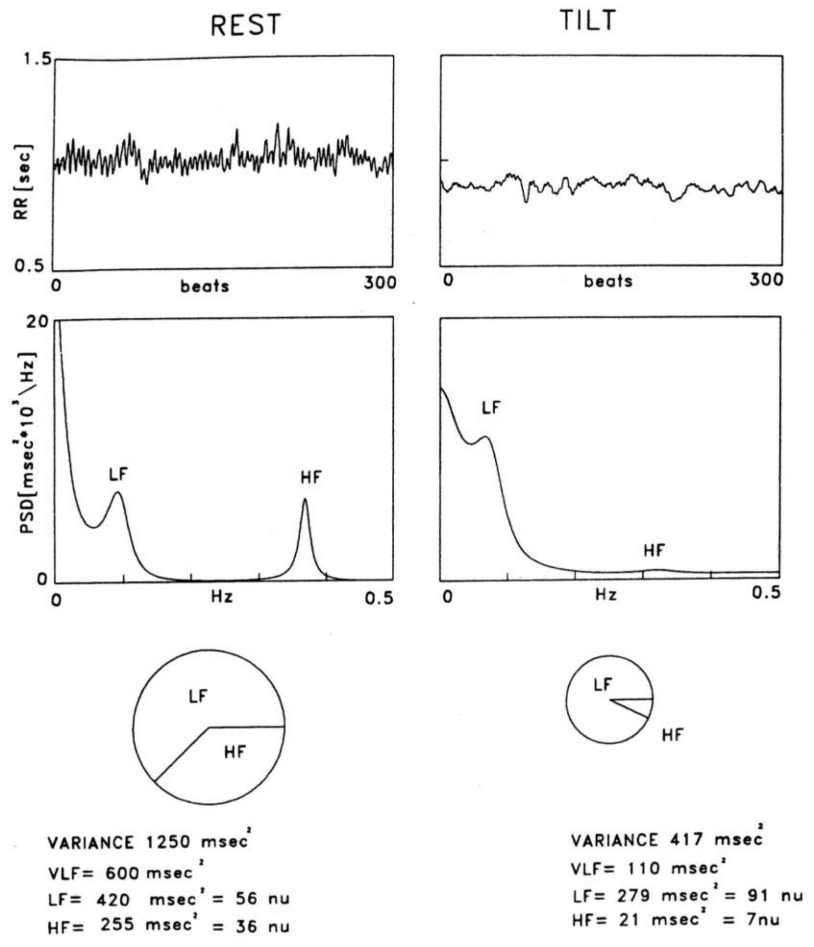
Variáveis no domínio da freqüência

Variável	Unidade	Descrição	Freqüência
Potência total	ms^2	Variância ou potência total dos eventos no segmento temporal	-
MBF	ms^2	Potência na banda de muito baixa freqüência	≈≤ 0,04 Hz
BF	ms^2	Potência na banda de baixa freqüência	0,04-0,15 Hz
BF norm	Unidades arbitrárias	Potência na BF em unidades normalizadas (BF/(total-MBF))*100	0,15-0,40 Hz
AF	ms^2	Potência na banda de alta freqüência	0,15-0,40 Hz
AF norm	Unidades arbitrárias	Potência na AF em unidades normalizadas AF/(total-MBF)*100	0,15-0,40 Hz
BF/AF	Adimensional	Razão entre BF [ms^2]/AF[ms^2]	

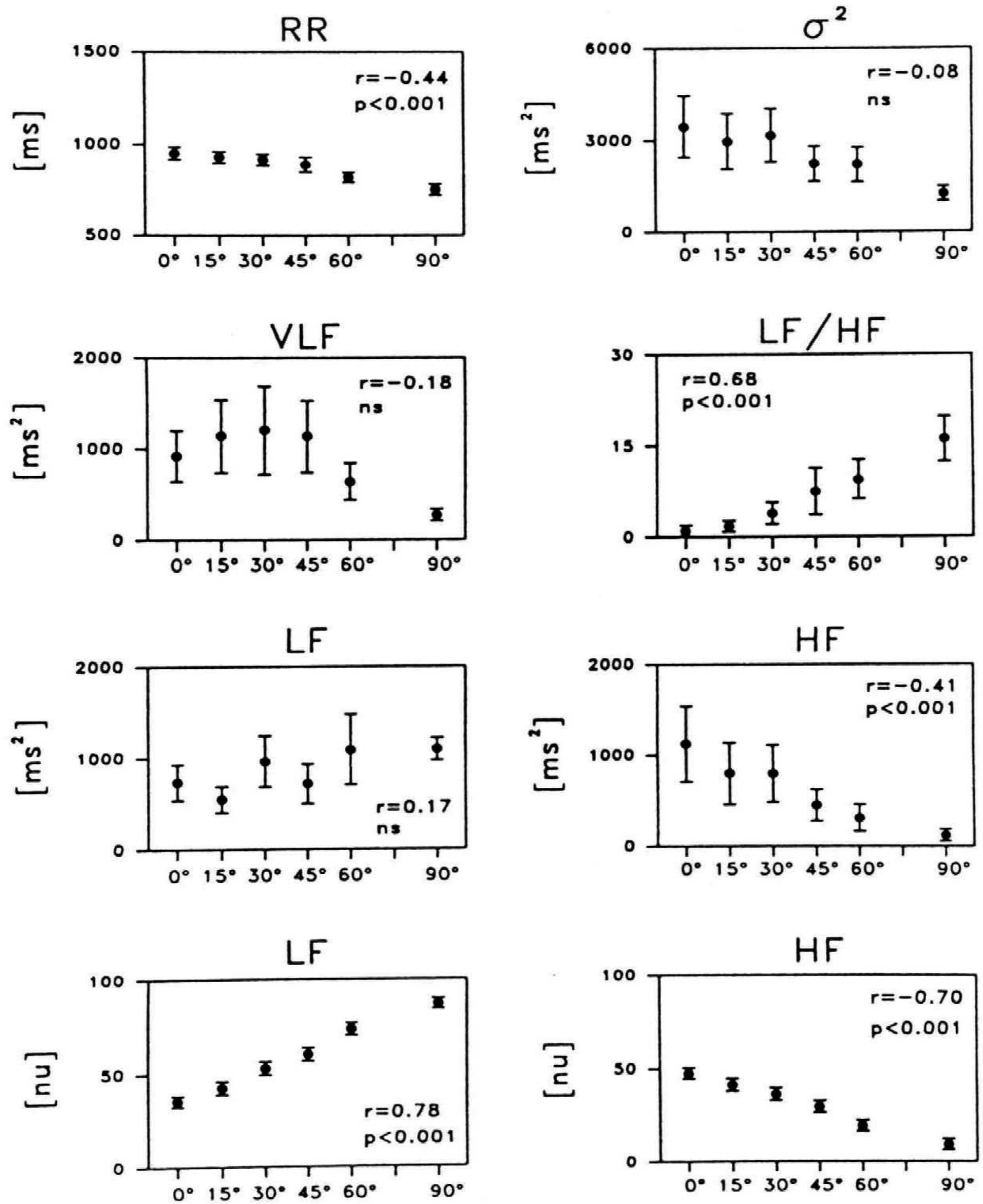
Interpretação da contribuição das bandas de baixa e alta freqüências

	LF Mayer	HF respiração Hering
IP	simpático + parassimpático	parassimpático
PAS	Simpático + vasomotor	"débito cardíaco" "volume sistólico"

Japundzic *et al*.(1990), J Auton Nerv Syst, 30(2):91-100.

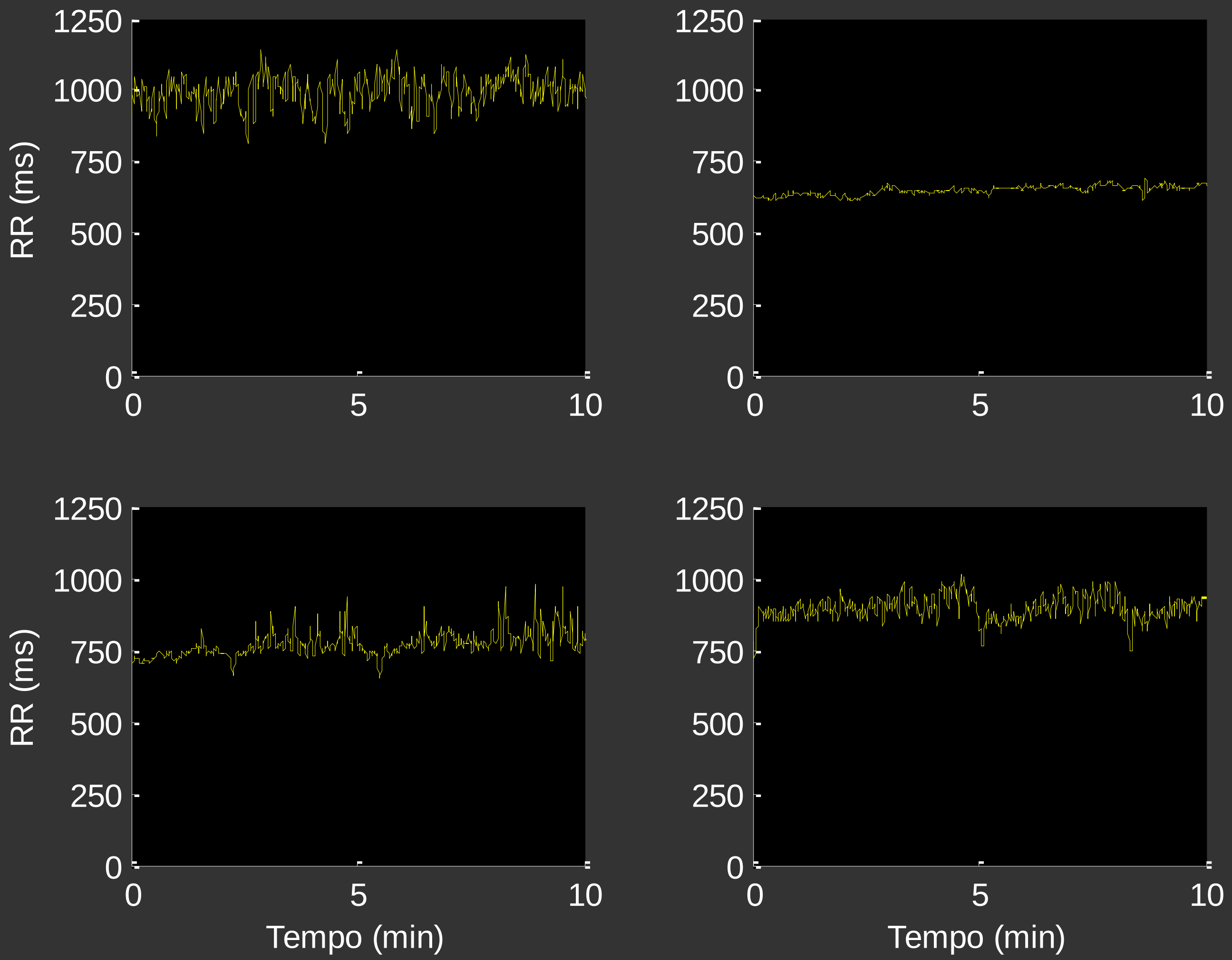


(From Malliani et al, *Cardiac Electrophysiol Rev 1997;1:343-346*)

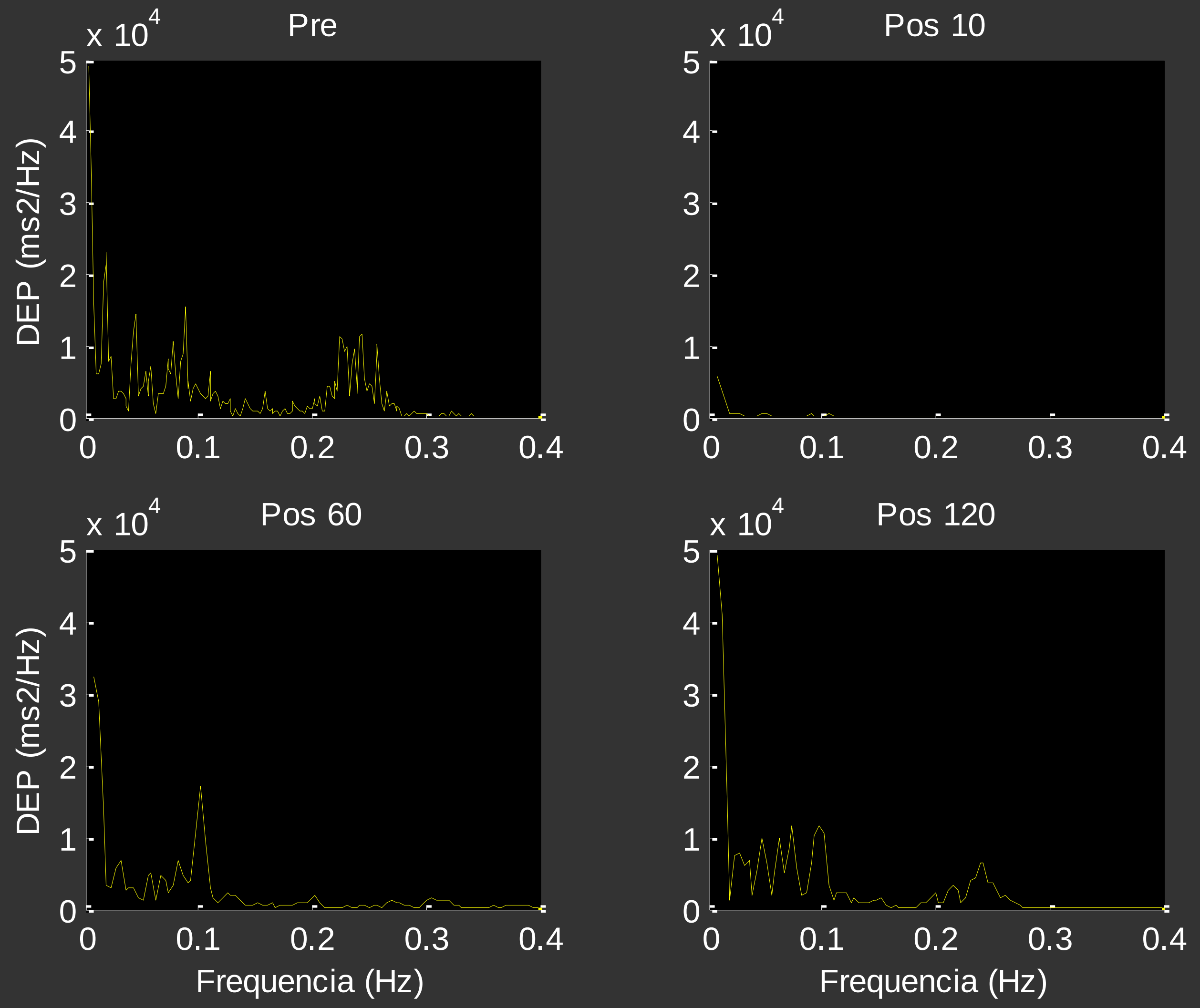


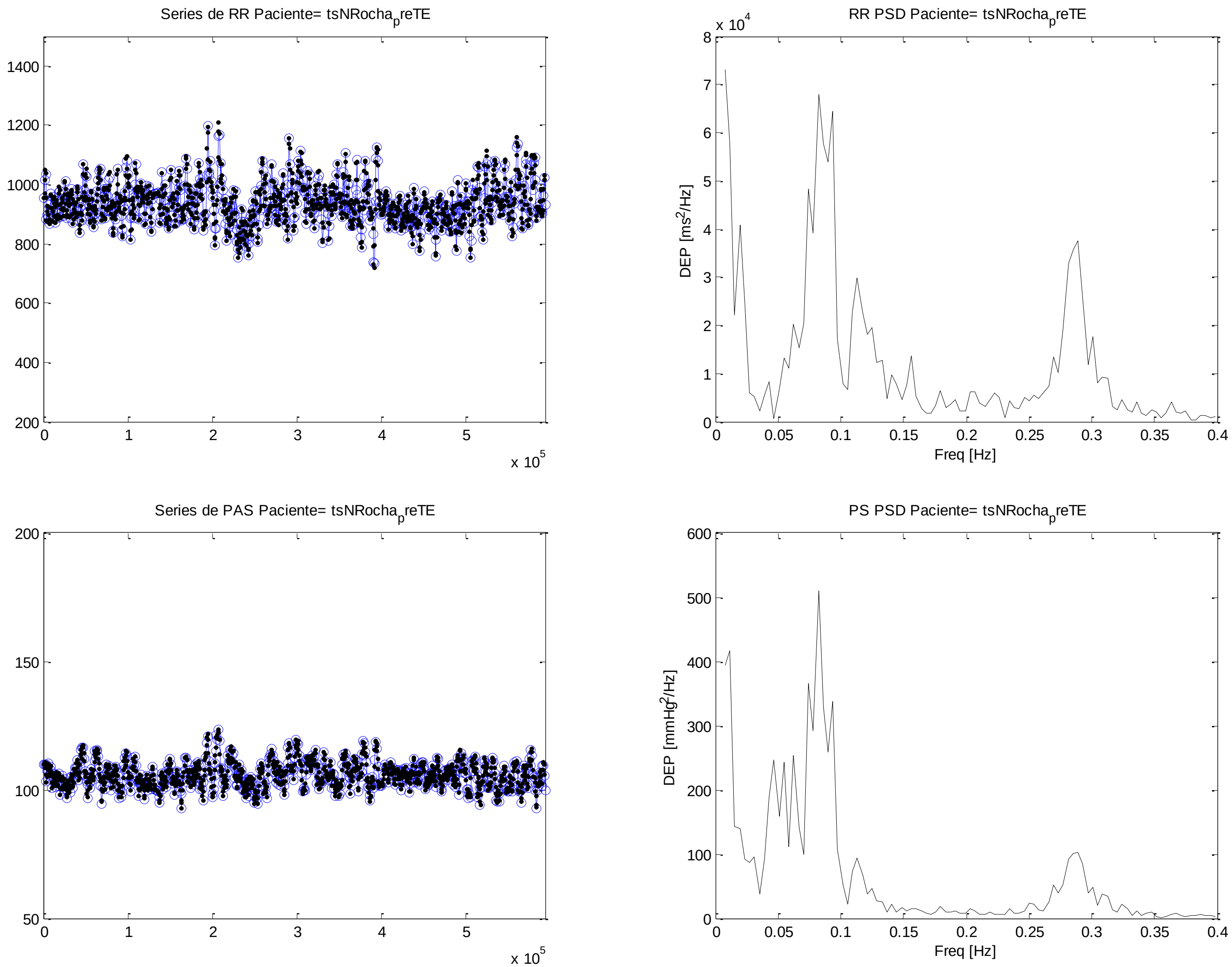
(From Montano et al, *Circulation 1994;90:1826-1831*)

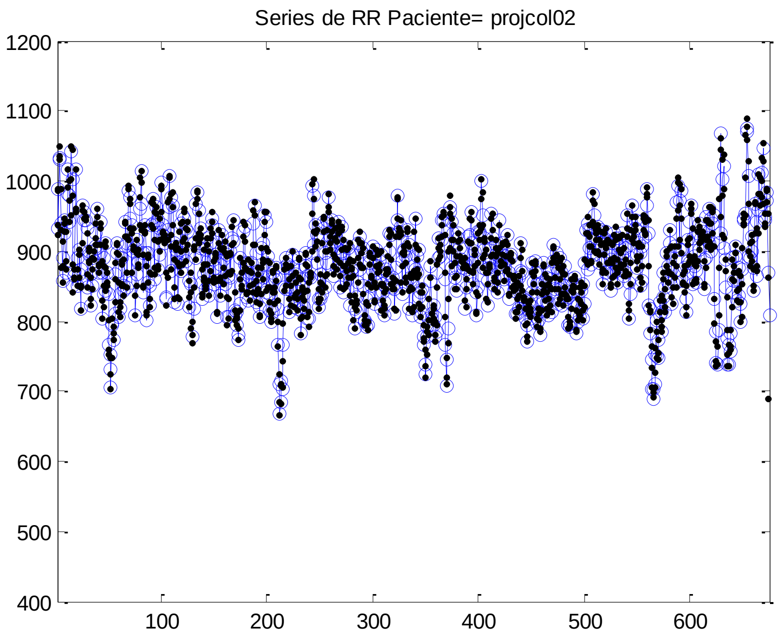
POST EXERCISE RR INTERVALS
up to 120 min

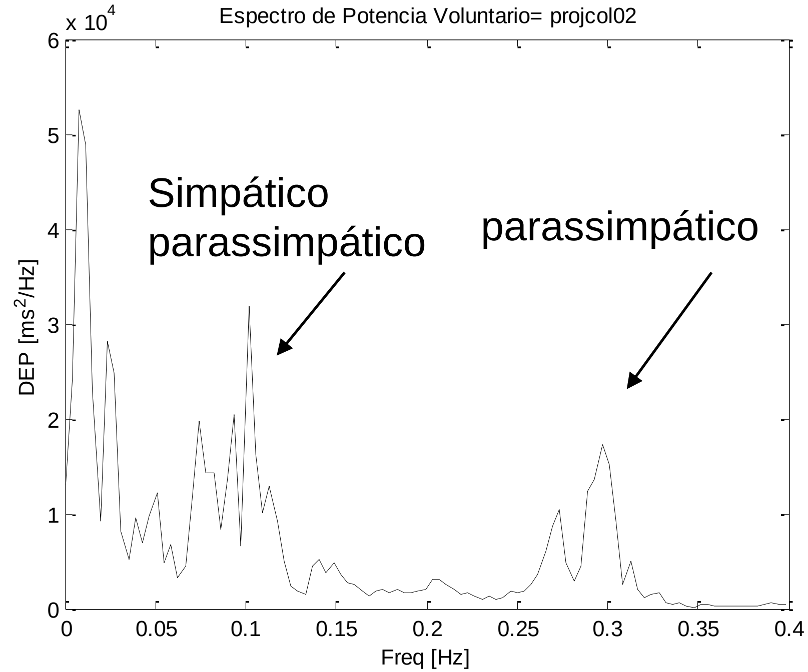


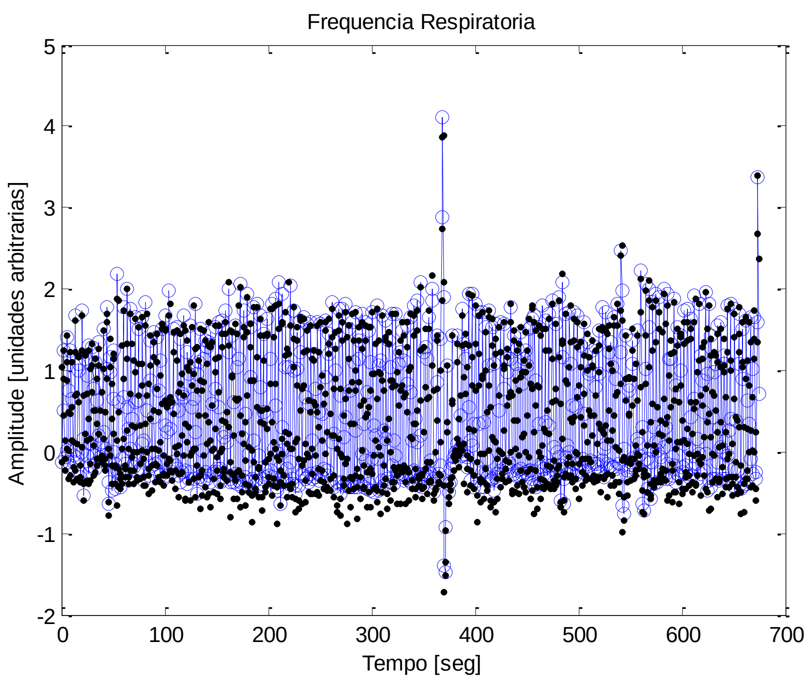
SPECTRAL ANALYSIS
heart rate variability
Fourier Transformation

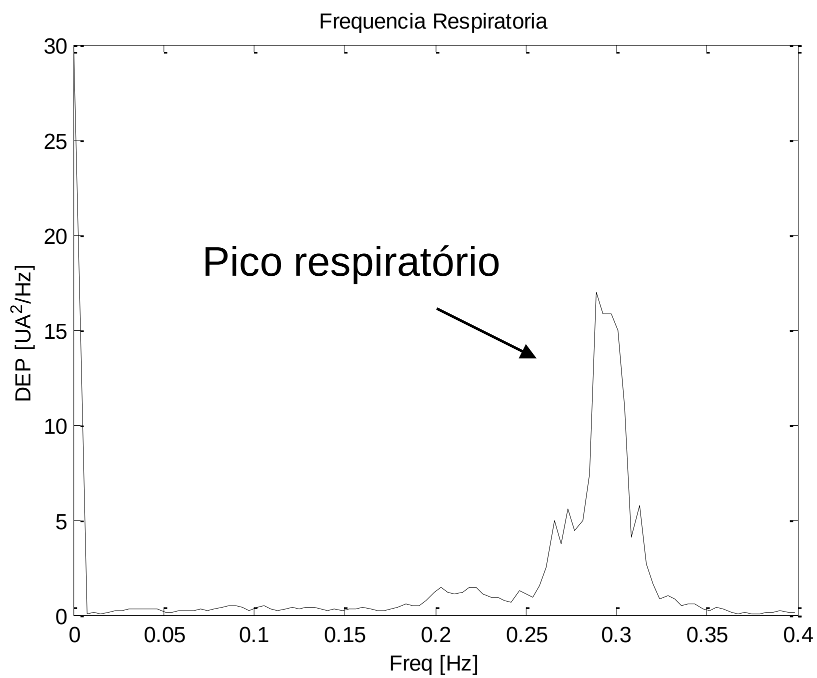


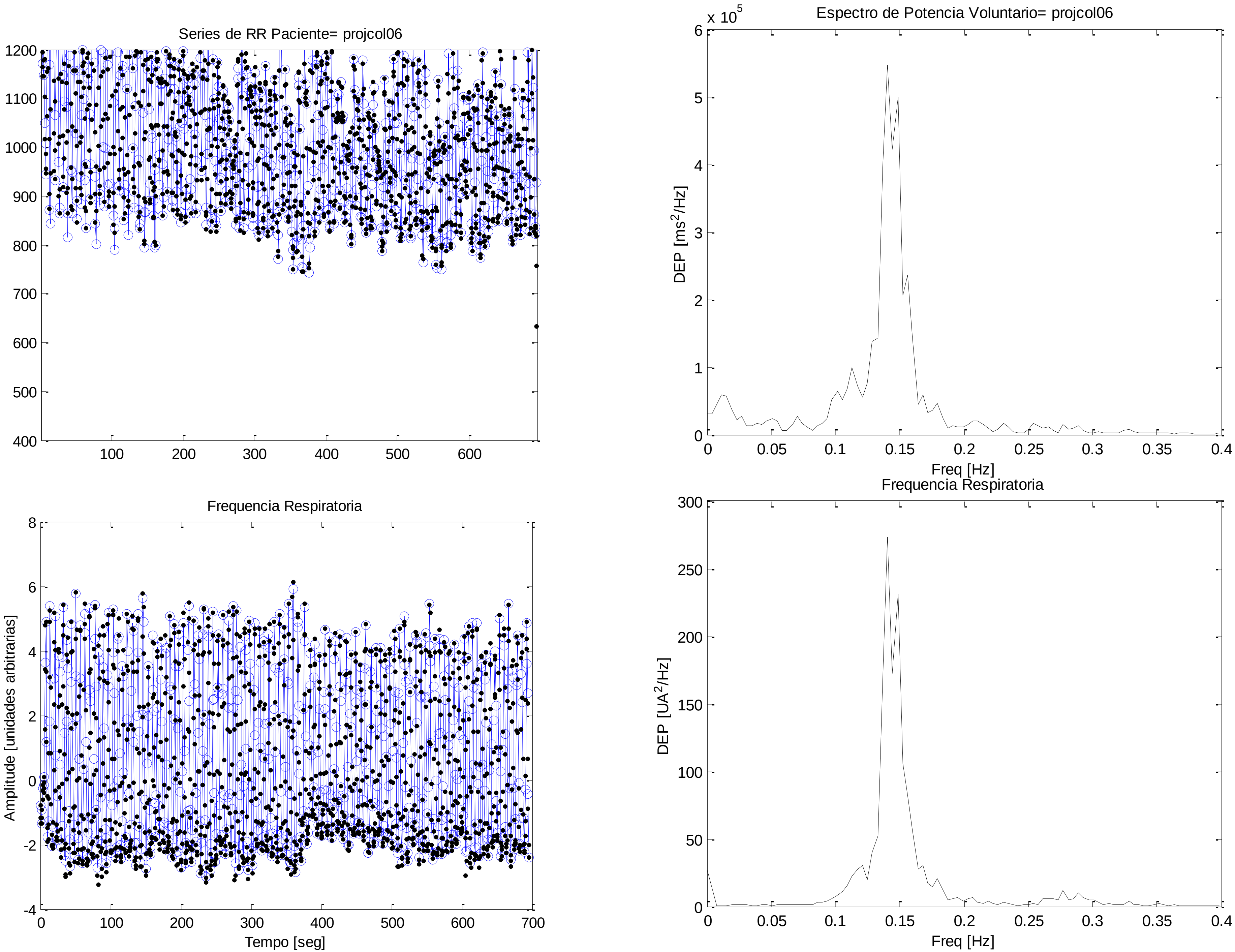

Series de RR Paciente= tsNRocha_preTE
x 10^5
RR PSD Paciente= tsNRocha_preTE
x 10^4
DEP [ms^2/Hz]
Freq [Hz]
Series de PAS Paciente= tsNRocha_preTE
x 10^5
PS PSD Paciente= tsNRocha_preTE
DEP [mmHg^2/Hz]
Freq [Hz]


Series de RR Paciente= projcol02
1200
1100
1000
900
800
700
600
500
400
100
200
300
400
500
600

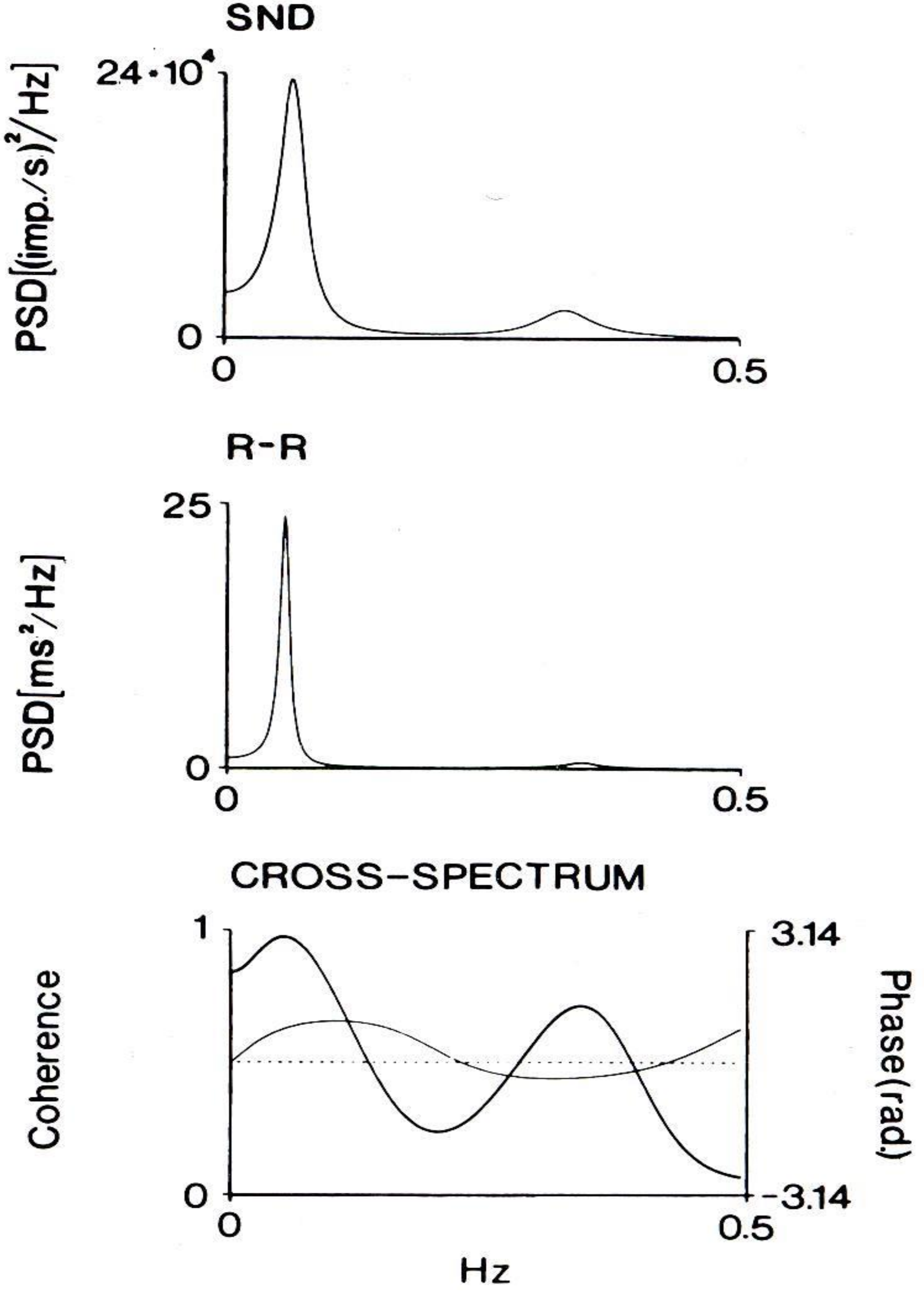

Espectro de Potencia Voluntario= projcol02
x 10^4
DEP [ms^2/Hz]
Freq [Hz]
Simpático
parassimpático
parassimpático
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4


Frequencia Respiratoria
Amplitude [unidades arbitrarias]
Tempo [seg]
0
100
200
300
400
500
600
700


Frequencia Respiratoria
DEP [UA^2/Hz]
Freq [Hz]
Pico respiratório
30
25
20
15
10
5
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4

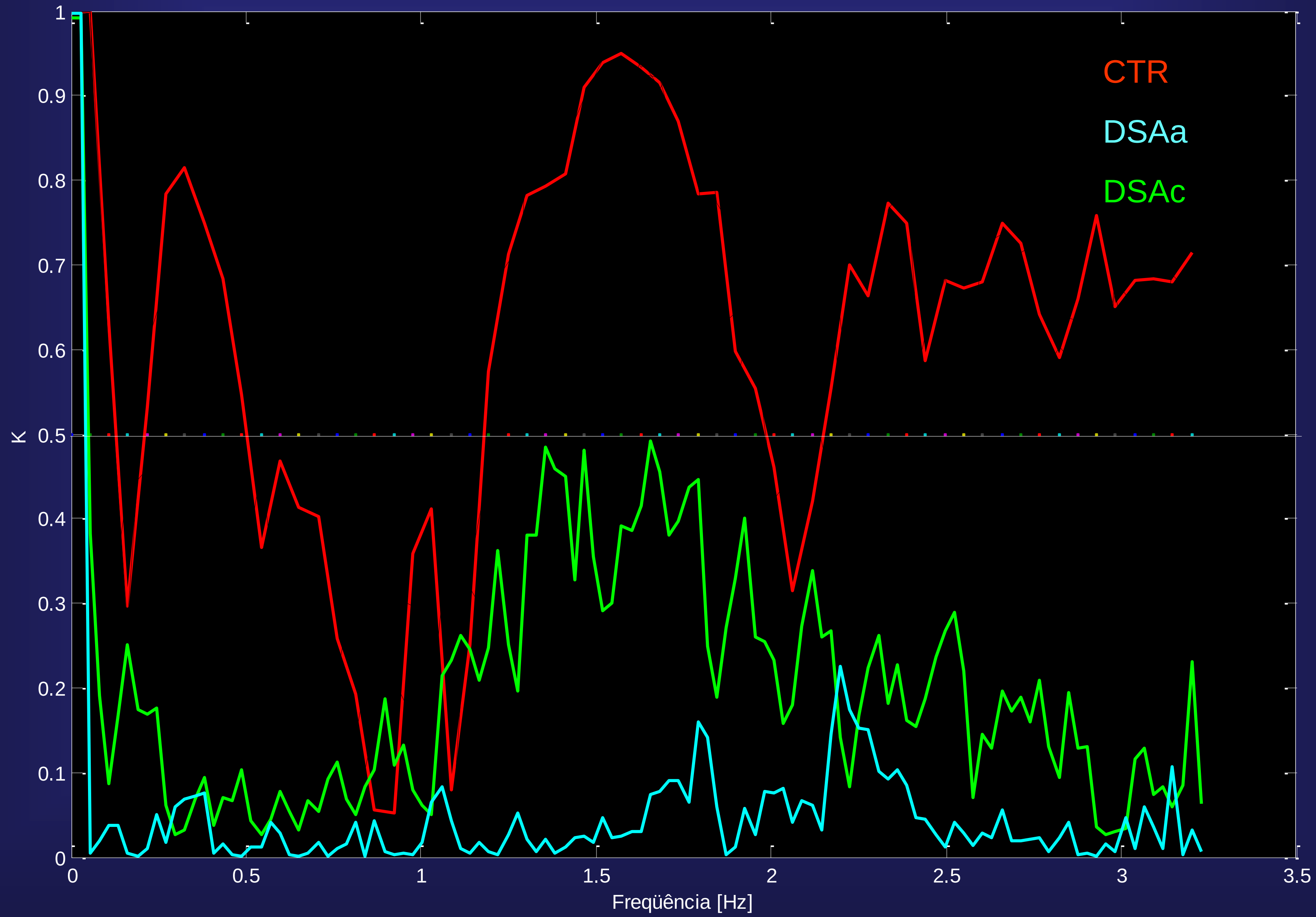


Series de RR Paciente= projcol06
1200
1100
1000
900
800
700
600
500
400
100
200
300
400
500
600
Espectro de Potencia Voluntario= projcol06
x 10^5
DEP [ms^2/Hz]
Freq [Hz]
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
Frequencia Respiratoria
Amplitude [unidades arbitrarias]
Tempo [seg]
8
6
4
2
0
-2
-4
700
Frequencia Respiratoria
DEP [UA^2/Hz]
Freq [Hz]
300
250
200
150
100
50



(From Montano et al. *J Auton Nerv Syst* 1992; 40: 21-32)

CORRELAÇÃO-CRUZADA
COERÊNCIA



ANÁLISE ESPECTRAL
MÉTODOS

- FFT - Transformada Rápida de Fourier: decomposição de um sinal em seus componentes periódicos de freqüência através de séries de senos e cosenos
  - vantagem: independe de condições *a priori*
  - desvantagem: apresenta perda de resolução para freqüências muito baixas quando em trechos curtos
- Modelamento Autorregressivo: modelamento paramétrico que se baseia na dependência entre os eventos
  - vantagem: pode ser aplicado a trechos curtos de sinal e apresenta os componentes em freqüência mais importantes
  - desvantagem: depende da ordem do modelo

ANÁLISE ESPECTRAL
MÉTODOS

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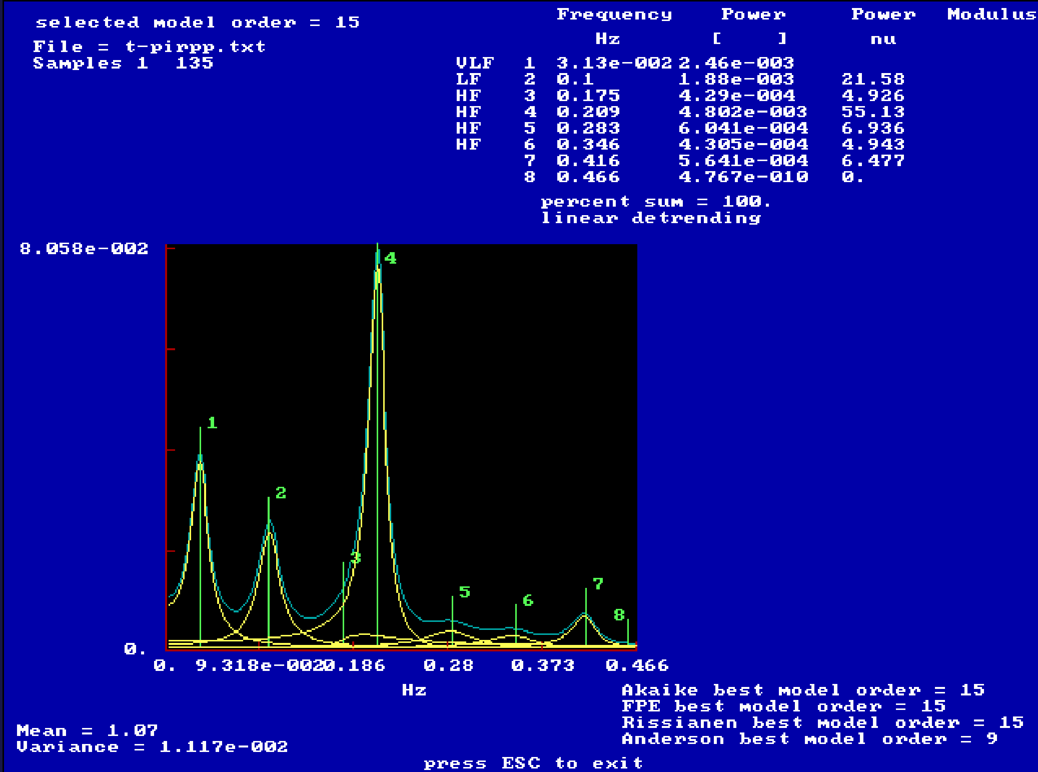
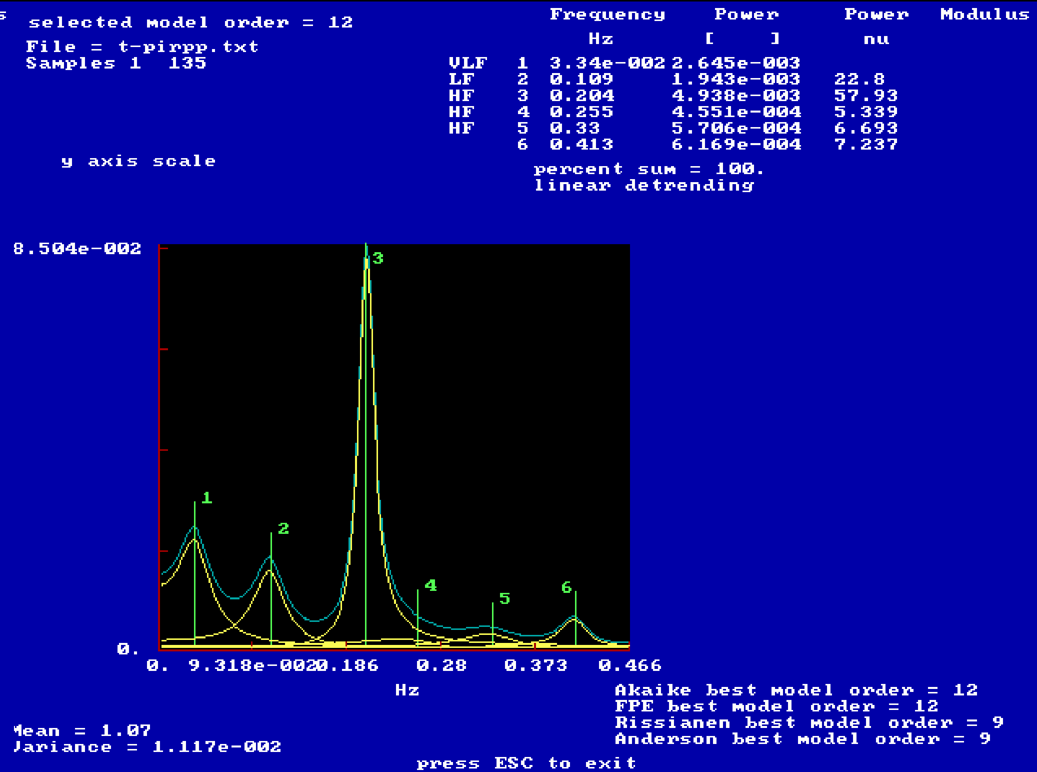
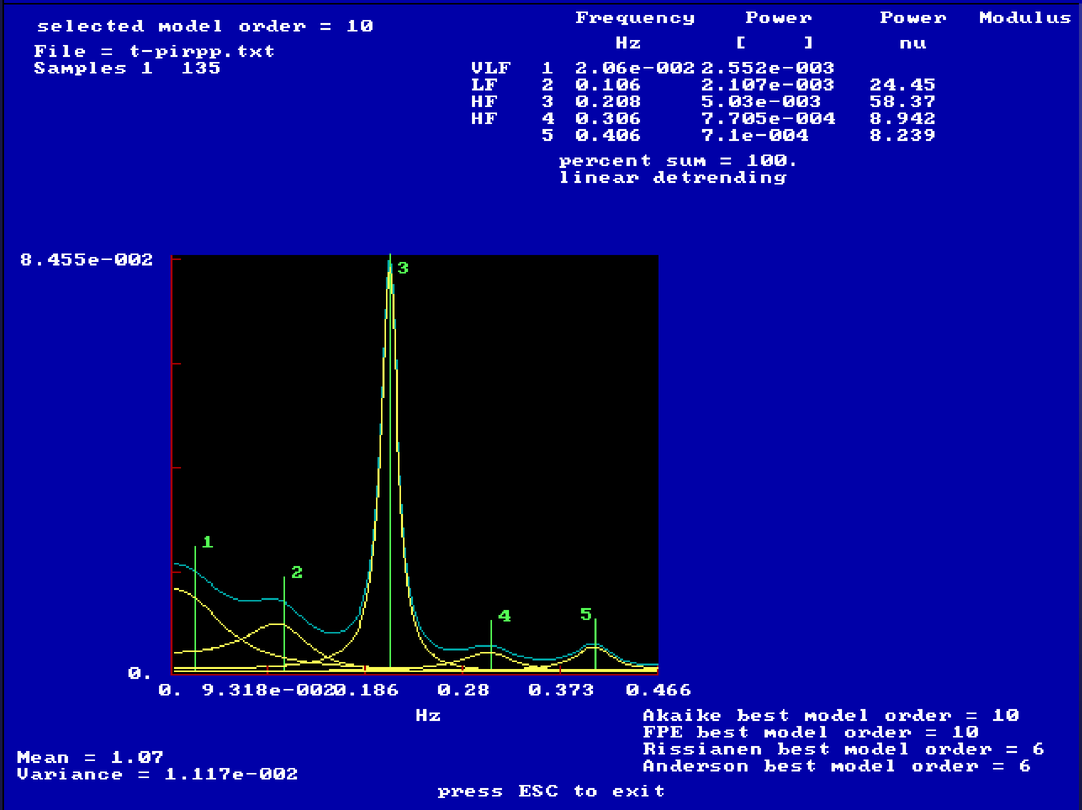
  - desvantagem: depende da ordem do modelo

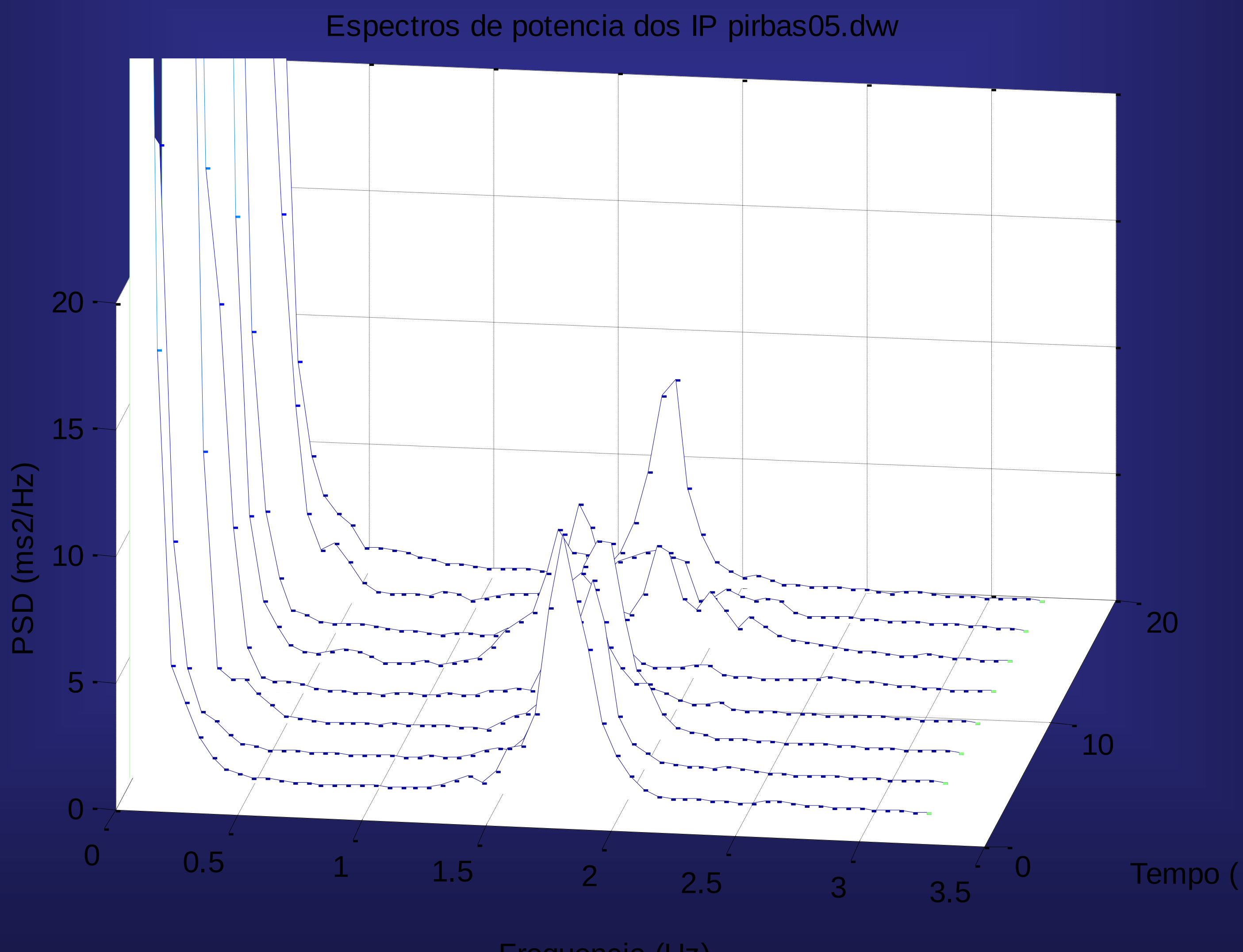






MODELO AR DEPENDÊNCIA DA ORDEM DEFINIDA

ANÁLISE ESPECTRAL
FFT

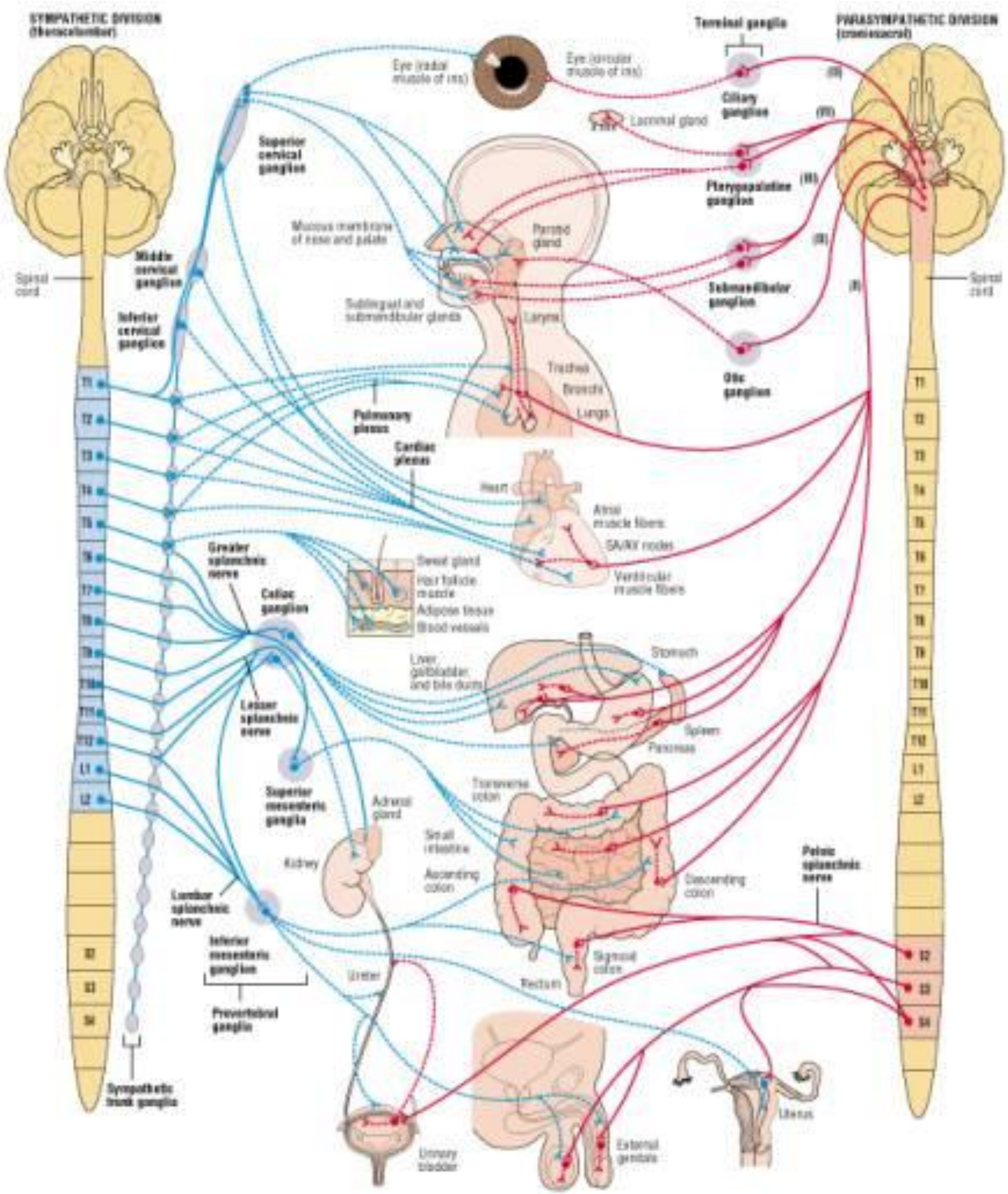


CONSIDERAÇÕES

- A utilização da FFT e do modelo AR para análise espectral fornecem informações e aplicabilidade semelhantes no estudo do controle cardiovascular
- A aplicação de um ou outro método depende da definição *a priori* dos parâmetros a serem estudados, levando-se em consideração tempo de registro e as informações de interesse
- O estudo da FC e PA no domínio da freqüência deve ser complementar ao domínio do tempo
- O desenvolvimento de ferramentas computacionais permite o domínio de tecnologias e amplia as possibilidades de aplicação das mesmas

Existe relevância clínica para o uso da frequência cardíaca?

The Autonomic Nervous System



Pergunta:

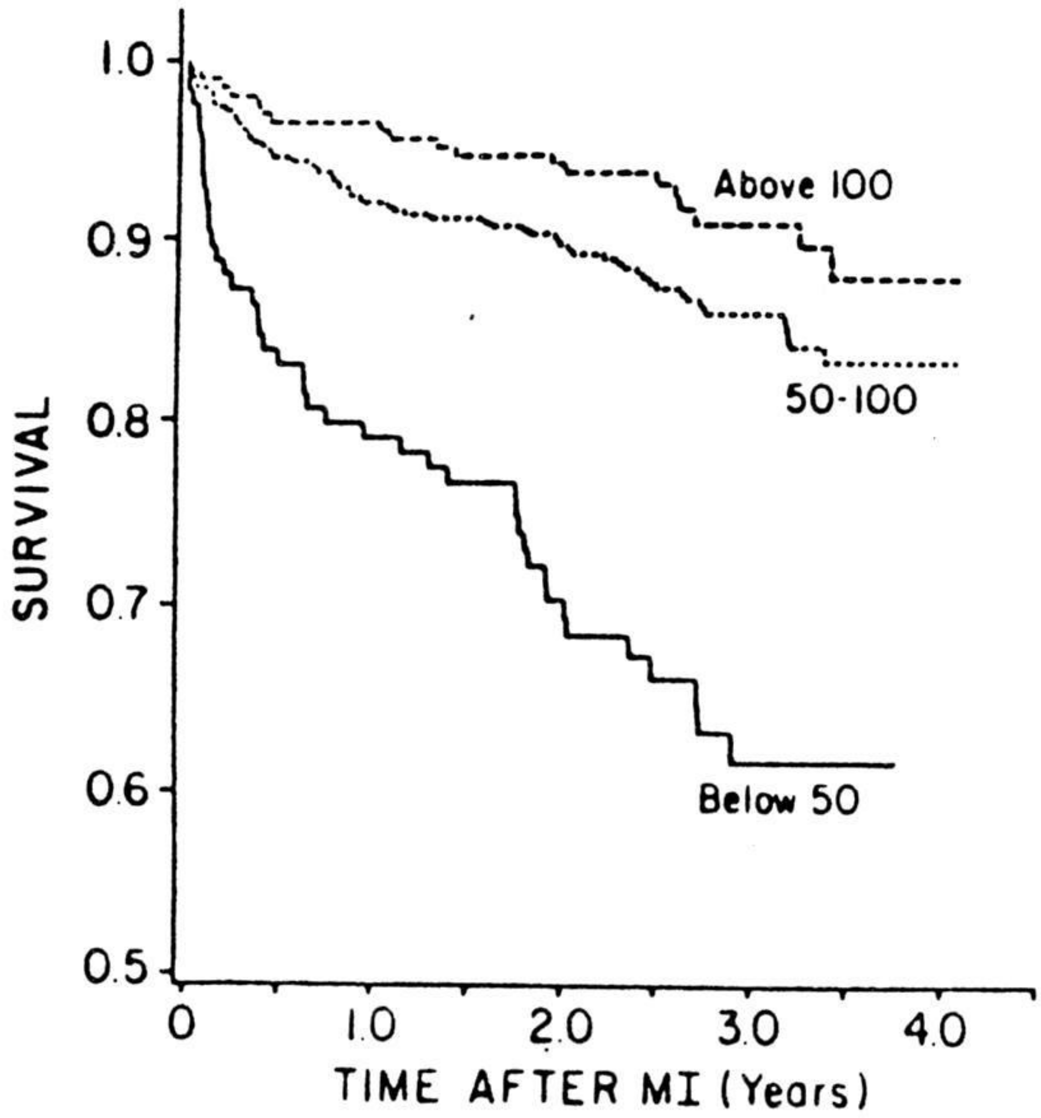
Por que a variabilidade da FC é útil para predizer risco?

hipótese:

HRV é uma janela para os mecanismos autonômicos de regulação cardiovascular

Table 1
Studies of vagal function and mortality

Studies (1st author)	Subject and sample size	Measures employed	Controlled variables	Relative risk
Habib, 1999	Over 30,000 men and women	HR	Gender and ethnicity	3-fold greater risk if HR > 90 bpm relative those with HR < 60 bpm
Cole et al., 1999	$n = 2428$; 63% men	HR recovery	Age, sex, the use or nonuse of medications, the presence or absence of myocardial perfusion defects on thallium scintigraphy, standard cardiac risk factors, resting heart rate, the change in heart rate during exercise, workload achieved	Unadjusted: Not stated
				Adjusted: 4.0 [CI, 3.0–5.2]; $p < 0.001$
Cole et al., 2000	$n = 5234$; gender not reported	HR recovery	Age, gender, chronotropic response to exercise, habitual exercise, smoking, resting blood pressure, resting HR, cholesterol level, education and income	Unadjusted: Not stated
				Adjusted: 2.58 [CI, 2.06–3.20]
Nishime et al., 2000	$n = 9454$; 77% men	HR recovery	Resting systolic blood pressure considered as a continuous variable, body mass index; use of nondihydropyridine calcium channel blockers, and lipid-lowering drugs, diabetes, insulin use, known hypercholesterolemia, documentation of total cholesterol value, known prior coronary heart disease, prior myocardial infarction, prior coronary artery bypass graft surgery, reason for test (screening or not), and presence of chronic obstructive pulmonary disease	Unadjusted: 4.16 [CI, 3.33–5.19]; $p < 0.001$



(From Kleiger R et al, *Am J Cardiol* 1987, 107: 565-570)

Available online http://ccforum.com/content/9/2/R124

Research

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Coronary artery bypass surgery and longitudinal evaluation of the autonomic cardiovascular function

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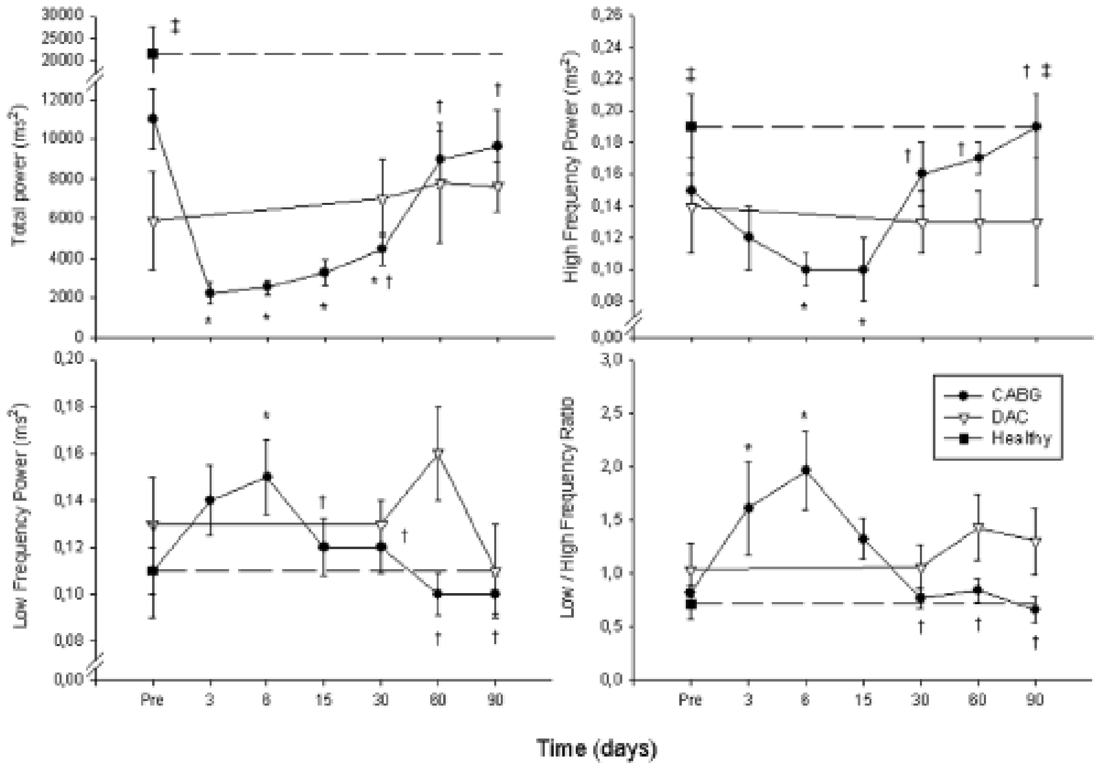
Figure 2



Longitudinal evaluation of heart rate variability in patients undergoing coronary artery bypass grafting surgery. Longitudinal results of spectral analysis of heart rate variability in the three groups: CABG, patients who underwent coronary artery bypass grafting; CAD, patients with coronary artery disease who did not undergo surgery; healthy, control subjects without CAD. Total power (a) and low-frequency power (b) indicate both adrenergic and parasympathetic modulation of heart rate; high-frequency power (c) represents the parasympathetic component; and the low-frequency/high-frequency ratio (d) represents autonomic balance that modulates heart rate. *$P < 0.05$ versus CABG preoperative value; †$P < 0.05$ versus CABG day 3 or 6; ‡$P < 0.05$ versus CABG and CAD, except high frequency, for which ‡$P < 0.05$ versus CAD.

HRV – Hypertension

Impairment in Cardiac Autonomic Regulation Preceding Arterial Hypertension in Humans

Insights From Spectral Analysis of Beat-by-Beat Cardiovascular Variability

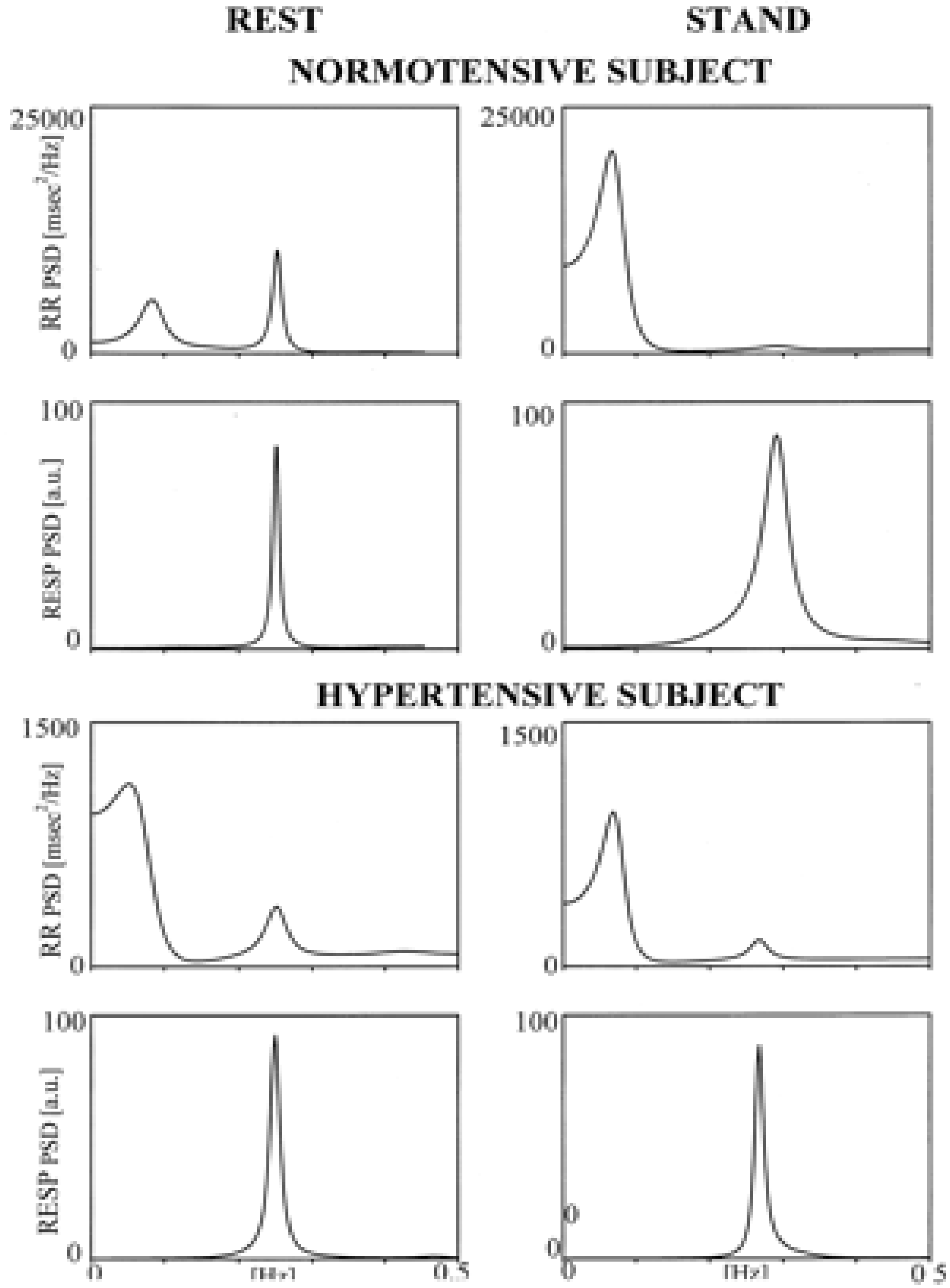
Daniela Lucini, MD, PhD; Giuseppe Sandro Mela, MD; Alberto Malliani, MD; Massimo Pagani, MD

300 subjects:

- **100 normotensive (mean SAP 103)**
- **100 normotensive (mean SAP 133)**
- **100 hypertensive (mean SAP 163)**

→ **Spectral analysis of HRV Rest/stand**

(*Circulation* 2002, 106: 2673-2679)



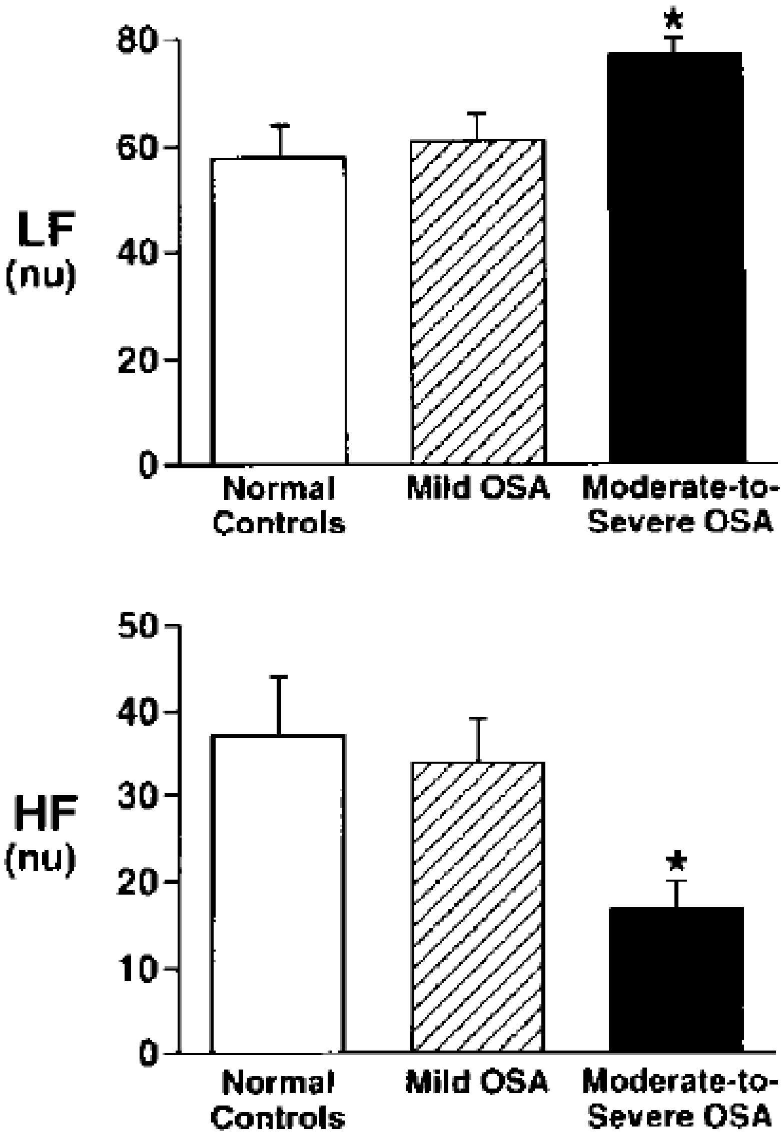
(Lucini D et al, *Circulation* 2002, 106: 2673-2679)

HRV – Obstructive Sleep Apnea

Fact 1:
OSA is associated with an increased cardiovascular morbidity/mortality

Fact 2:
OSA patients have an increased sympathetic activity not only at night but also during daytime

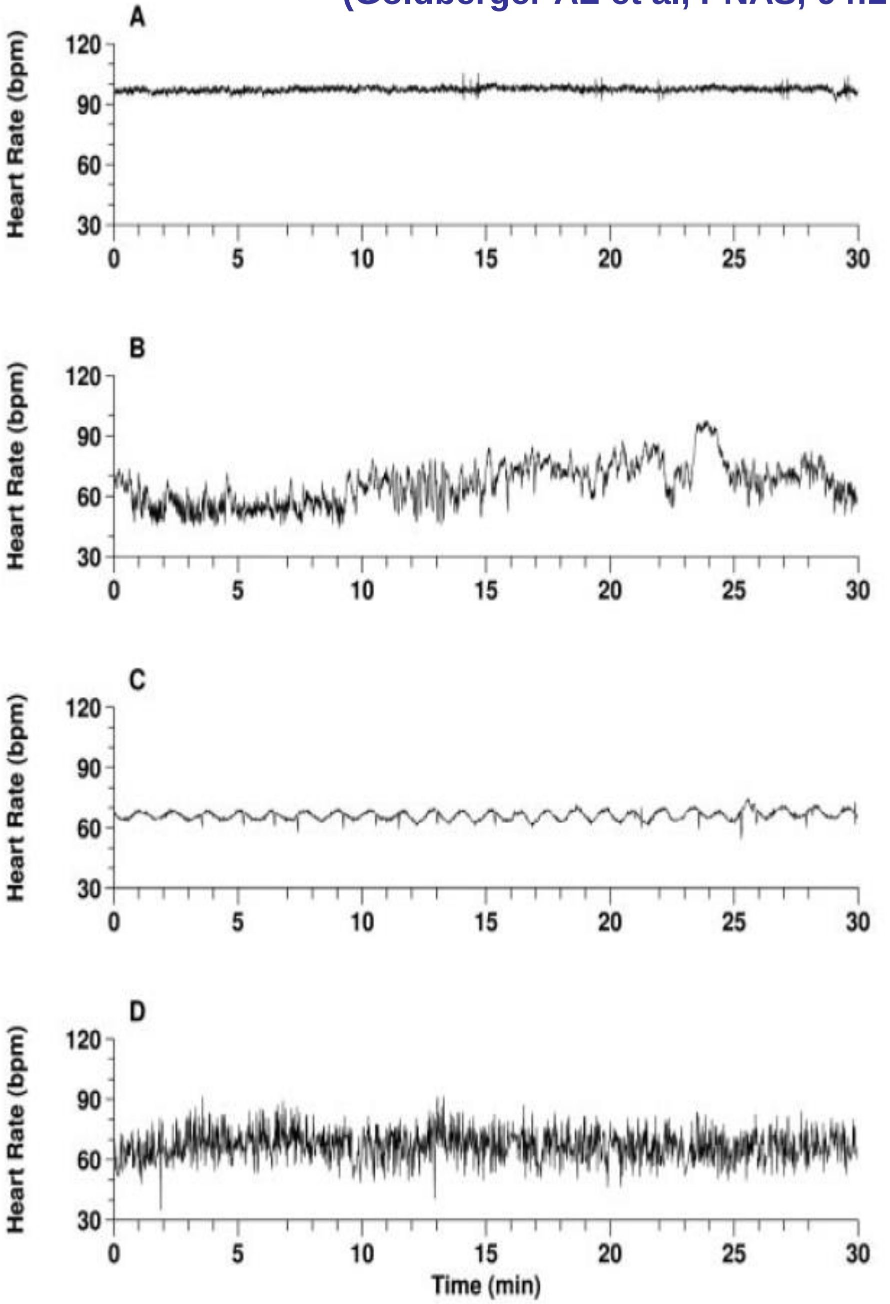
Hypothesis:
the heightened sympathetic activity is the link between OSA and cardiovascular diseases



(From Narkiewicz K et al, *Circulation* 1998, 98: 1071-1077)

HEART RATE VARIABILITY IN HEALTH AND DISEASE: A time series test

(Goldberger AL et al, PNAS, 94:2464-2472, 2002)



Congestive heart failure

Healthy

Congestive heart failure
(Cheyne-Stokes breathing)

Atrial fibrillation

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Autonomic Neuroscience: Basic and Clinical 113 (2004) 24–31

AUTONOMIC NEUROSCIENCE: Basic & Clinical

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Cholinergic stimulation with pyridostigmine increases heart rate variability and baroreflex sensitivity in rats

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Received 4 March 2004; received in revised form 16 April 2004; accepted 5 May 2004

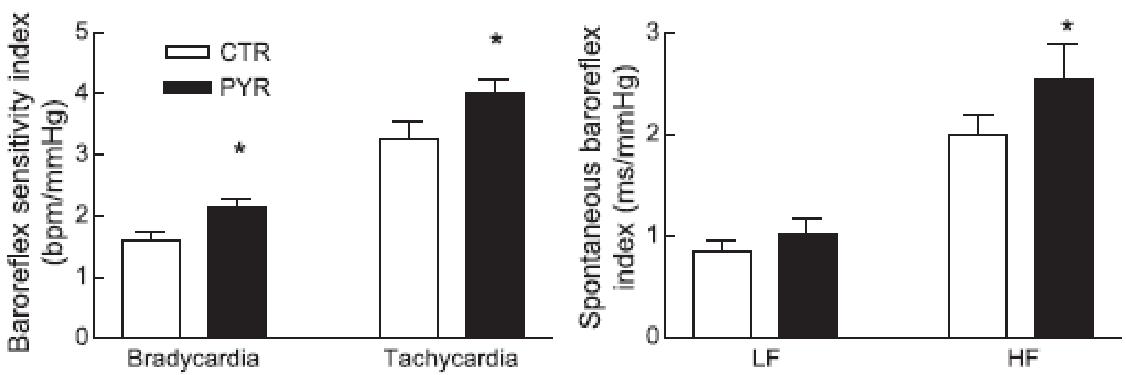

Fig. 2. Arterial baroreflex sensitivity in control (CTR, empty bars) and pyridostigmine-treated (PYR, full bars) rats. Left: indexes indicating the reflex bradycardia and tachycardia in response to vasoactive drugs. Right: spontaneous baroreflex in the low-frequency (LF) and high-frequency (HF) bands (α-index). *$P<0.05$ For CTR vs. PYR. Values are mean ± S.D.

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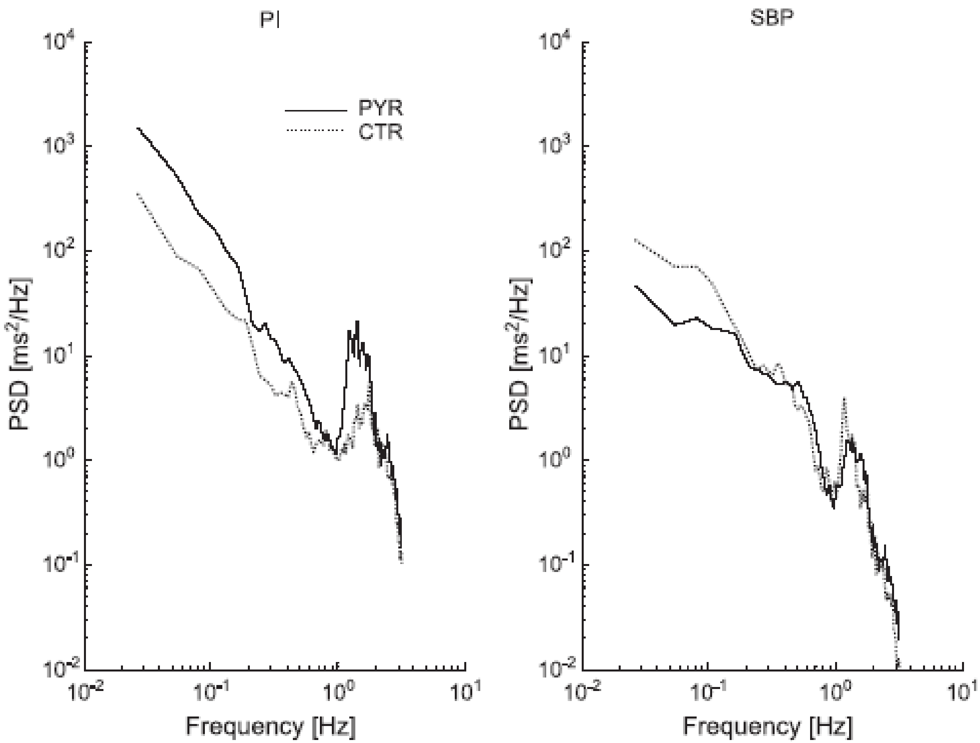
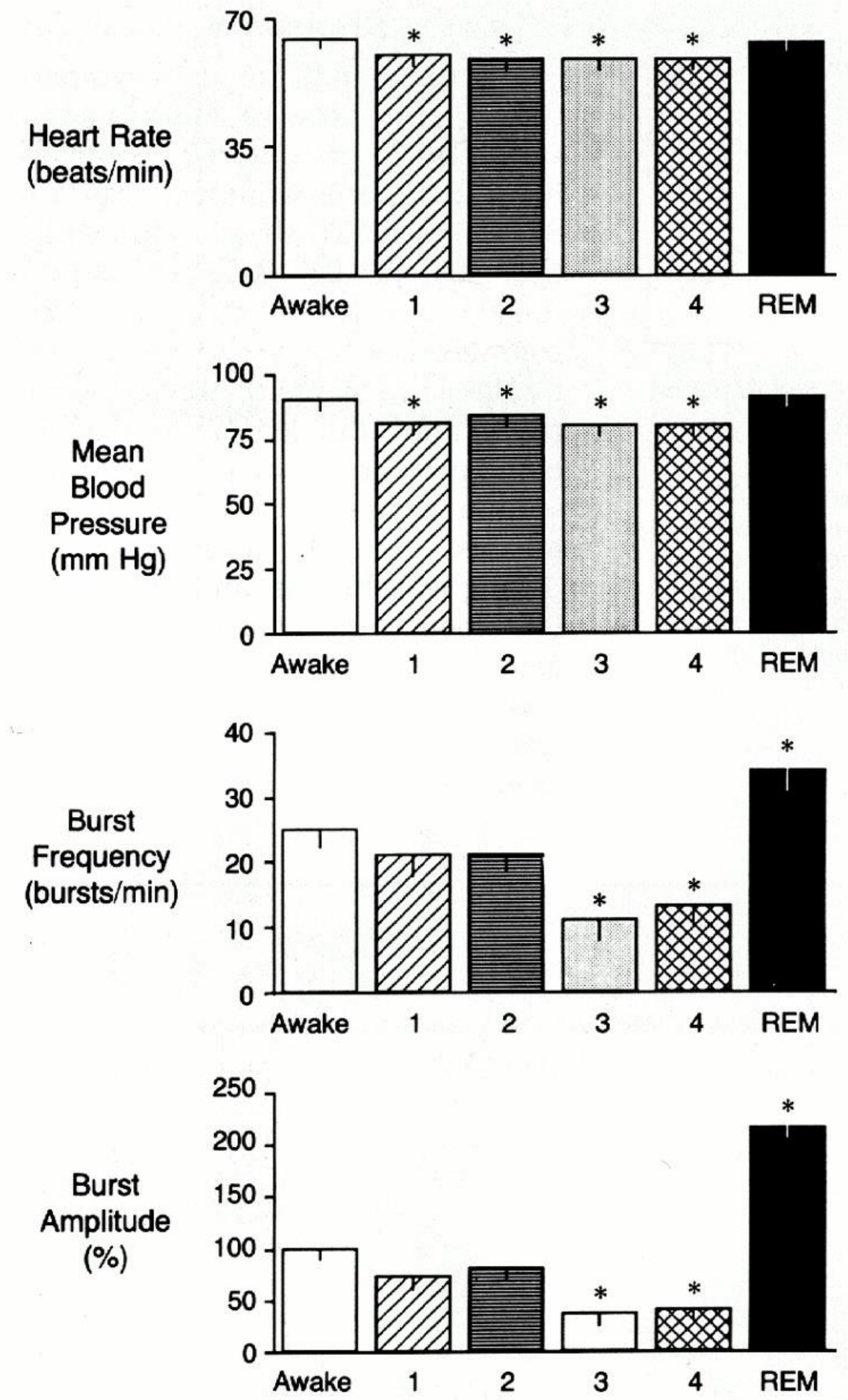


Fig. 1. Spectral analysis of the pulse interval (PI) and systolic blood pressure (SBP) signals recorded for 20 min in representative control (CTR: dotted line) and pyridostigmine-treated (PYR-treated: solid line) rats. Note the larger area under the curve for the treated rat for PI variability.

SLEEP

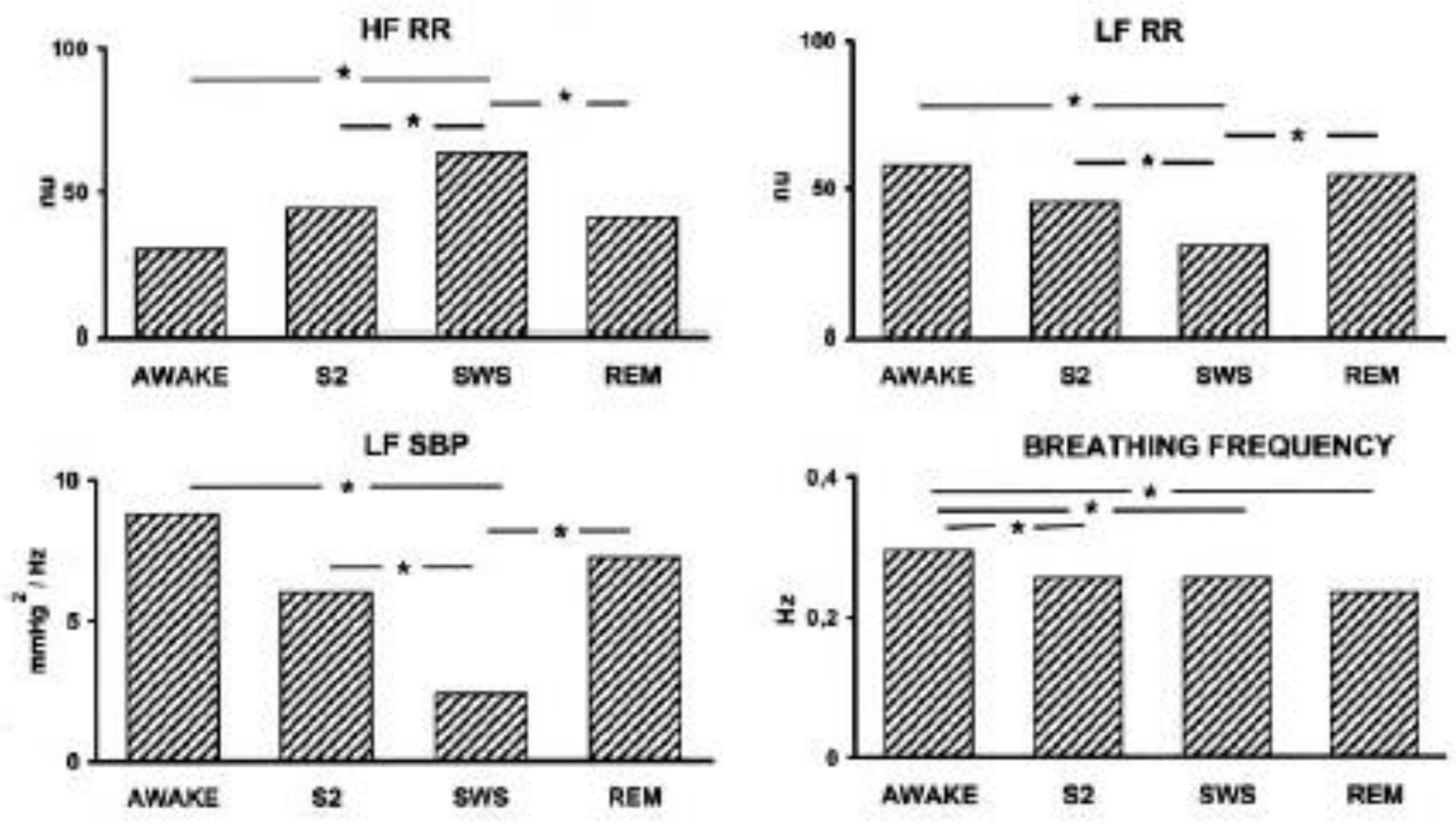
Cardiovascular and

sympathetic changes



(From Somers V. K. et al. *N Engl J Med* 1993;328:303-307

HRV during the different sleep stages



(Iellamo F. et al, *Hypertension* 2004, 43:814-819)

AUTONOMIC MODULATION IN HEART FAILURE

To evaluate autonomic control of circulation in HF subjects after maximal exercise.

- **Maximal Cardiopulmonary Ramp Test**

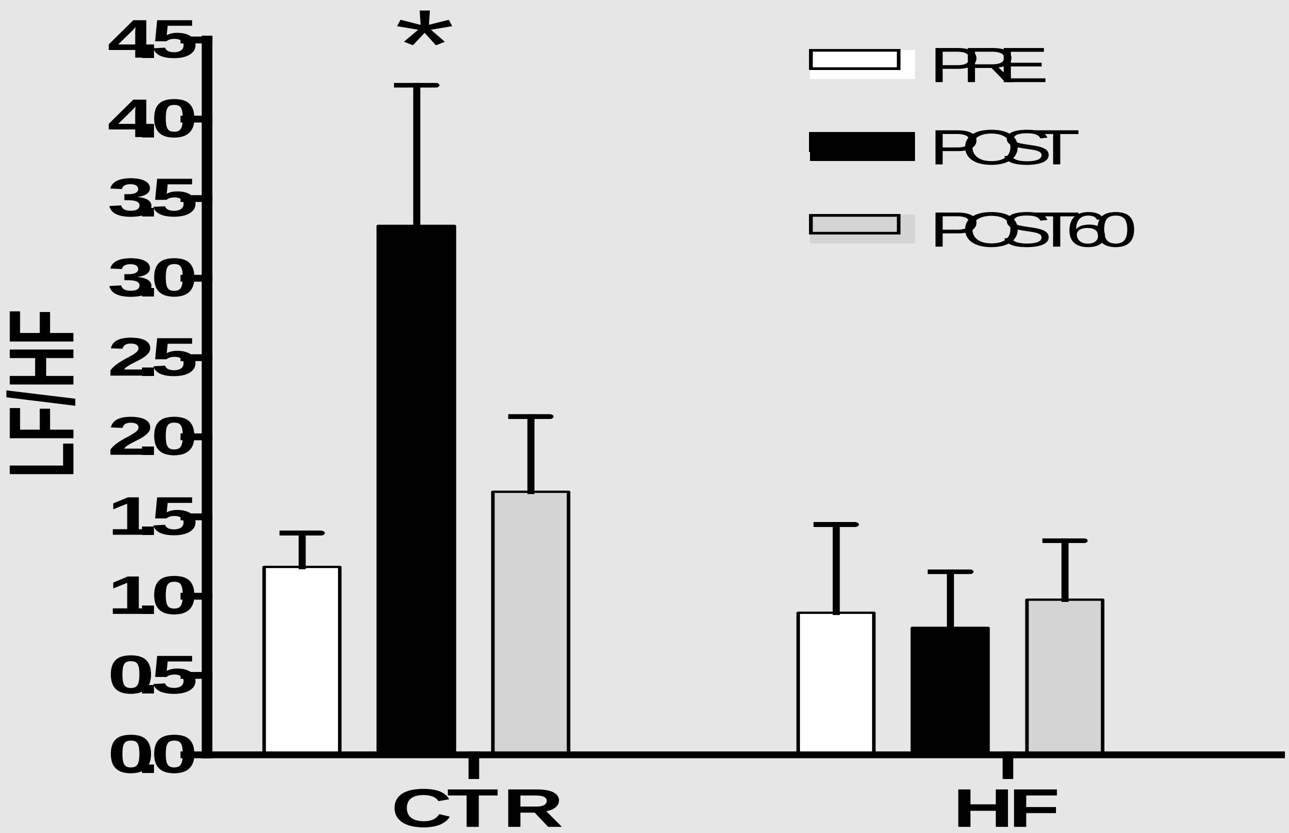
- Heart rate (HR) was recorded beat-by-beat for 5 minutes (Polar Electro Oy, Finland), before (PRE), immediately (POST) and 60 minutes (POST60) after cardiopulmonary test

- **RR time series** were analysed in

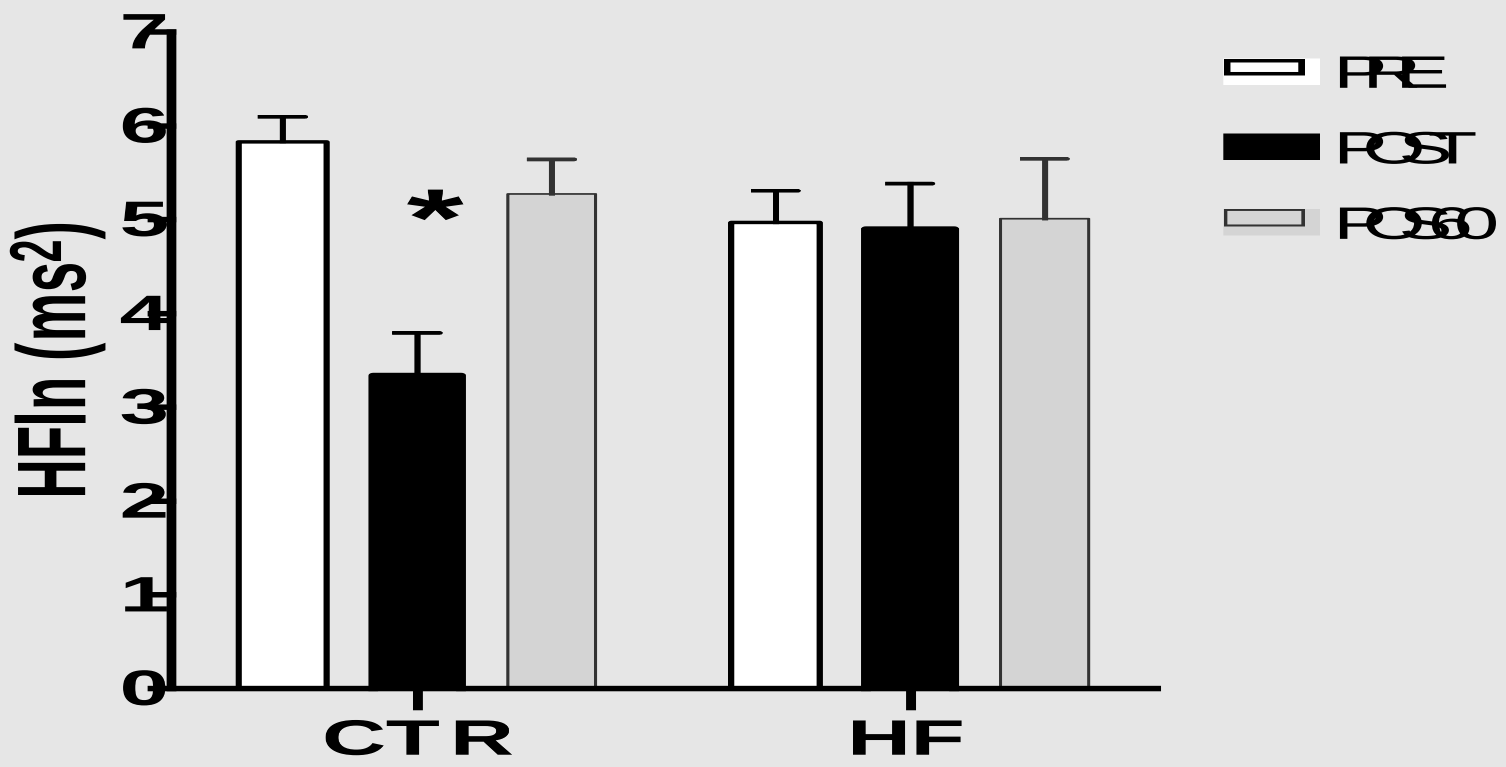
  time domain: mean RR, standard deviation and rMSSD

  frequency domain: Fast Fourier Transformation (Welch's method, Hanning window, 50% overlap). Spectral power calculated by integration in the low (LF= 0,04-0,15 Hz) and high (HF= 0,15-0,40 Hz) frequency bands in absolute units after natural logarithm transformation

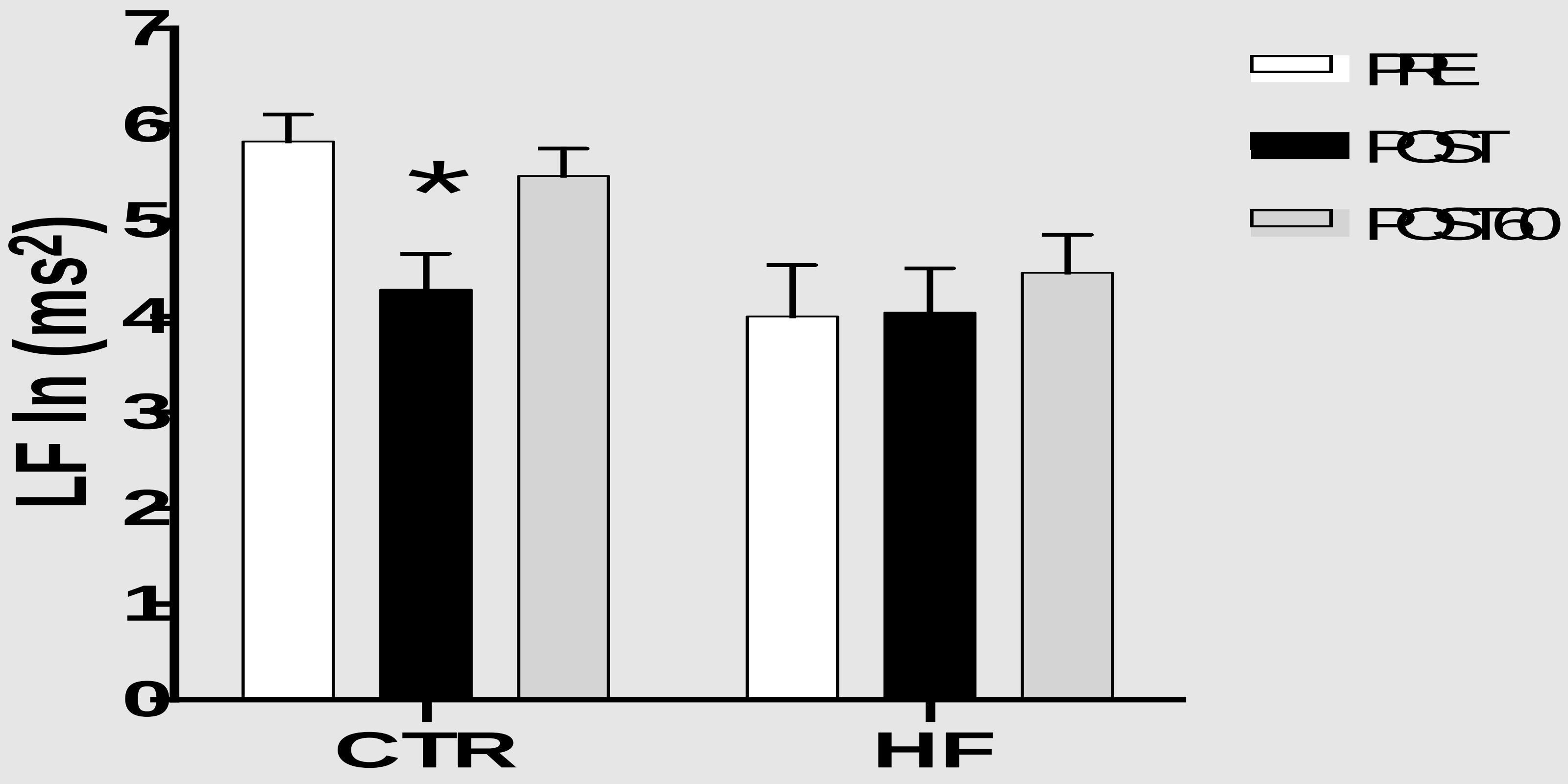
AUTONOMIC BALANCE



PARASYMPATHETIC MODULATION OF HEART RATE



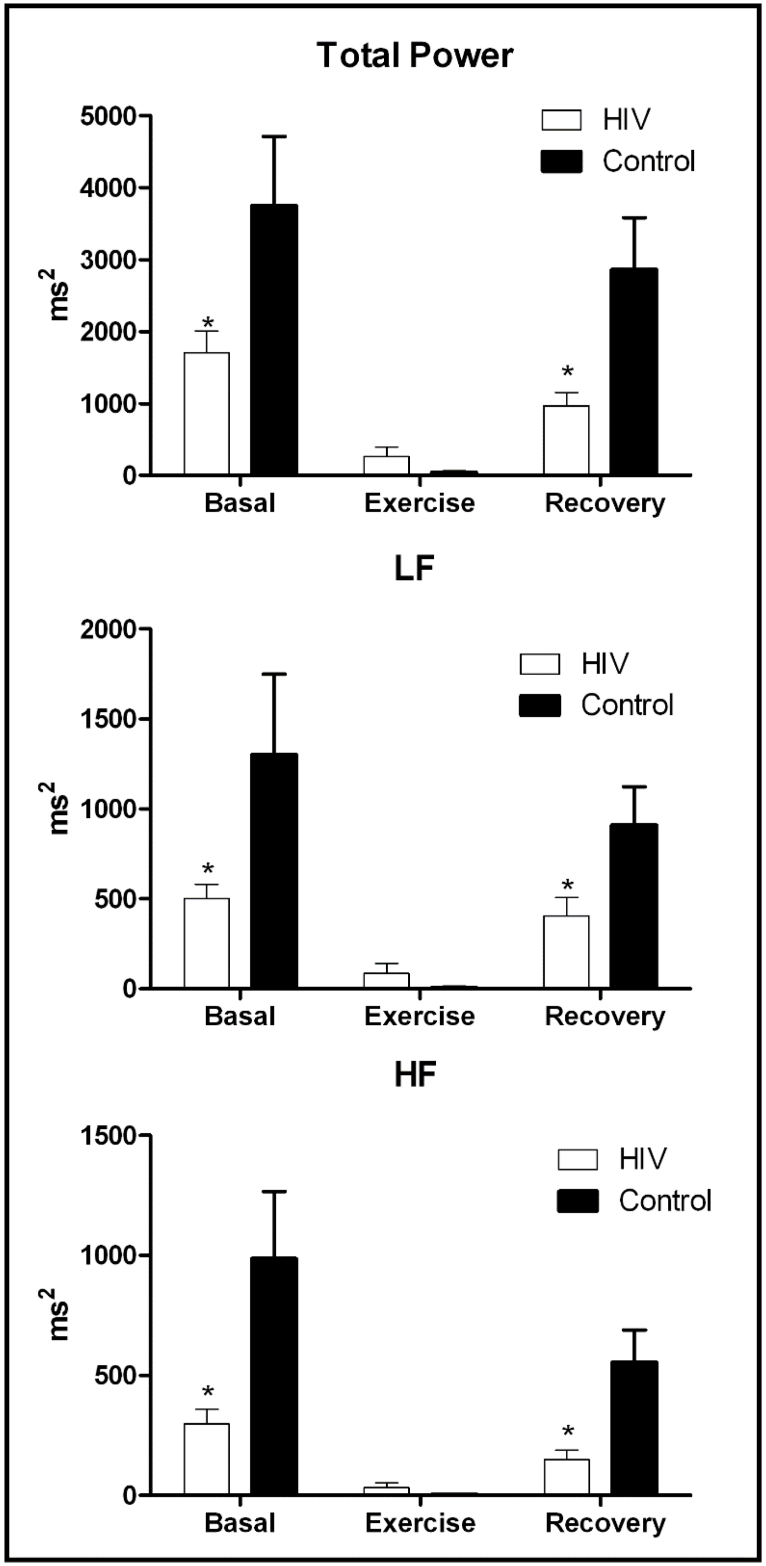
SYMPATHETIC MODULATION OF HEART RATE

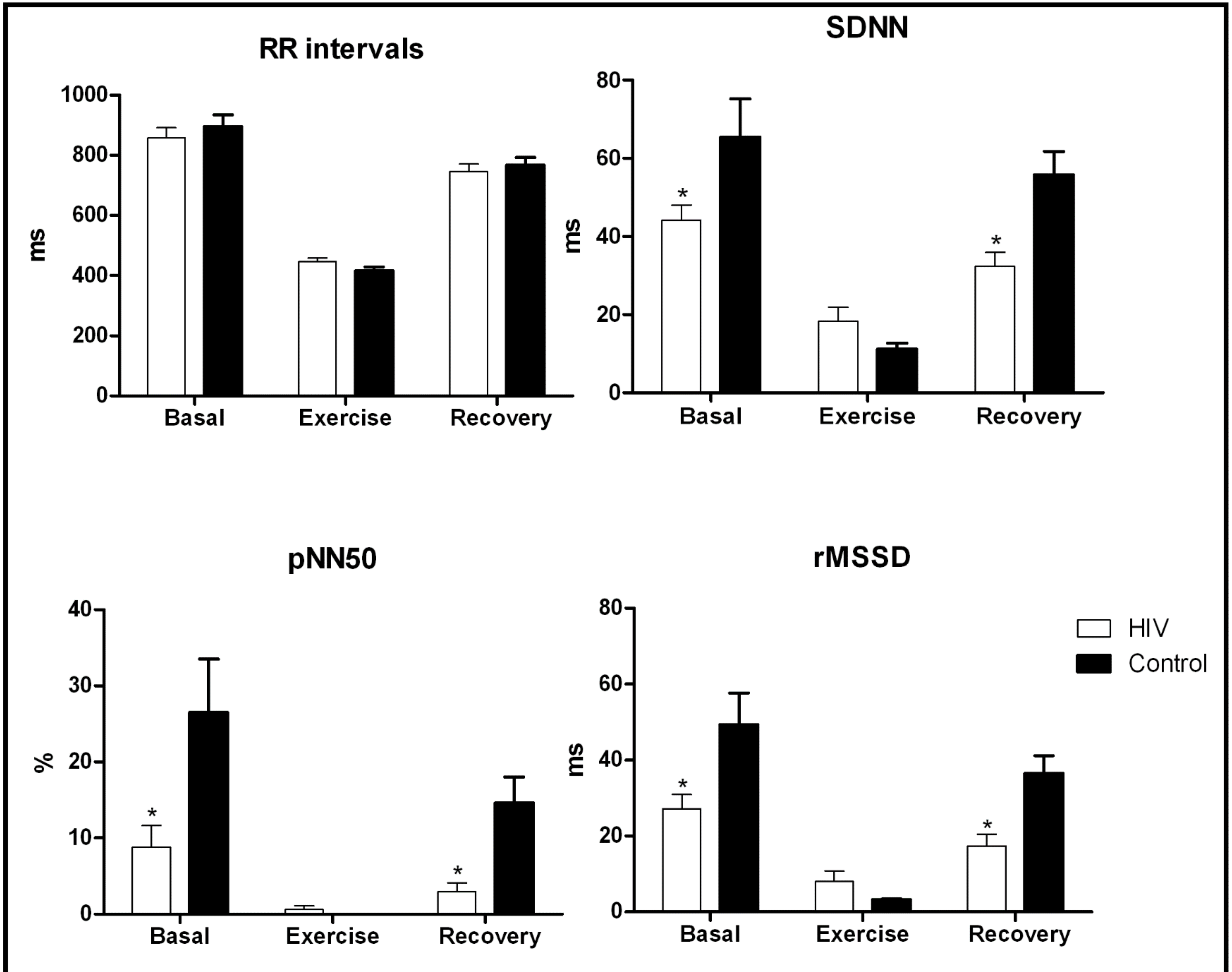


Autonomic Modulation Following Exercise is Impaired in HIV Patients

J. Borges, P.Soares, P. Farinatti

Borges J et al. Autonomic Modulation Following Exercise … Int J Sports Med



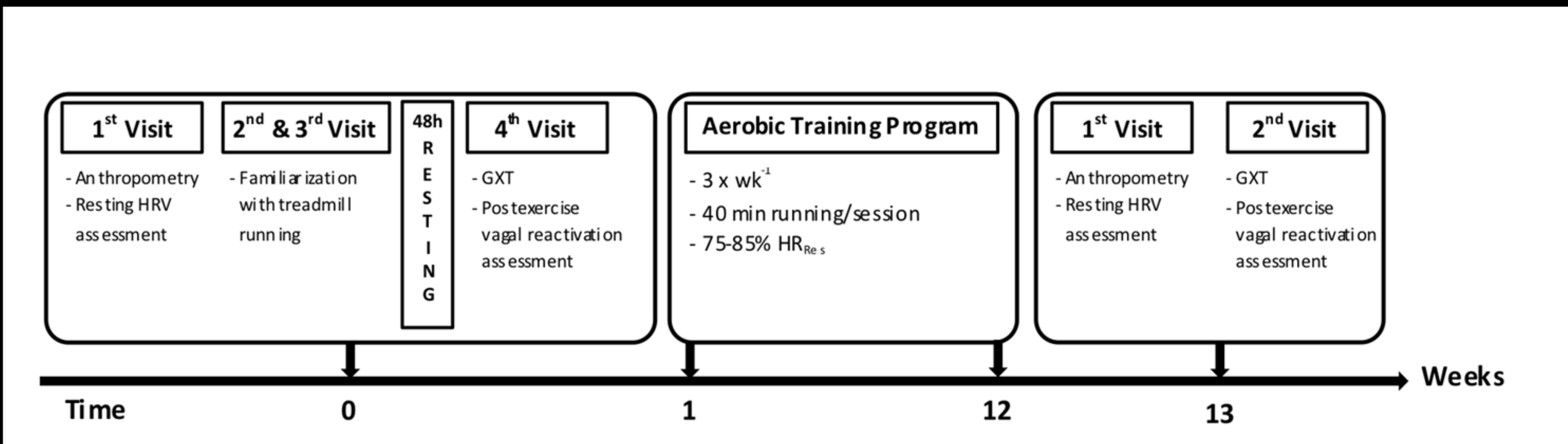


RR intervals
1000
800
600
400
200
0
ms
Basal
Exercise
Recovery
SDNN
80
60
40
20
0
ms
*
*
Basal
Exercise
Recovery
pNN50
40
30
20
10
0
%
*
*
Basal
Exercise
Recovery
rMSSD
80
60
40
20
0
ms
*
*
Basal
Exercise
Recovery
HIV
Control

Efeitos do exercício

FC basal e pós-exercício

Exercise training and initial values of cardiac autonomic modulation



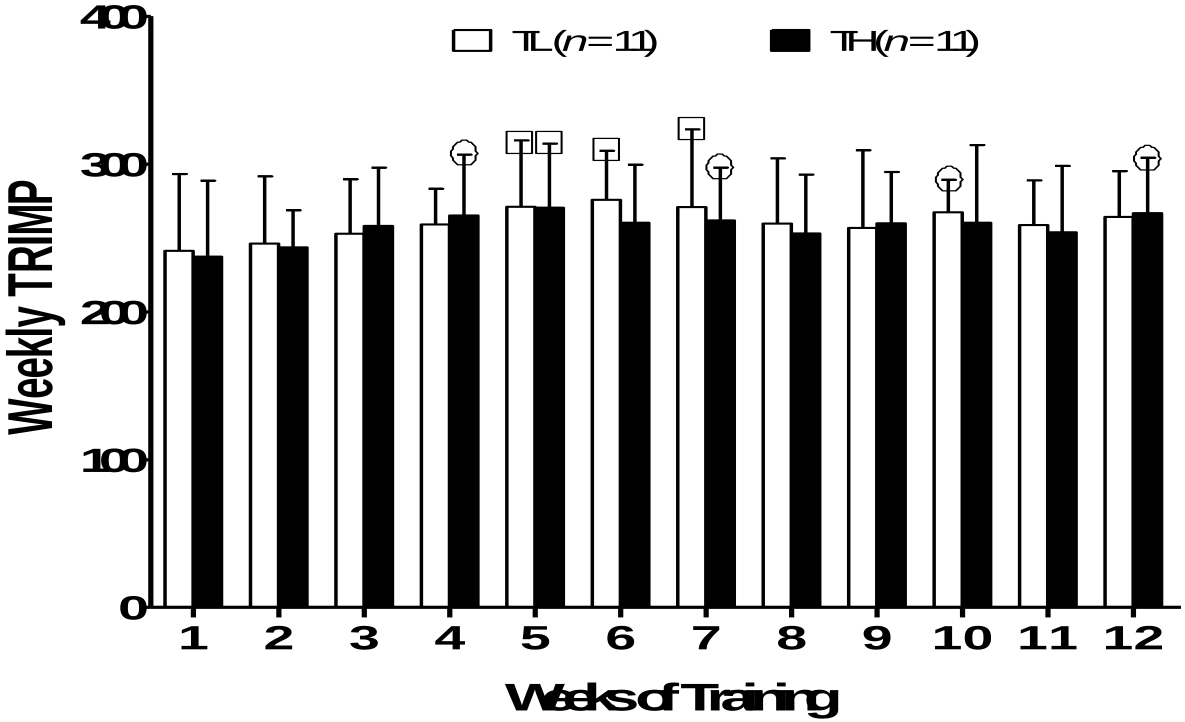
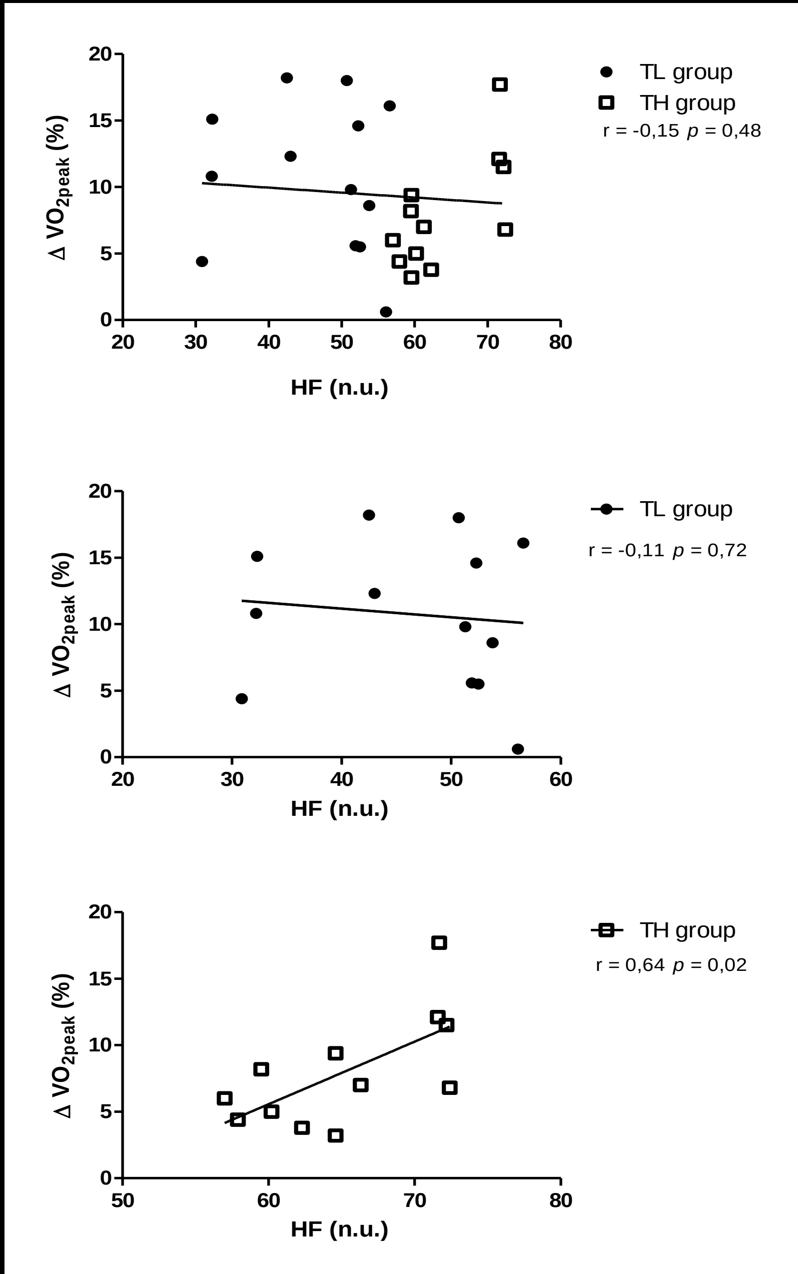


Figure 1 – Intensity and duration of training, as quantified by the training impulse (TRIMP) index, during the 12 weeks of training accomplished by the training groups with low (TL) and high (TH) cardiac vagal modulation at baseline. *Open circles* indicate significant difference in comparison to week 1 training load (P < 0.05). *Open squares* indicate significant difference in relation to Weeks 1 and 2 training load (P < 0.05). Values are Mean ± SD.

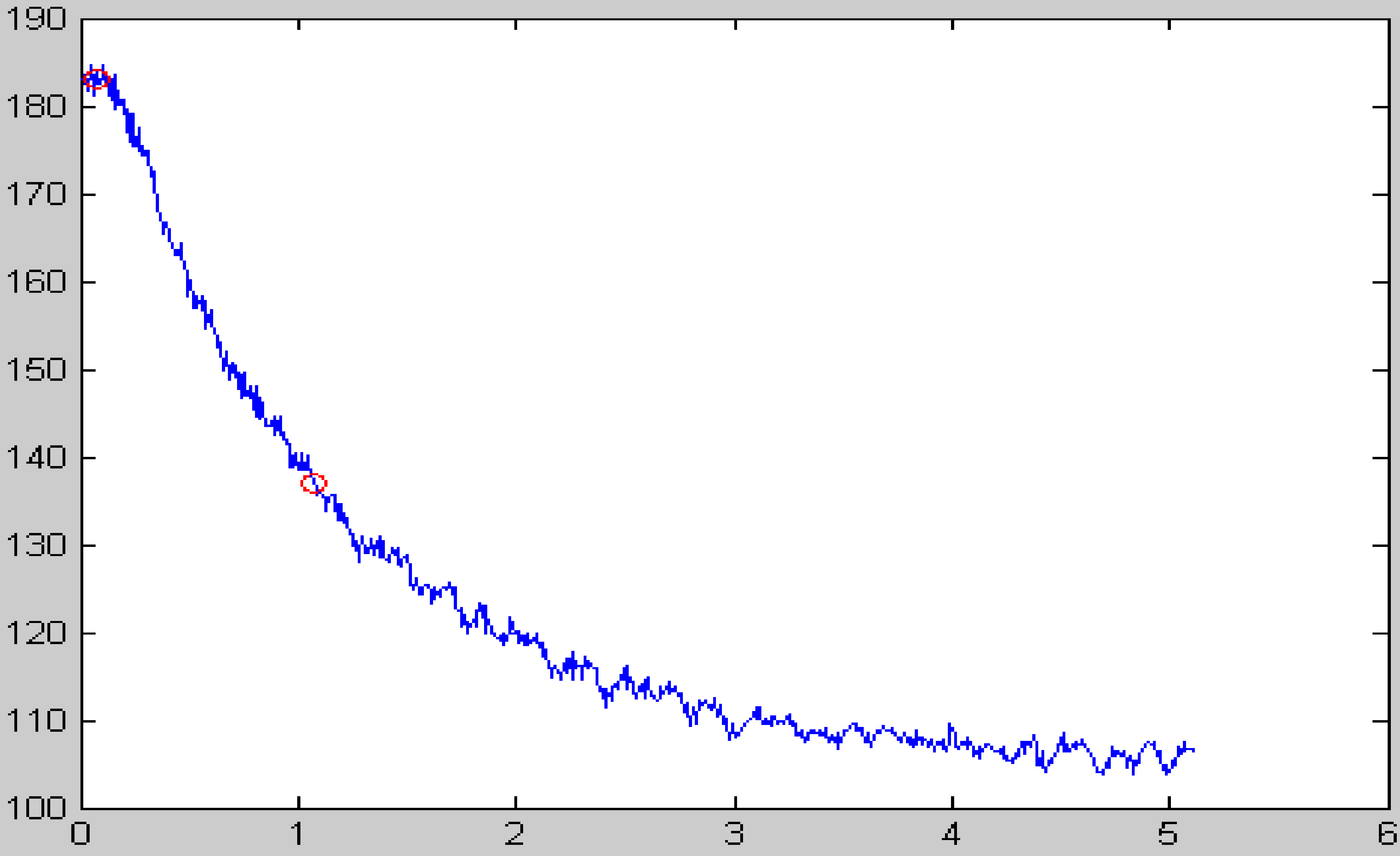
Exercise training
HRV vs VO_{2max}



Moderate to high intensity aerobic training improved VO_{2peak} despite differences in baseline vagal control in young fit subjects, but only those with low HF power increased parasympathetic autonomic control. An elevated baseline vagal control may be related to higher VO_{2peak} gains due to aerobic training.

Figure – Correlation coefficients between aerobic conditioning gains (Δ Vo_{2peak}) after 12 weeks and pre-training high-frequency power (HF, n.u.), considering pooled data (*n*=25) of both trained groups (A) and separate data of trained group with lower HF power (TL, *n*=13) (B) and trained group with higher HF power (TH, *n*=12) (C).

Jbahia



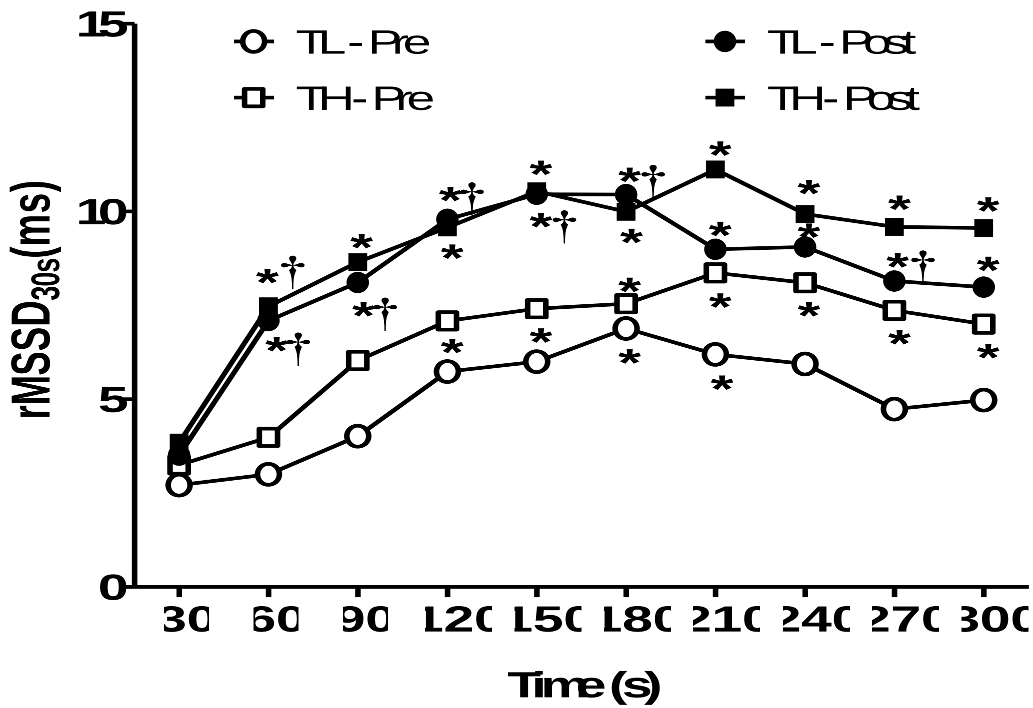
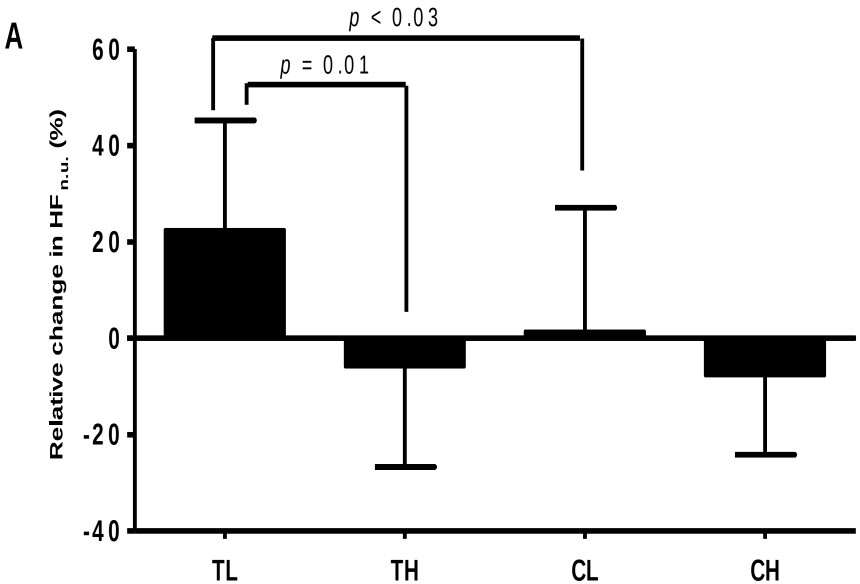


Figure 2 – Mean values of the square root of the mean squared difference of successive R-R intervals, measured in successive 30s-intervals ($rMSSD_{30s}$), presented by training groups of low (TL) and high (TH) baseline vagal modulation, before (Pre) and after (Post) the training protocol. * Significant difference in comparison to $rMSSD_{30s}$ at 30 s ($P < 0.05$). † Significant difference between Pre and Post values within groups ($P < 0,05$). To improve figure clarity, the error bars were omitted.



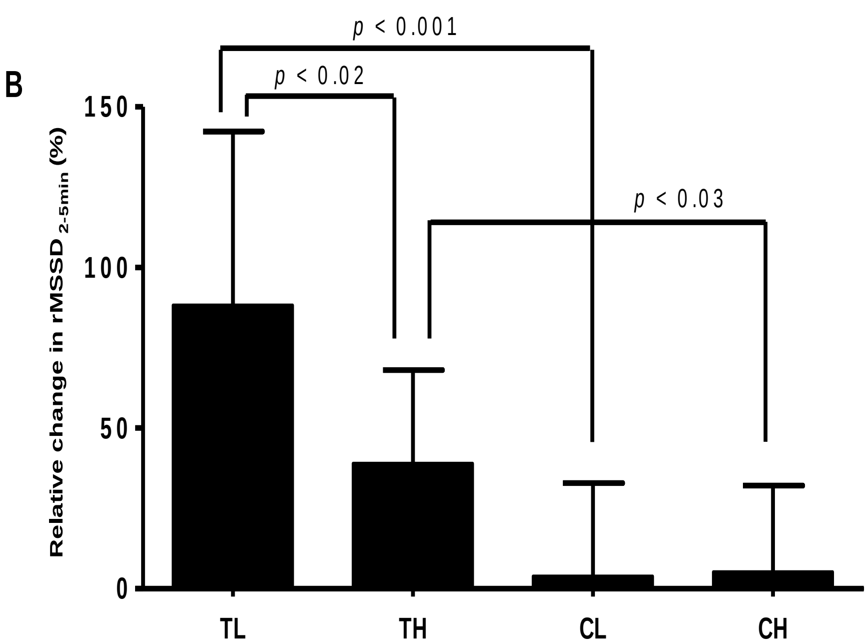
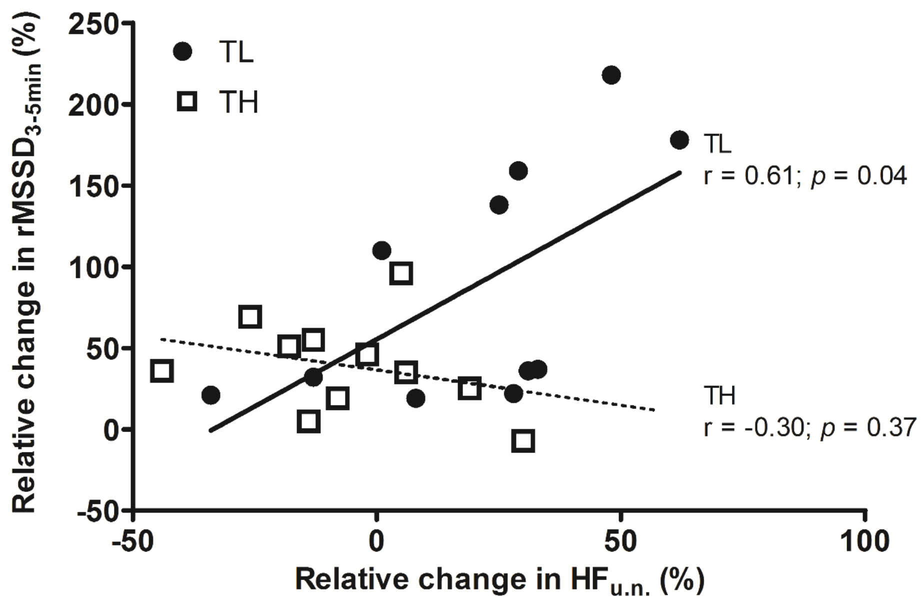
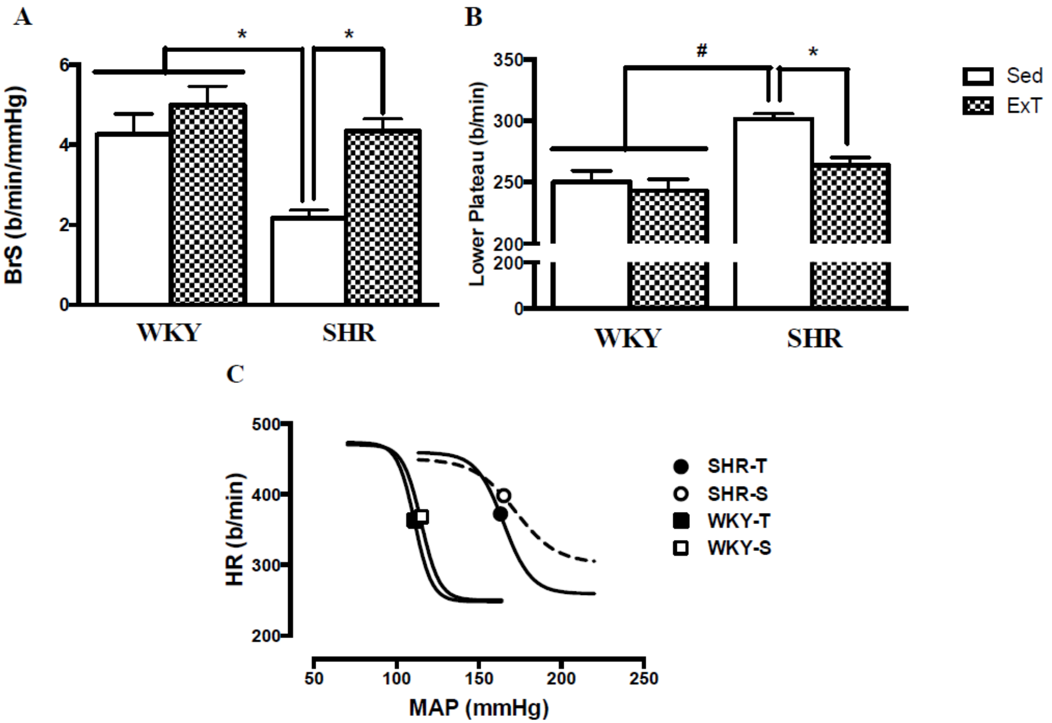


Figure 4 – Mean values ($\pm$ SD) of (**A**) the relative change in high-frequency power of HRV (Δ% $HF_{n.u.}$), and (**B**) the relative change in the square root of the mean squared difference of successive R-R intervals during the last 2 min of the 5 min postexercise recovery time (Δ% $rMSSD_{2\text{-}5min}$), for the low (TL) and high (TH) baseline vagal modulation training groups and the low (CL) and high (CH) baseline vagal modulation control groups, as a result of training. Significant differences are disclosed in the figure.

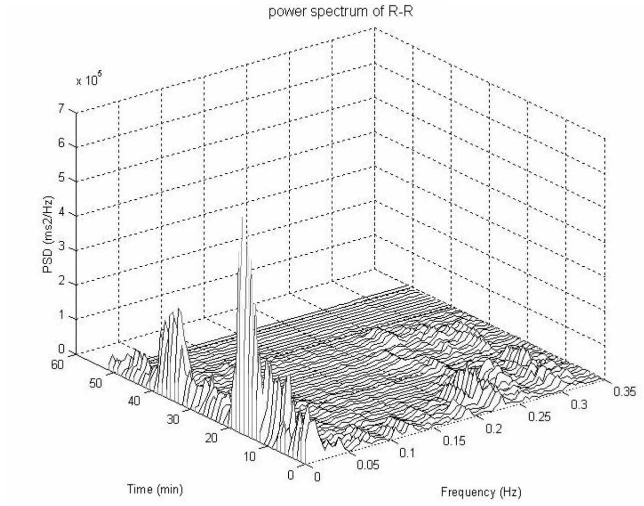
Duarte et al MSSE 2015

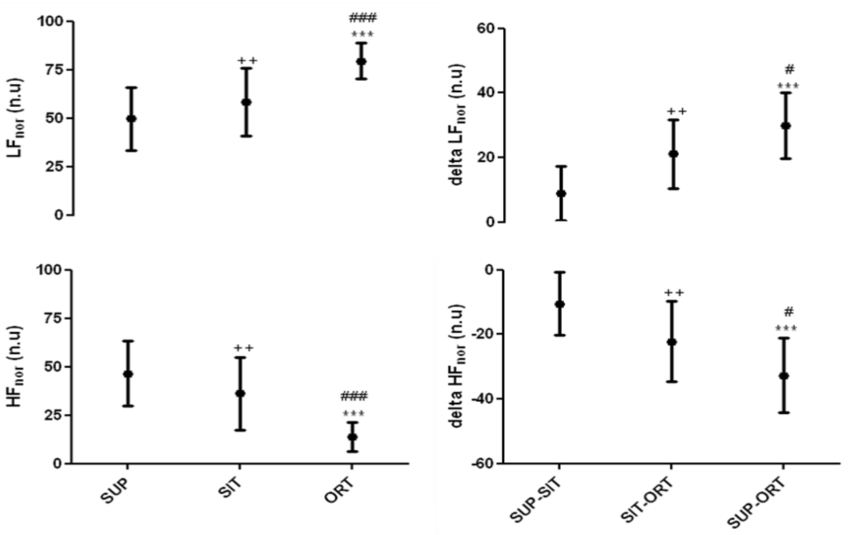


Duarte et al MSSE 2015



Masson et al. 2015





J Strength Cond Res. 2015 May;29(5):1415-21

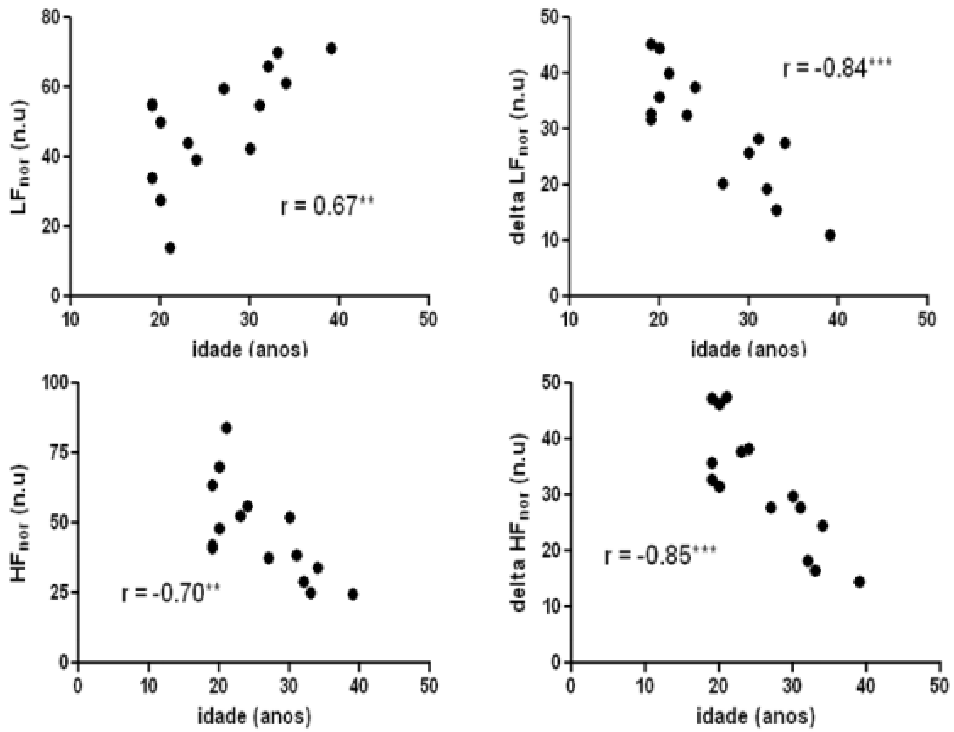
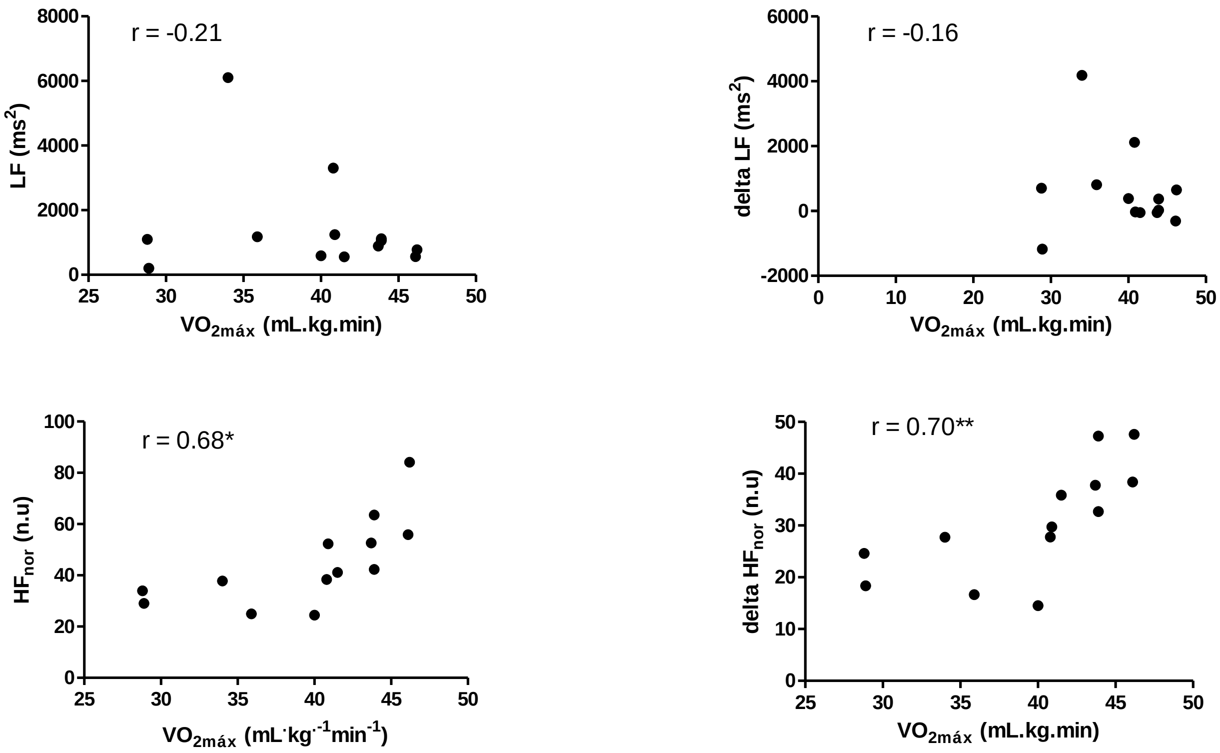


FIGURA 4 – Diagrama de dispersão de LFnor, HFnor, ΔLFnor e ΔHFnor com a idade.

J Strength Cond Res. 2015 May;29(5):1415-21



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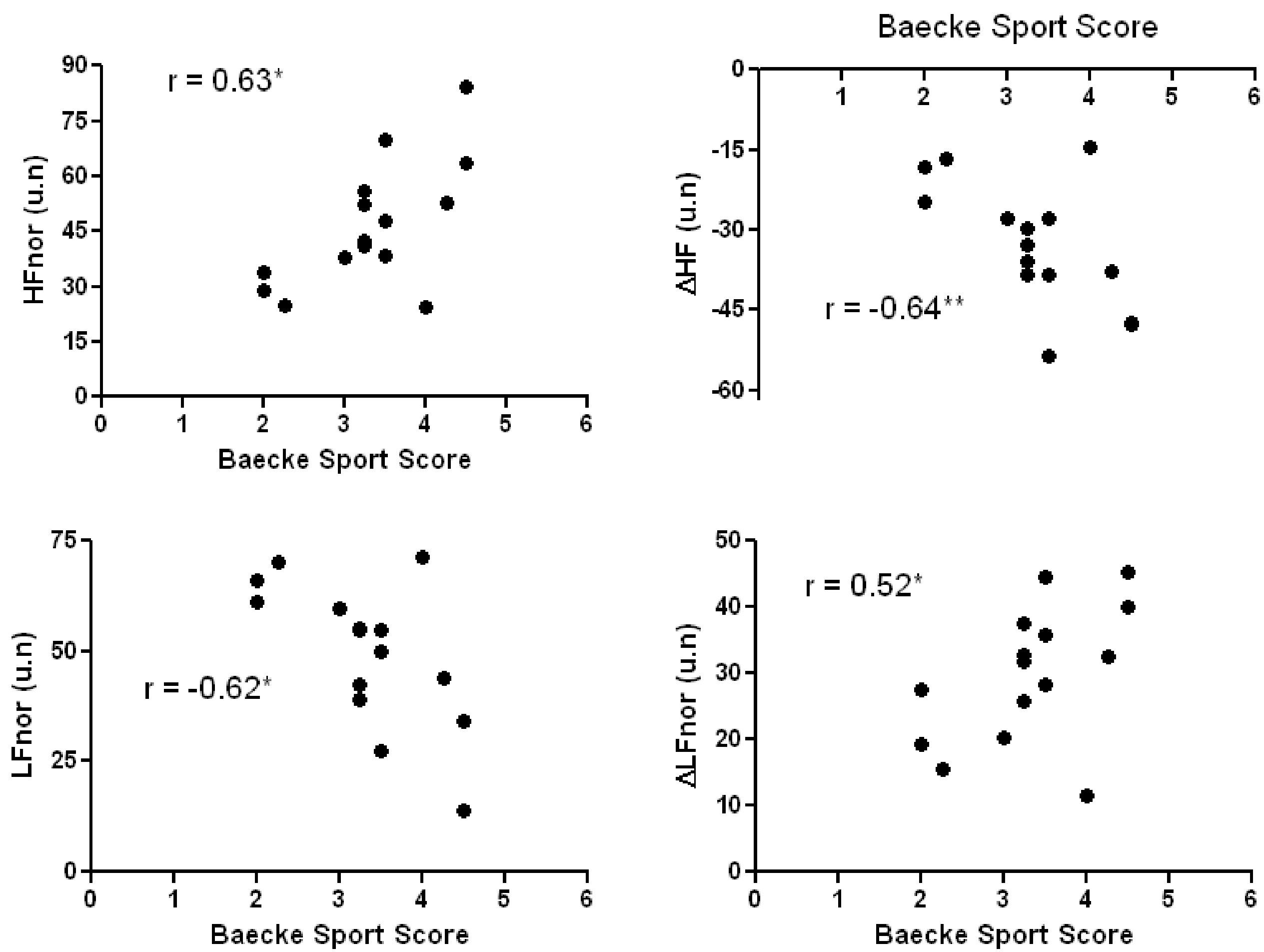

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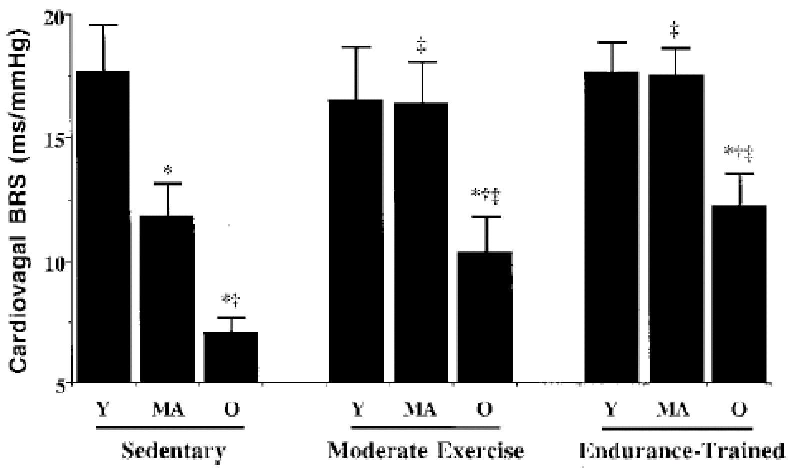

Figure 3. Cardiovagal baroreflex sensitivity of subjects in the cross-sectional study

* $P < 0.05$ *vs.* young subjects (Y) within same activity group; † $P < 0.05$ *vs.* middle-aged subjects (MA) within same activity group; ‡ $P < 0.05$ *vs.* sedentary subjects of same age group; Y, young; MA, middle age; O, older.

Monahan et al J Physiol 2000; 529.1: pp263-71

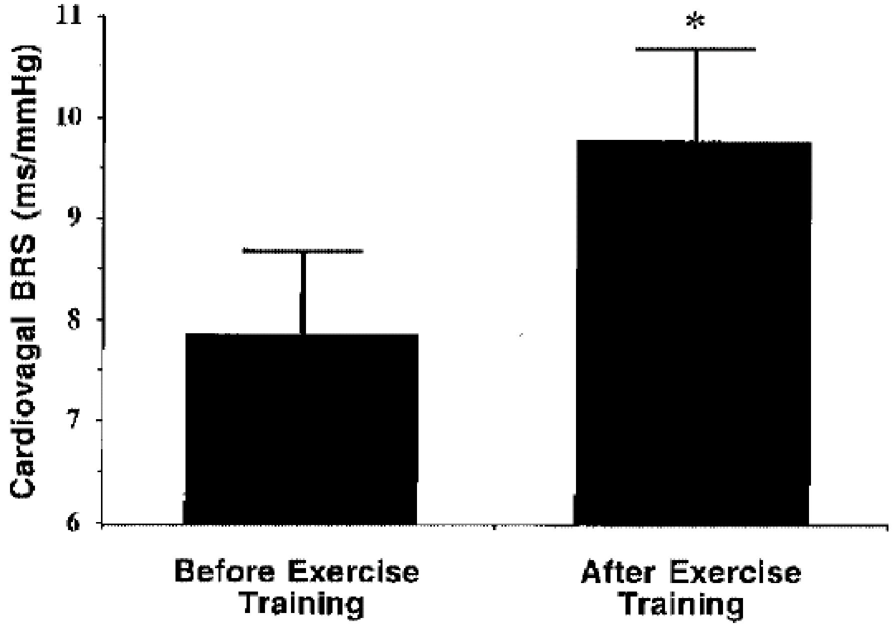

Figure 4. Cardiovagal baroreflex sensitivity before and after the aerobic exercise intervention

* $P < 0{\cdot}05$ *vs.* before exercise.

Monahan et al J Physiol 2000; 529.1: pp263-71

HRV - THE "INFORMATION DOMAIN":

- **provides info on autonomic neural control mechanisms in cardiovascular as well as non-cardiovascular diseases**
- **provides info on responses to therapy**
- **provides info on cardiovascular risk (morbidity/mortality)**
- **provides predictive info on disease development**

HRV – Limitations of spectral analysis

In conditions characterized by an extremely low variability (e.g. CHF) assessment of SVB by linear analysis might be limited by irregularity and instability of signals.

Moreover, spectral analysis is not able to provide info on complexity of variability signals. This is characterized by:

regularity (recurrence of a pattern in a signal)

synchronization (when two mechanisms operate synchronously and pace the activity of each other)

coordination (between control mechanisms, necessary to allow adequate system functioning) ***(*Porta et al*, Med Biol Eng Comp, 2002)***

HRV – Non-linear dynamics

- **Power-law scaling (1/f)**
- **Detrended fluctuation analysis**
- **Correlation dimension**
- **Shannon entropy**
- **Approxymate entropy**
- **………..**

New Journal of Physics
The open-access journal for physics

Detrended fluctuation analysis of a systolic blood pressure control loop

C E C Galhardo[1,3], T J P Penna[1,3], M Argollo de Menezes[1] and P P S Soares[2]

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[2] Instituto Biomédico, Universidade Federal Fluminense, R. Prof. Hernani Melo n. 101, 24210-130, Niteroi, RJ, Brazil
[3] INCT-SC, Instituto Nacional de Ciência e Tecnologia de Sistemas Complexos, R. Dr Xavier Sigaud 150, Rio de Janeiro 22290-180, Brazil
E-mail: marcio@mail.if.uff.br

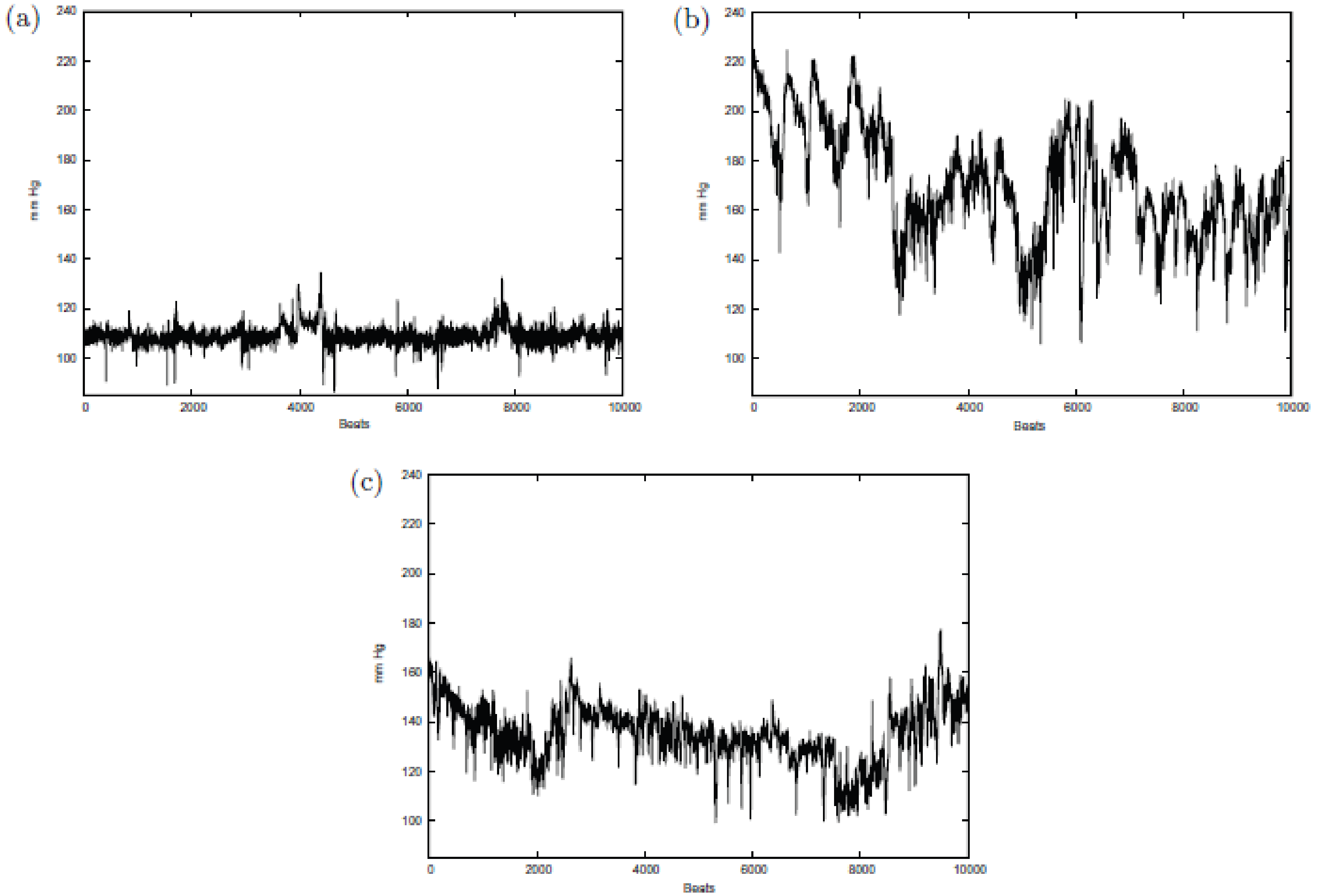


Figure 3. (a) Fluctuations of arterial systolic blood pressure from a rat in the control group. Blood pressure oscillates about safe, steady levels. (b) One day after disrupting the pressure control loop with a surgical procedure, pressure fluctuates in a non-stationary fashion, reaching dangerously high values. (c) As a result of physiological adaptation, 20 days after surgical denervation of baroreceptors average blood pressure returns to safe levels and fluctuations are again stationary.

3. Fluctuation analysis and computer modeling

We used DFA [23, 25] to characterize long-term correlations in arterial systolic blood pressure. This method has been successfully applied to analyze diverse non-stationary physiological signals [25]–[28], [37, 38] and we briefly describe it in the following: let $\{P(t)\}$ be the systolic blood pressure time series and P_{ave} its time average. Define the integrated time series $\{y(t)\}$ with

$$y(t) = \sum_{k=1}^{t} (P(k) - P_{\text{ave}}). \tag{1}$$

Divide the integrated series in boxes of equal sizes n and, for each box, calculate the detrended profile subtracting from the original signal a l-degree polynomial least-squares fit, $y_n^l(t)$ (in the following, DFA-l will stand for DFA with l-degree polynomials [39]). At each box of size n, calculate the fluctuation

$$F(n) = \sqrt{\frac{1}{N} \sum_{t=1}^{N} \left(y(t) - y_n^l(t)\right)^2}. \tag{2}$$

A power-law relation $F(n) \sim n^{\alpha}$ implies different correlation patterns for different values of α: when $0 < \alpha < 1/2$, the signal is stationary and long-range anti-correlated, with $\alpha = 1/2$ for a white noise (and $\alpha = 3/2$ for its integral, the Brownian motion), $\alpha > 1/2$ for long-range correlated signals, while the paradigmatic $1/f$ noise corresponds to $\alpha = 1$. This value of α also marks the borderline between stationary and non-stationary behavior: for $\alpha \geqslant 1$, one has non-stationary signals, with sub-diffusive ($\alpha < 3/2$), diffusive ($\alpha = 3/2$) or super diffusive ($\alpha > 3/2$) behavior.

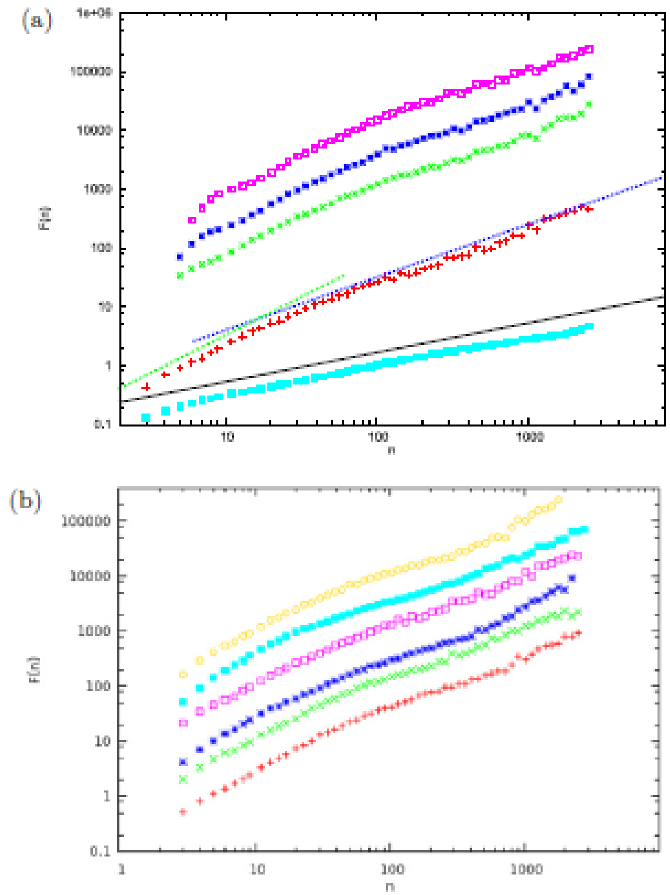


Figure 4. (a) DFA of systolic blood pressure time series for a typical rat in the control group. There is a crossover from non-stationary to stationary, long-range correlated behavior at $n \approx 35$: for short timescales we have $\alpha \approx 1.18$ and for large timescales $\alpha \approx 0.93$. We apply DFA-1 (red crosses), DFA-2 (green times), DFA-3 (blue stars) and DFA-4 (pink open squares) to the series and find that the crossover always exists, although at different scales. We also applied DFA-1 to shuffled data (bottom curve), for which $\alpha \approx 0.5$ as for a white noise. (b) DFA-1 for all rats in the control group. In both figures, curves are shifted vertically for better visibility. The curves $y = Ax^{\alpha}$ with $\alpha = 0.5$ (full black line), 0.9 (dashed blue line) and 1.3 (dashed green line) are plotted as guides to the eye.

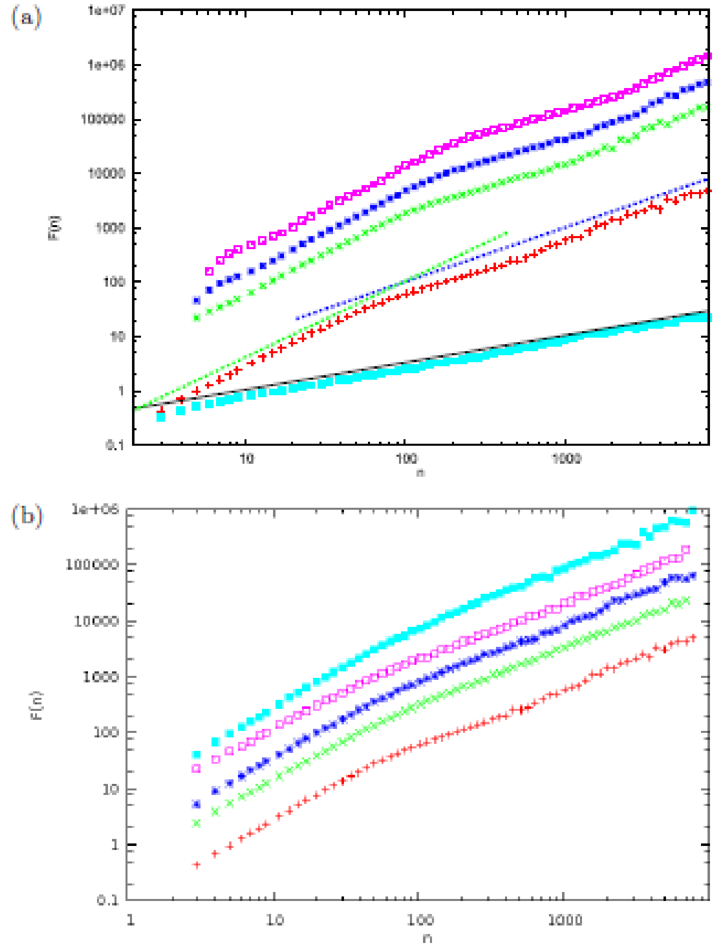


Figure 6. (a) DFA of systolic blood pressure time series for a typical rat in the chronic group: 20 days after surgical denervation, stationarity is recovered at large timescales and fluctuations crossover from non-stationary ($\alpha \approx 1.42$) to stationary, long-range correlated ($\alpha \approx 0.99$) at $n \approx 100$. This result suggests that, although the fast response from the baroreceptors in the heart is lost, physiological adaptation re-establishes homeostatic regulation. We apply DFA-1 (red crosses), DFA-2 (green times), DFA-3 (blue stars) and DFA-4 (pink open squares) to the series and find that the crossover always exists, although at different scales. We also applied DFA-1 to shuffled data (bottom curve), for which $\alpha \approx 0.5$ as in white noise. (b) DFA-1 for all rats in the chronic group. In both figures, curves are shifted vertically for better visibility. The curves $y = Ax^{\alpha}$ with $\alpha = 0.5$ (full black line), 1.0 (dashed blue line) and 1.4 (dashed green line) are plotted as guides to the eye.

Autonomic changes after sucessive bouts of maximal exercise in simulated rowing

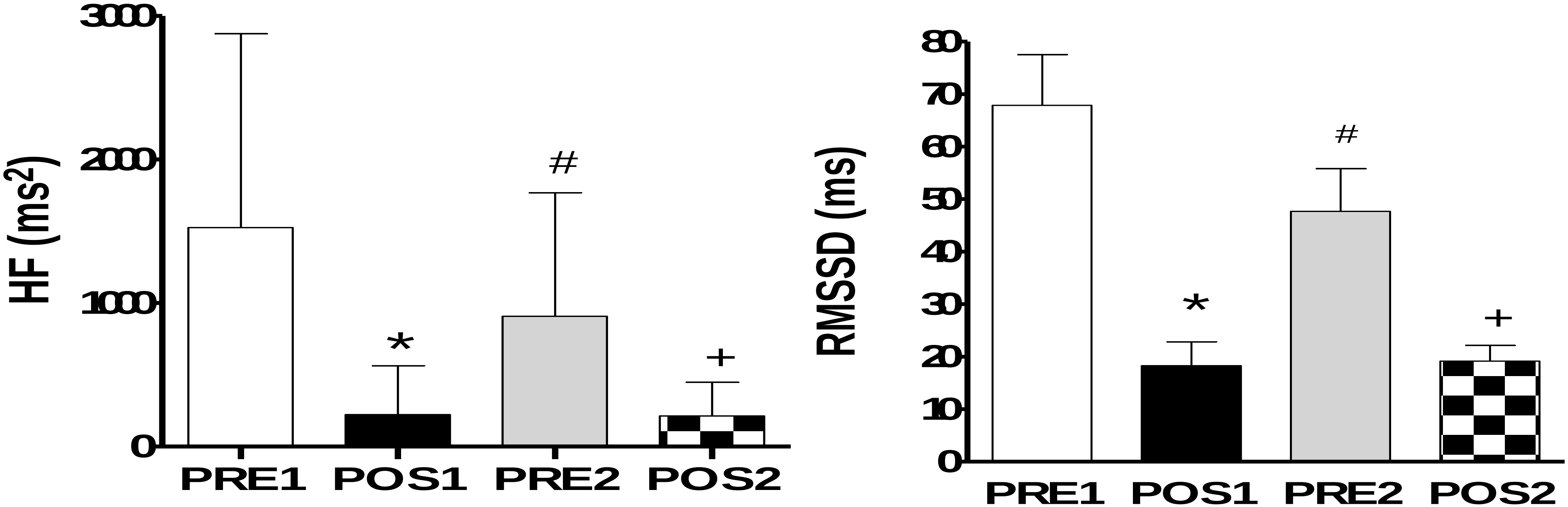
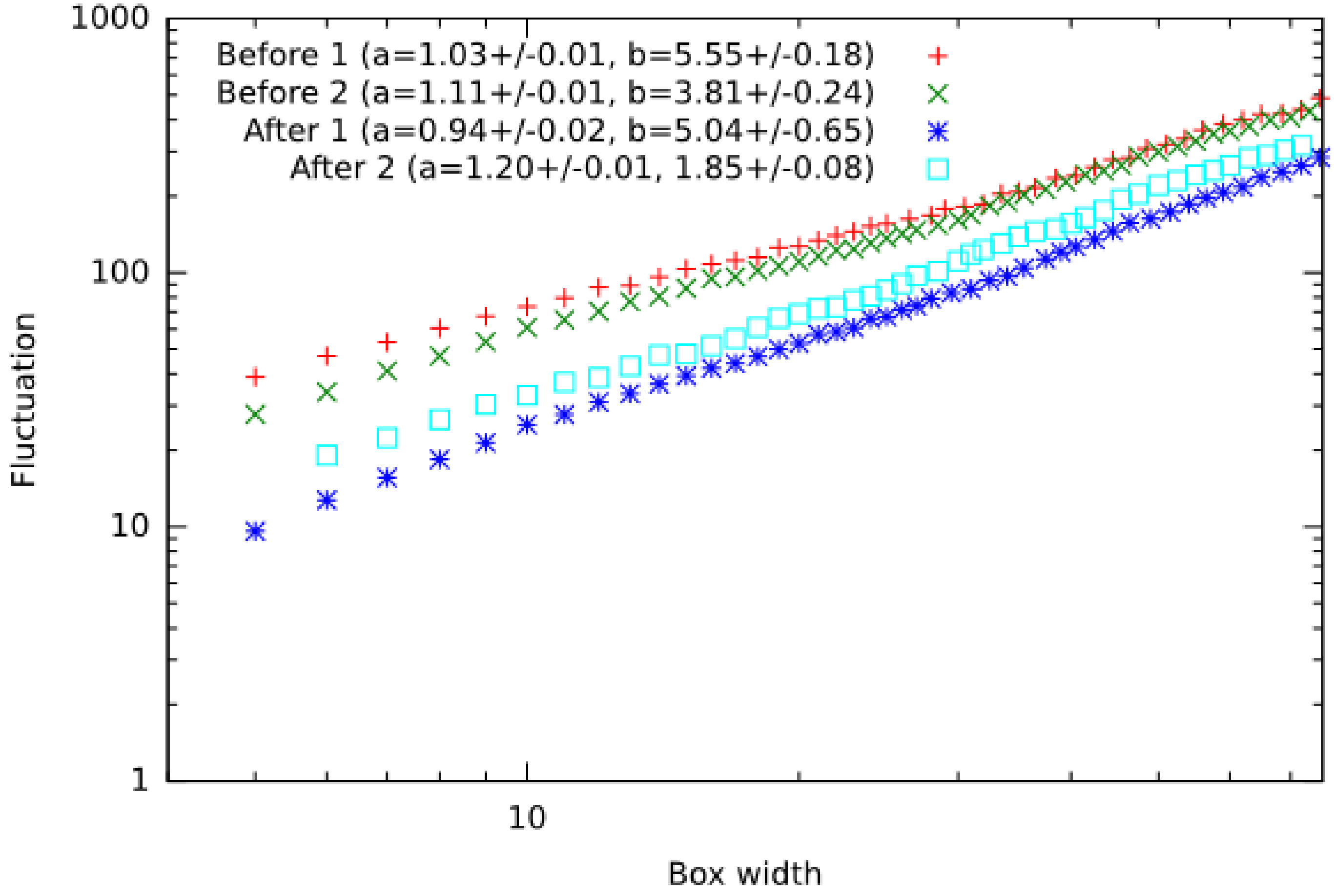


Figure 1 – High frequency power (HF) ate left, and the root mean squared of the sum of sucessive differences (rMSSD) right at moments PRE1, POS1, PRE2 and POS2. + POS2 vs PRE2; # PRE2 vs PRE1; * PRE1 vs POS1, $p < 0.05$.

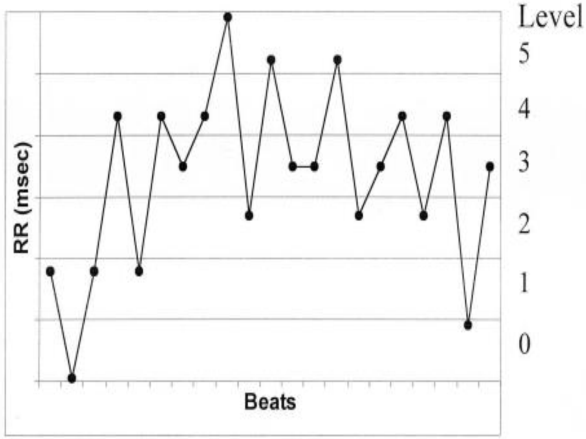
Detrended fluctuation analysis



Symbolic Dynamics of Heart Rate Variability
A Probe to Investigate Cardiac Autonomic Modulation

(*Circulation*. 2005;112:465-470.)

Stefano Guzzetti, MD; Ester Borroni, MD; Pietro E. Garbelli, MD; Elisa Ceriani, MD;
Paolo Della Bella, MD; Nicola Montano, MD; Chiara Cogliati, MD; Virend K. Somers, MD;
Alberto Mallani, MD; Alberto Porta, PhD



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0 1 4
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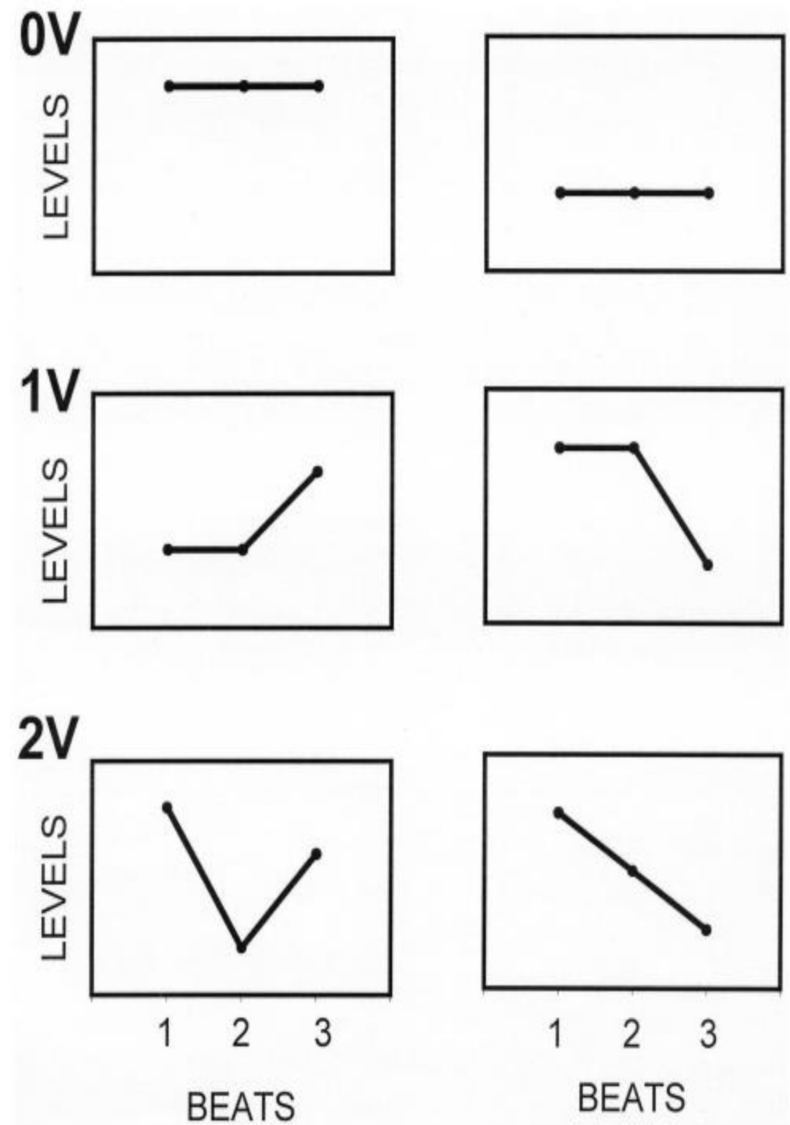
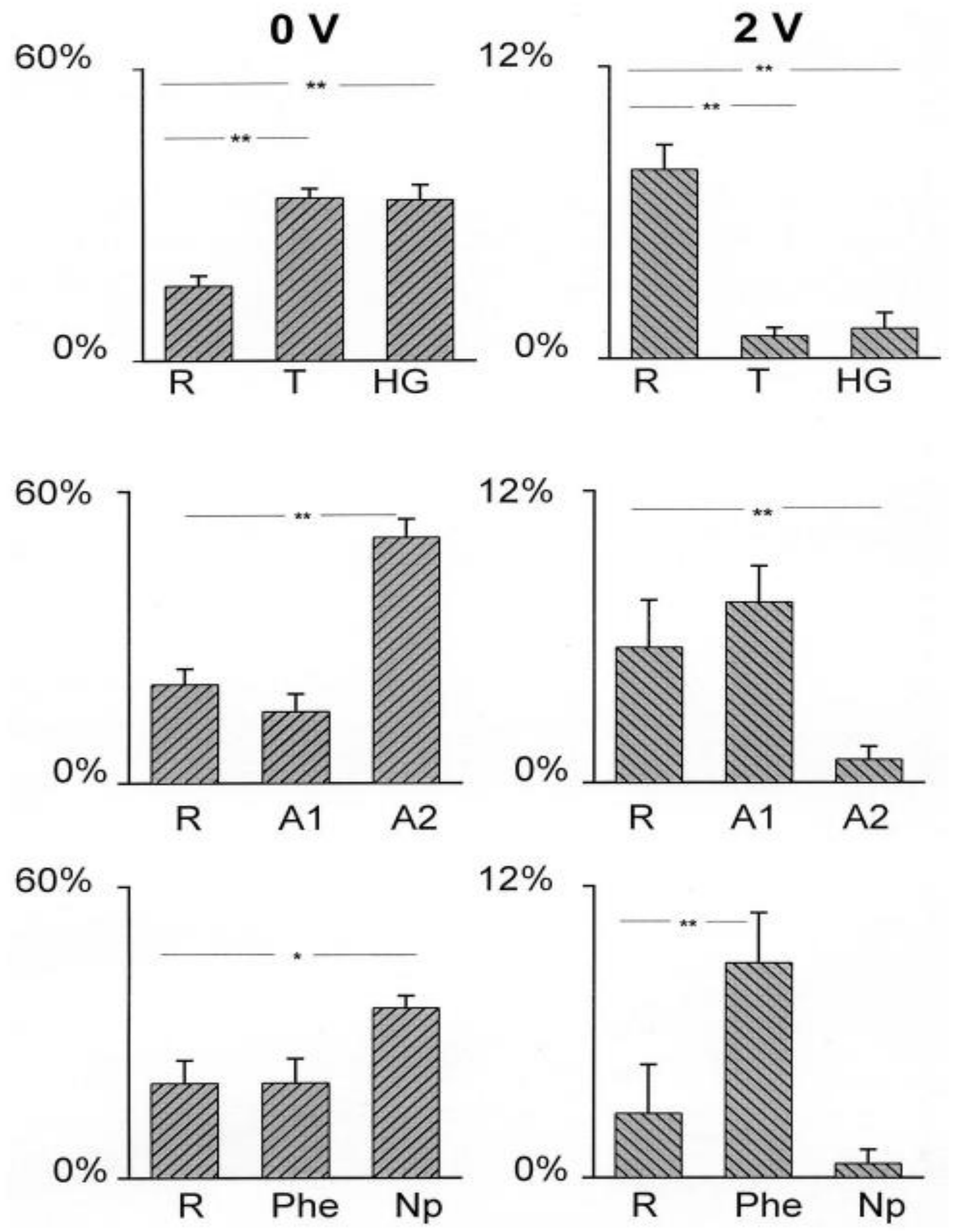


SYMBOLIC ANALYSIS AND AUTONOMIC STIMULI

R = rest
T = tilt
HG = handgrip
A1 = atropine low
A2 = atropine high
Phe = phenilephrine
Np = nitroprusside



(Guzzetti et al, *Circulation*, 112:465-470, 2005)

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European Journal of Internal Medicine xxx (xxxx) xxx–xxx

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Original Article

Cardiac autonomic modulation at rest and during orthostatic stress among different systemic sclerosis subsets

Gabriel Dias Rodrigues[a,b], Eleonora Tobaldini[c,d], Chiara Bellocchi[d,e], Alessandro Santaniello[e], Monica Caronni[e], Adriana Severino[e], Marco Froldi[d], Lorenzo Beretta[e], Pedro Paulo da Silva Soares[a,b], Nicola Montano[c,d,*,1]

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Table 2
Comparison of HRV indexes at rest between SSc and age-matched healthy control group.

	SSc (n = 69)	HC (n = 36)	p-value
Spectral analysis			
Total power (ms^2)	933 ± 1107[a]	1769 ± 1973	< 0.01
LFnu	57 ± 22[a]	38 ± 22	< 0.001
HFnu	34 ± 19[a]	57 ± 21	< 0.001
LF/HF	3.27 ± 4.23[a]	1.12 ± 1.60	< 0.001
Symbolic analysis			
0 V (%)	36.76 ± 17.74[a]	16.55 ± 9.84	< 0.001
1 V (%)	43.48 ± 9.91[a]	49.60 ± 5.70	< 0.001
2UV (%)	13.39 ± 7.95[a]	21.37 ± 8.55	< 0.001
2LV (%)	6.37 ± 5.22[a]	12.49 ± 6.28	< 0.001
Conditional entropy			
RO	0.36 ± 0.10[a]	0.27 ± 0.08	< 0.001
CE	0.86 ± 0.24[a]	1.10 ± 0.12	< 0.001

HRV: heart rate variability; SSc: systemic sclerosis; HC: age-matched healthy control group; HFnu: high frequency normalized unity; LFnu: low frequency normalized unity; 0 V%: patterns with no variations; 1 V%: patterns with one variation, 2LV%: patterns with two like variations, 2ULV%: patterns with two unlike variations; RO: regulatory index; CE: conditional entropy index; es: effect size. Unpaired test t.

[a] Differences from HC. $\alpha < 0.05$.

Table 3

Comparison of HRV indexes at rest and HRV adjustments from orthostatic stress between SSc subsets and age-matched healthy control group.

	dcSSc (n = 18)	lcSSc (n = 39)	EaSSc (n = 12)	HC (n = 36)	p-value
Spectral analysis					
Total power (ms^2)					
SUP	439 ± 248	1553 ± 2858	1430 ± 1173[a]	1769 ± 1973[a]	0.04
ΔORT%	0.08 ± 0.68	0.38 ± 1.35	0.31 ± 1.23	0.82 ± 3.40	0.97
LFnu					
SUP	61 ± 20	58 ± 22	54 ± 25	38 ± 22[a,b]	< 0.01
ΔORT%	0.18 ± 0.98	−0.07 ± 0.48	0.45 ± 0.92	1.42 ± 2.09[a,b]	< 0.001
HFnu					
SUP	34 ± 18	32 ± 16	42 ± 25	57 ± 21[a,b]	< 0.001
ΔORT%	−0.05 ± 0.63	0.01 ± 0.69	0.35 ± 1.84	−0.40 ± 0.51	0.09
LF/HF					
SUP	3.01 ± 3.02	3.20 ± 3.40	3.74 ± 5.81	1.12 ± 1.60[a,b]	< 0.001
ΔORT%	0.93 ± 2.71	1.22 ± 3.85	4.54 ± 8.85	9.08 ± 13.92[a,b]	< 0.01
Symbolic analysis					
0 V (%)					
SUP	35.11 ± 22.41	40.12 ± 17.11	30.63 ± 11.86	16.55 ± 9.84[a,b,c]	< 0.001
ΔORT%	0.35 ± 0.74	0.19 ± 0.97	0.79 ± 1.57	1.25 ± 2.33[b]	0.03
1 V (%)					
SUP	43.20 ± 11.88	42.16 ± 10.62	46.50 ± 3.79	49.60 ± 5.70[b]	< 0.01
ΔORT%	0.05 ± 0.43	0.05 ± 0.38	−0.07 ± 0.27	−0.03 ± 0.25	0.52
2UV (%)					
SUP	13.64 ± 9.13	12.63 ± 7.11	15.04 ± 9.02	21.37 ± 8.55[a,b]	< 0.001
ΔORT%	0.19 ± 0.91	0.52 ± 1.18	−0.30 ± 0.28[b]	−0.27 ± 0.58[b]	< 0.01
2LV (%)					
SUP	8.04 ± 6.77	4.65 ± 1.18	7.83 ± 4.77	12.49 ± 6.28[b]	< 0.001
ΔORT%	0.24 ± 1.74	1.37 ± 3.56	−0.38 ± 0.43	−0.10 ± 0.78[b]	0.02
Conditional entropy					
RO	0.39 ± 0.10	0.37 ± 0.11	0.33 ± 0.09	0.27 ± 0.08[a,b]	< 0.001
CE	0.87 ± 0.25	0.84 ± 0.21	0.92 ± 0.12	1.10 ± 0.12[a,b]	< 0.001

SSc: systemic sclerosis; lcSSc: limited cutaneous SSc; dcSSc: diffuse cutaneous SSc; EaSSc: Early SSc; HC: age-matched healthy control group; SUP: supine position; ORT: Orthostatic position HFun: high frequency normalized unity; LFun: low frequency normalized unity; 0 V%: patterns with no variations; 1 V%: patterns with one variation, 2LV%: patterns with two like variations, 2ULV%: patterns with two unlike variations; RO: regulatory index; CE: conditional entropy index. Both RO and CE analysis were performed at rest. ΔORT%: (HRV in SUP position – HRV in ORT position)/HRV in SUP position); ANOVA one-way for independent measures and Tukey post-hoc test.

[a] Differences from dcSSc.

[b] Differences from lcSSc.

[c] differences from EaSSc. $\alpha < 0.05$.

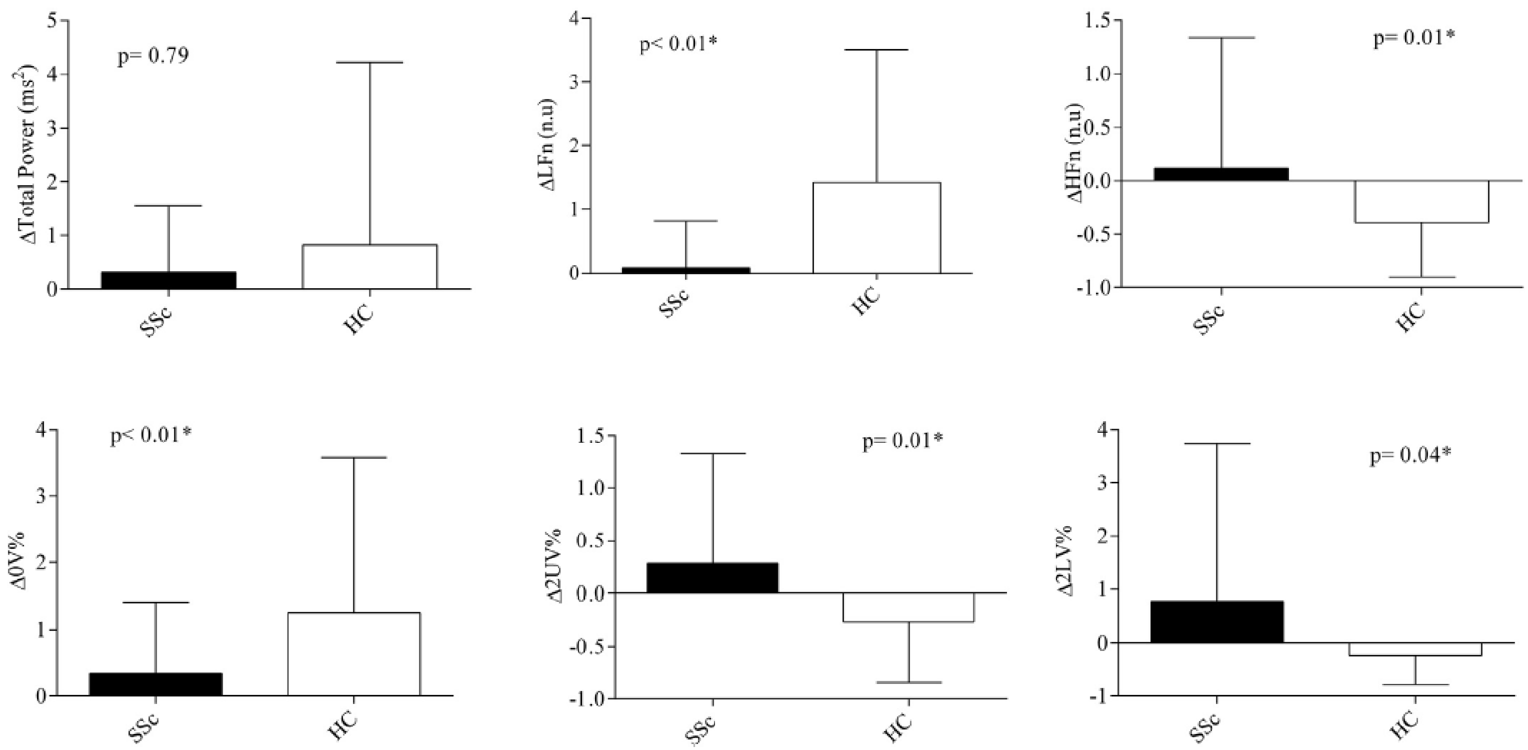
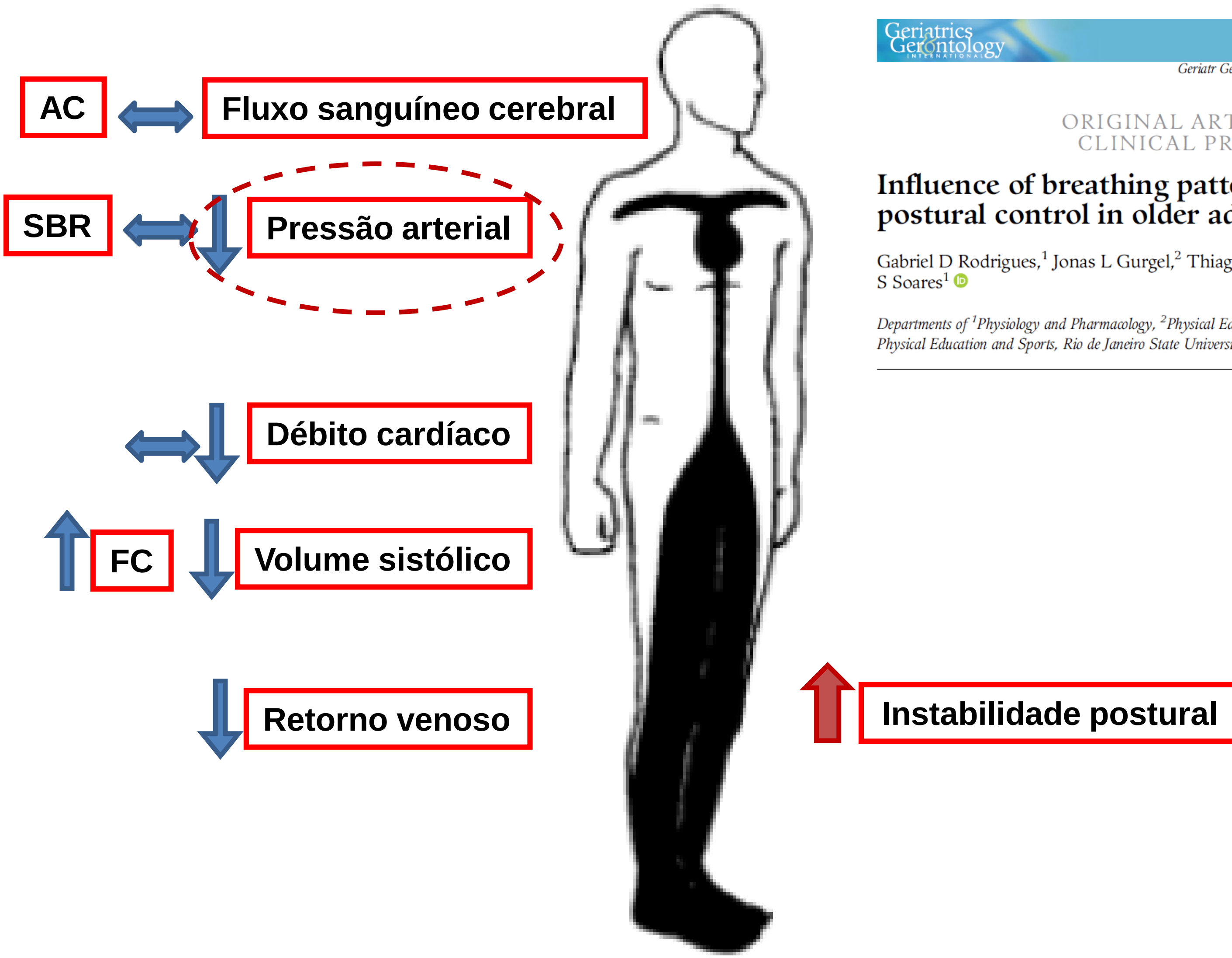
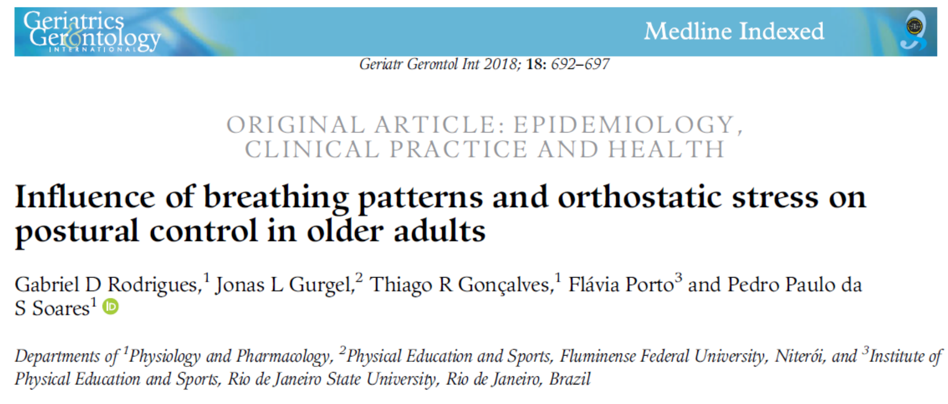


Fig. 1. Comparison of HRV adjustments from supine to orthostatic position between SSc and healthy control individuals. SSc: systemic sclerosis (n = 69); HC: age-matched healthy control group (n = 36); HFnu: high frequency normalized unity; LFnu: low frequency normalized unity; 0 V%: patterns with no variations; 2LV%: patterns with two like variations, 2ULV%: patterns with two unlike variations; ΔORT%: (HRV in SUP position – HRV in ORT position)/HRV in SUP position); Unpaired test t. *differences from HC. $\alpha < 0.05$.

PERSPECTIVAS E DESAFIOS

Ortostatismo → Desafio circulatório → *Physiological Pathway*




Geriatrics Gerontology International
Medline Indexed

Geriatr Gerontol Int 2018; 18: 692–697

ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

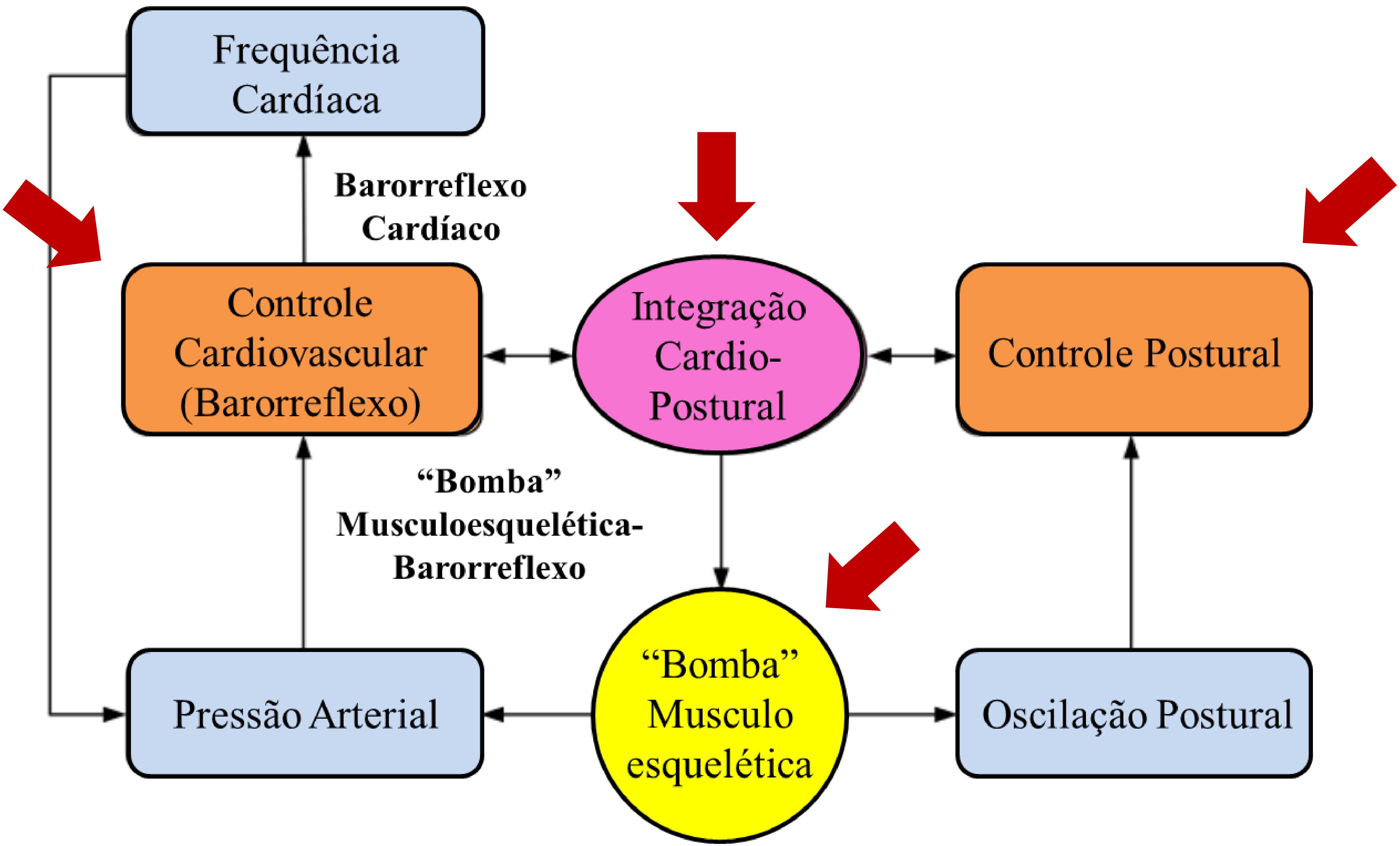
Influence of breathing patterns and orthostatic stress on postural control in older adults

Gabriel D Rodrigues,[1] Jonas L Gurgel,[2] Thiago R Gonçalves,[1] Flávia Porto[3] and Pedro Paulo da S Soares[1]

Departments of [1]Physiology and Pharmacology, [2]Physical Education and Sports, Fluminense Federal University, Niterói, and [3]Institute of Physical Education and Sports, Rio de Janeiro State University, Rio de Janeiro, Brazil

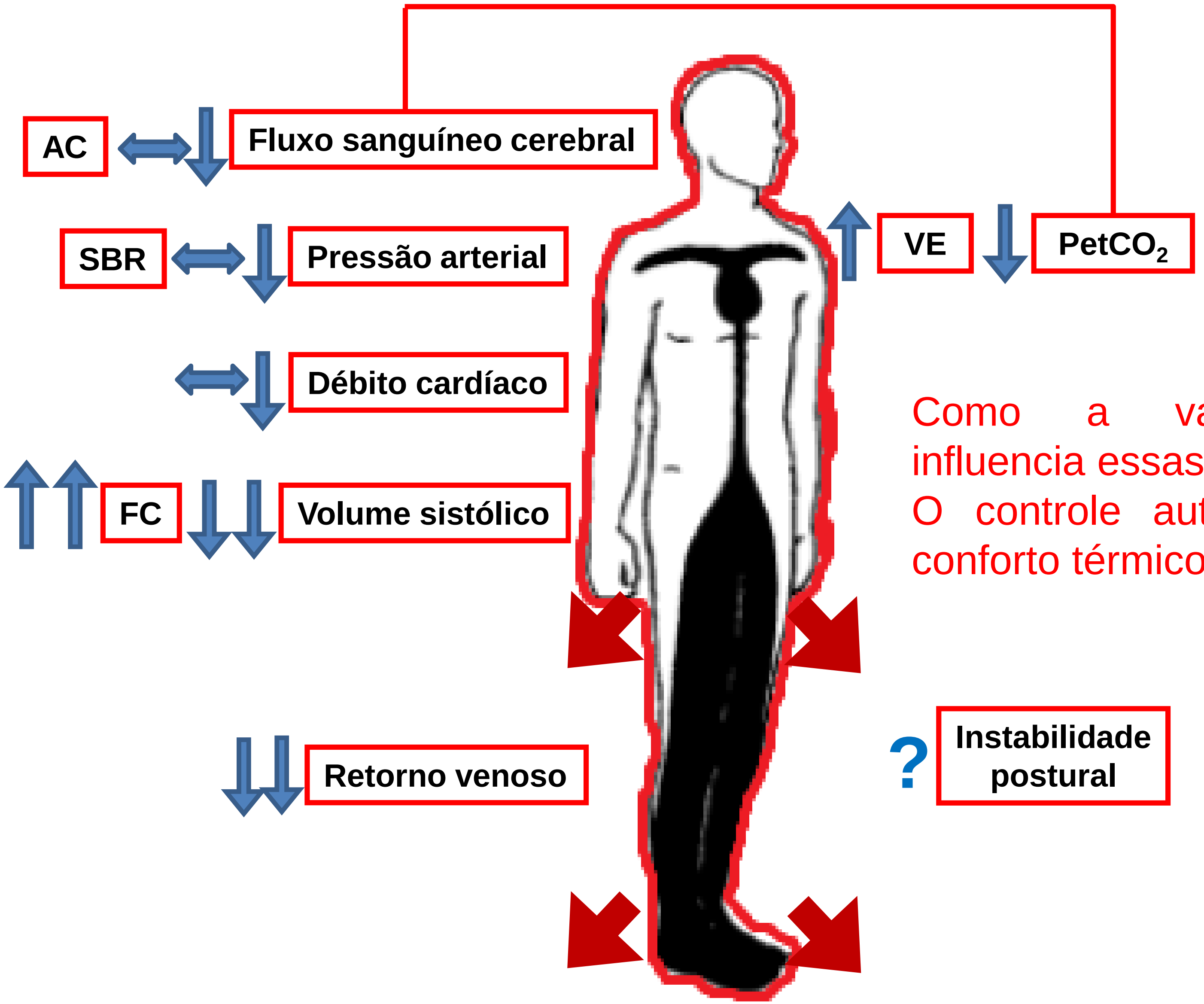
Convertino, 2014; Rodrigues, 2018a

Modelo de integração cardio-postural



Xu et al., 2017

Desafio ortostático → Estresse térmico → *Physiological Pathway*



Estresse térmico

Como a variabilidade inter-indivíduos influencia essas respostas?
O controle autonômico cardiovascular em conforto térmico tem valor preditivo?

Schlader et al., 2016

Desafio ortostático → Mecanismos compensatórios

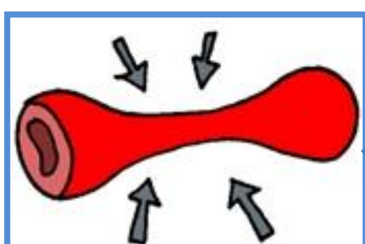
Fluxo sanguíneo cerebral

Pressão arterial

Débito cardíaco

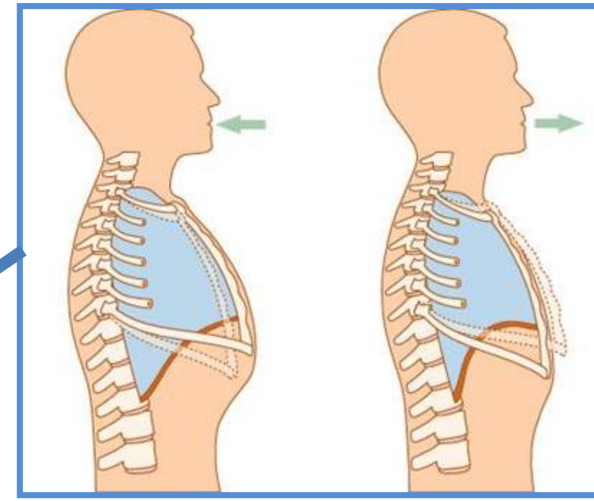
Volume sistólico

Retorno venoso

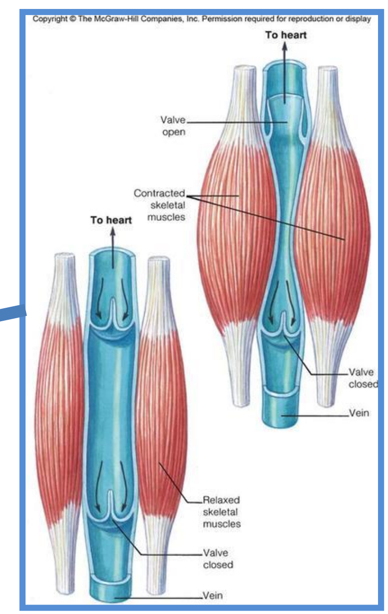


Venoconstrição simpática

Estresse Térmico



Bomba respiratória

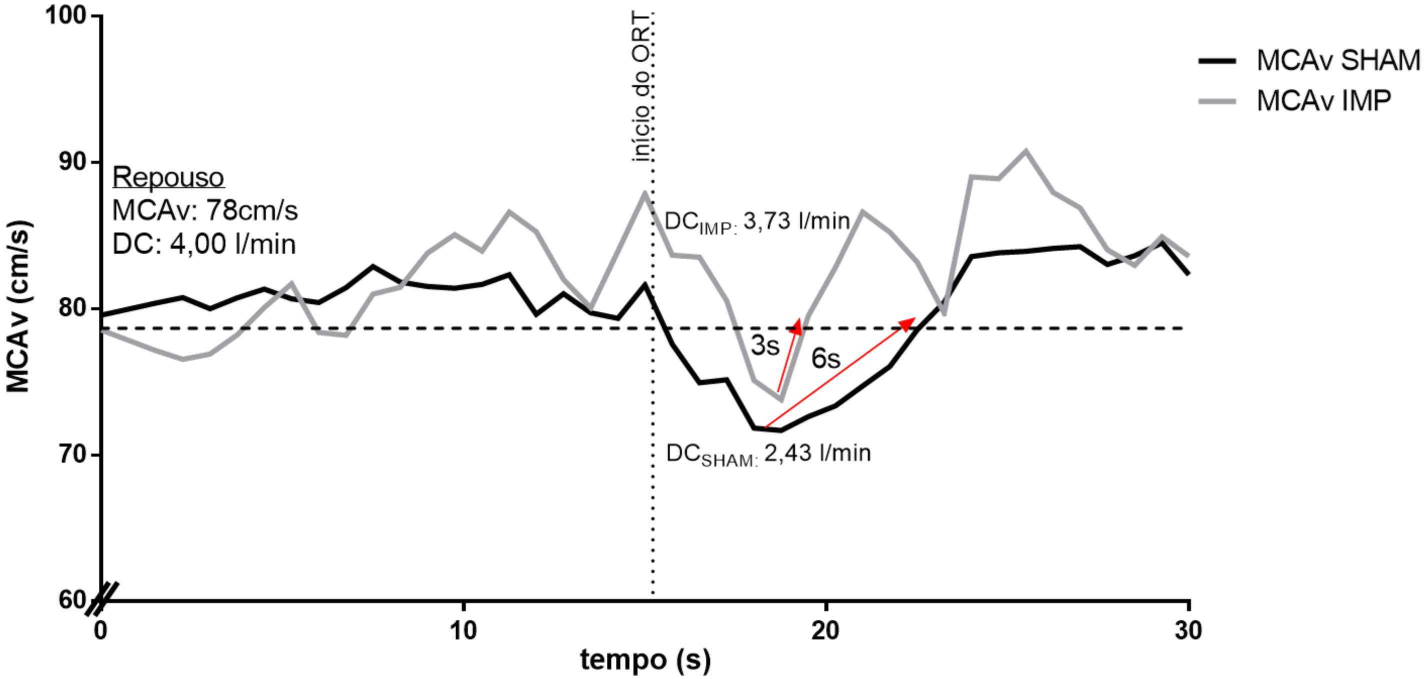


Bomba muscular

Schlader et al., 2016; Mohramn & Heller, 2014

Desafio ortostático → *Countermeasures*

Baixa impedância inspiratória (IMP; ~9 cmH_2O)



Rodrigues, 2018b; tese de doutorado

Corroborando com os resultados encontrados durante a manobra de hipotensão induzida (LBNP) em condições de conforto térmico (Rickards et al., 2007).

Como obter efeitos semelhantes durante a respiração espontânea?

Treinamento da musculatura inspiratória (TMI)

European Journal of Applied Physiology
https://doi.org/10.1007/s00421-018-3844-9

ORIGINAL ARTICLE

Inspiratory muscle training improves physical performance and cardiac autonomic modulation in older women

Gabriel Dias Rodrigues[1] · Jonas Lírio Gurgel[2] · Thiago Rodrigues Gonçalves[1] · Pedro Paulo da Silva Soares[1]

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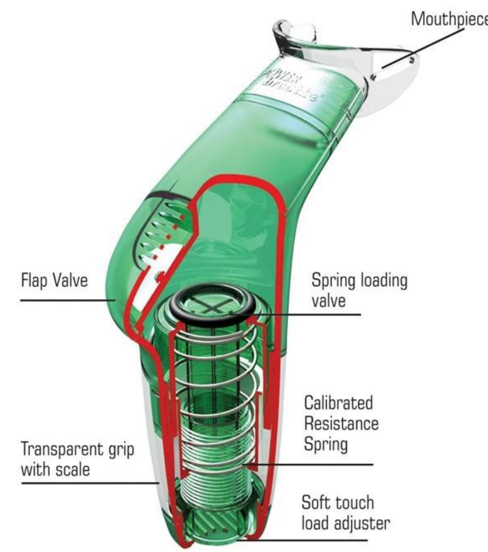
Modulação vagal cardíaca durante a respiração espontânea.



Rodrigues et al., 2018c.

Musculatura inspiratória → Bomba respiratória (McConnell, 2013)

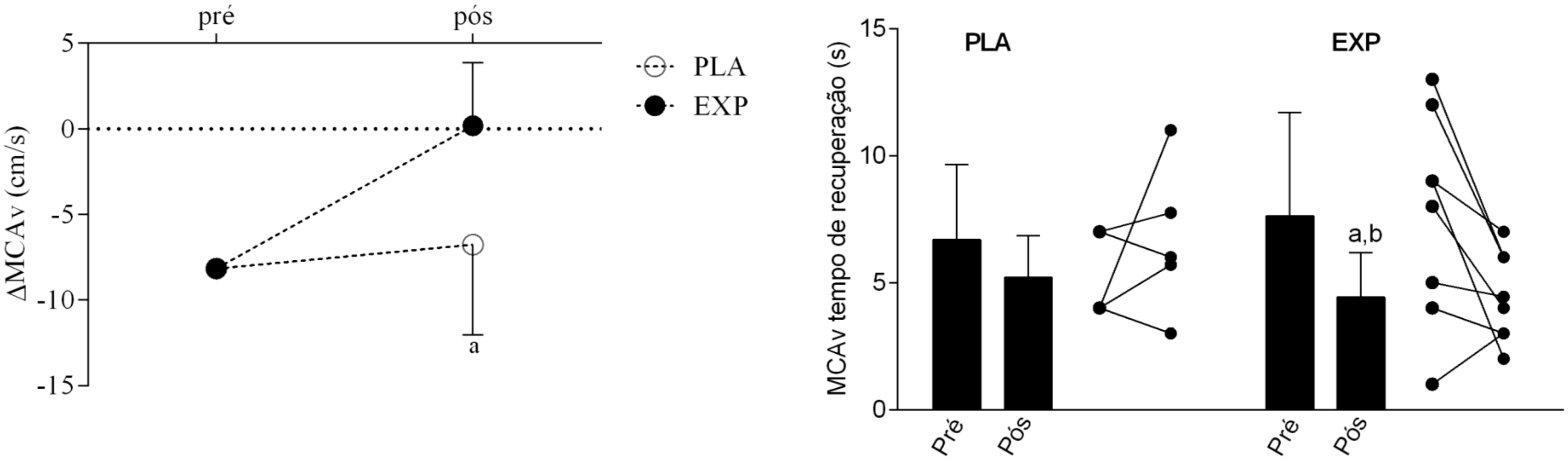


Figura 5. Comparações entre a queda da MCAv (ΔMCAv) e tempo para recuperação da MCAv durante o início ortostático entre os grupos EXP e PLA antes e após as intervenções em idosas.

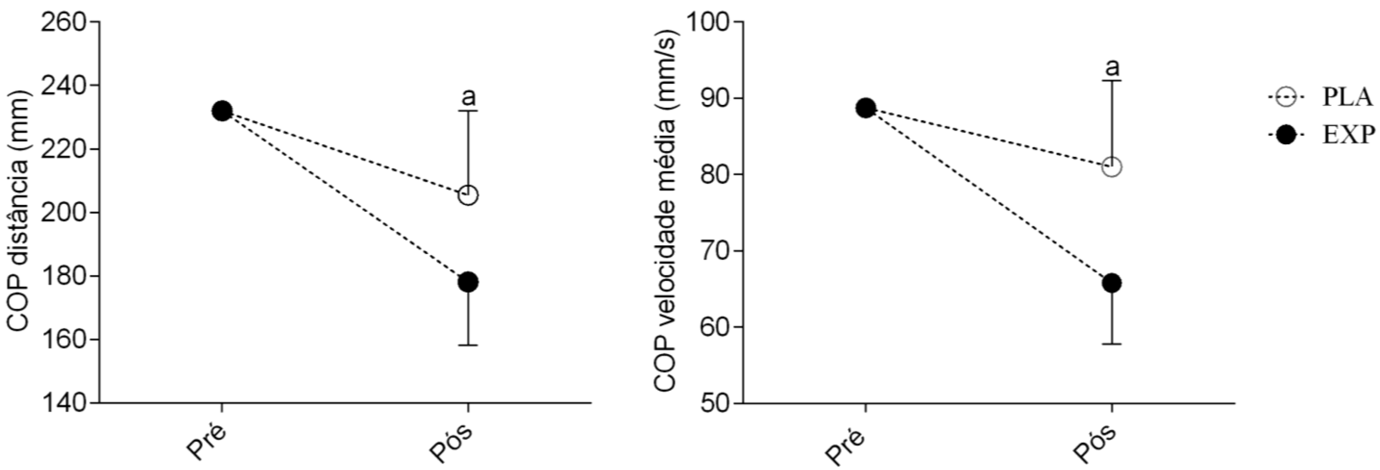


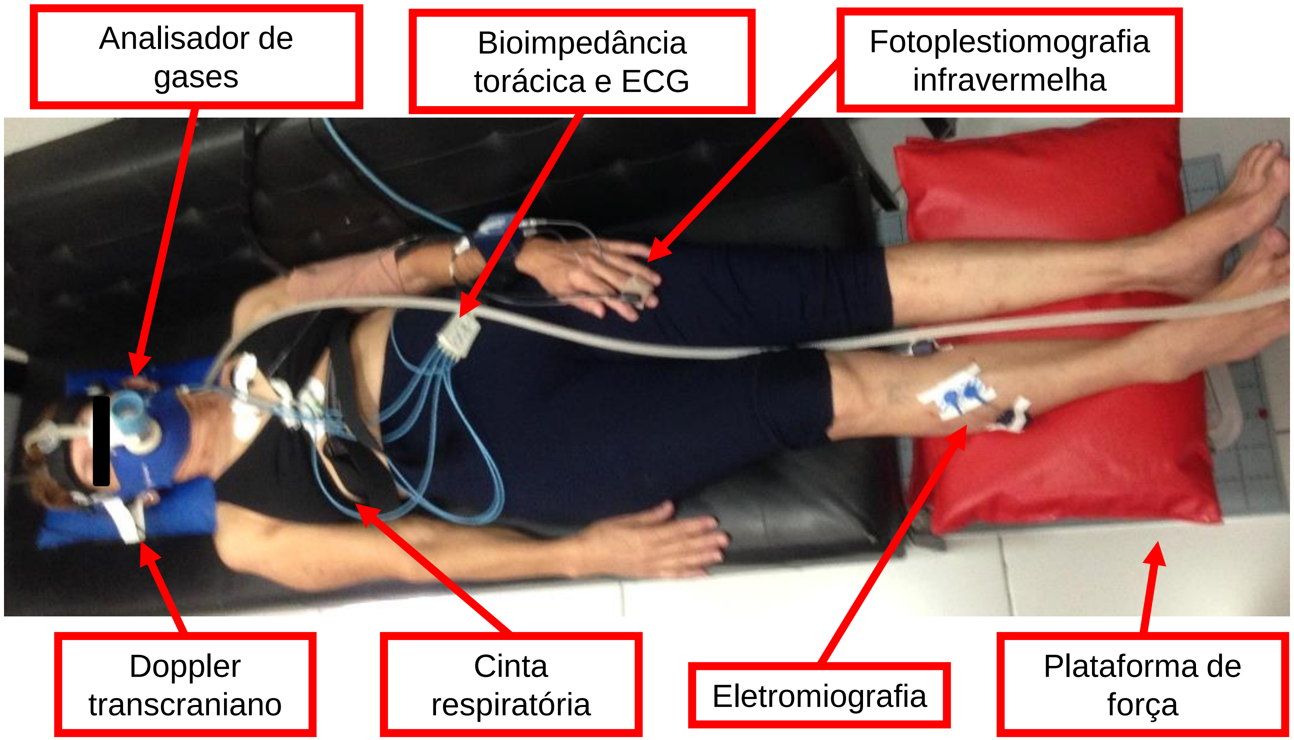
Figura 4. Comparações entre a distância percorrida e a velocidade média do centro de pressão do corpo (COP) antes e após as intervenções em idosas

Autorregulação cerebral
Controle postural

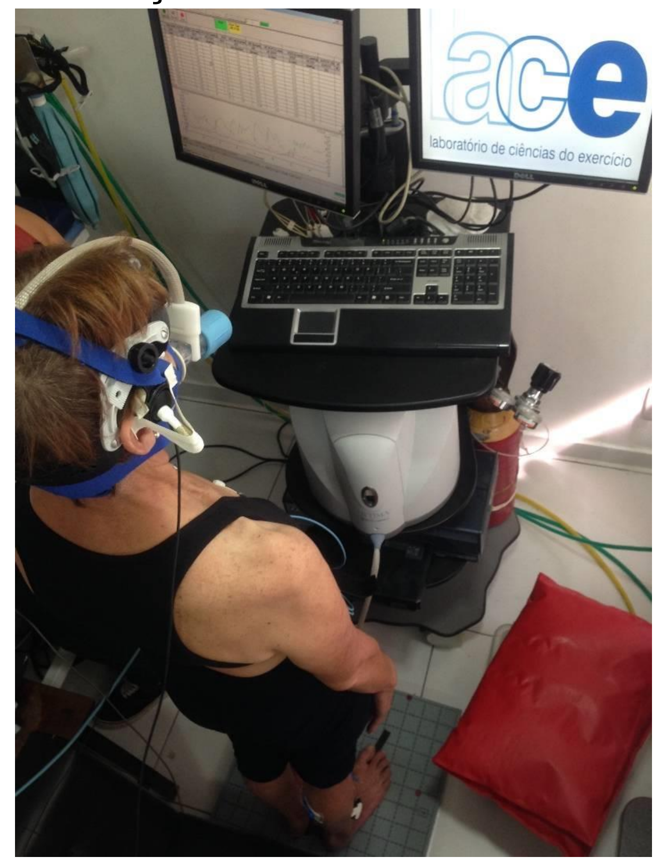
Rodrigues, 2018b; tese de doutorado.

Metodologia

Posição supina - 10min



Posição Ortostática- 10min

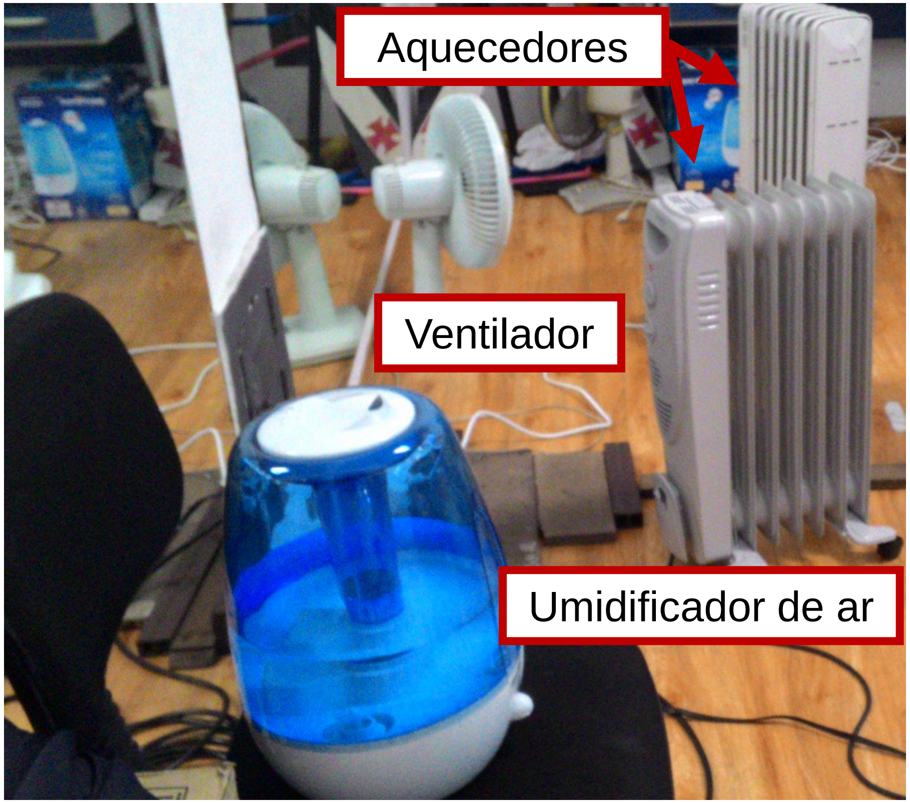


Ordem Randomizada

- Ambiente em conforto térmico ~22°C
- ~48h de intervalo
- Ambiente em estresse térmico ~32°C

Metodologia

Protocolo de aquecimento da sala



Variáveis ambientais → estação meteorológica portátil (Kestrel 4500, EUA).

A temperatura corporal → câmera infravermelha (Fluke Model Ti32; EUA).

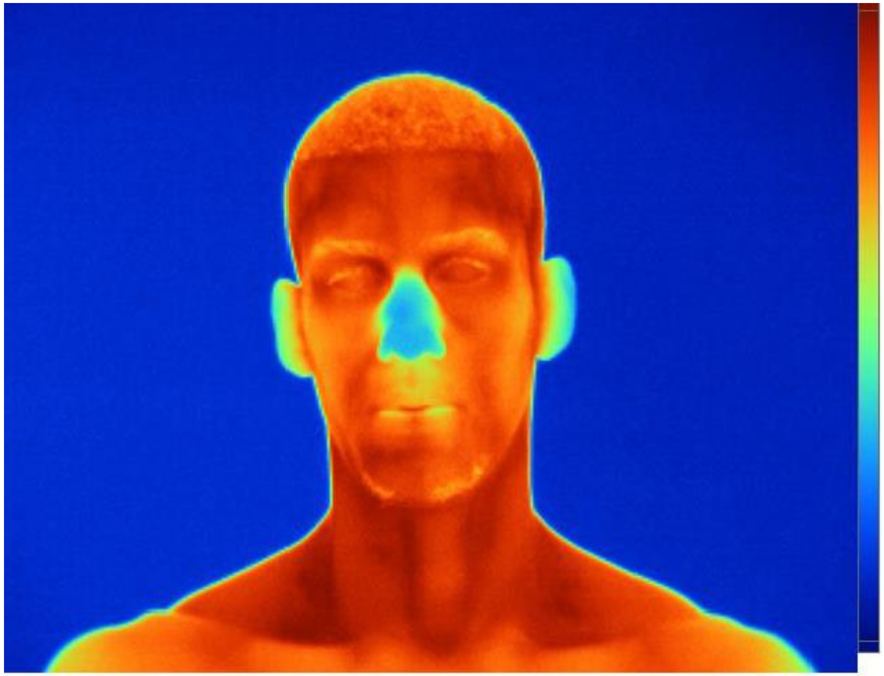


Ilustração de um voluntário em repouso (~22°C).

Campos, 2017; tese de doutorado

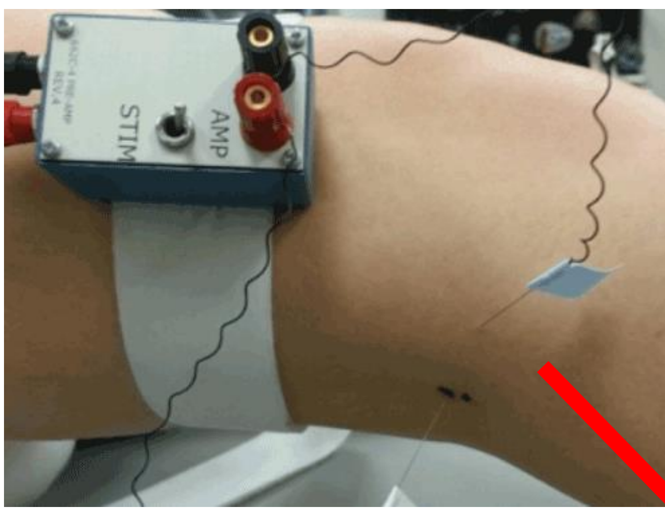
Metodologia

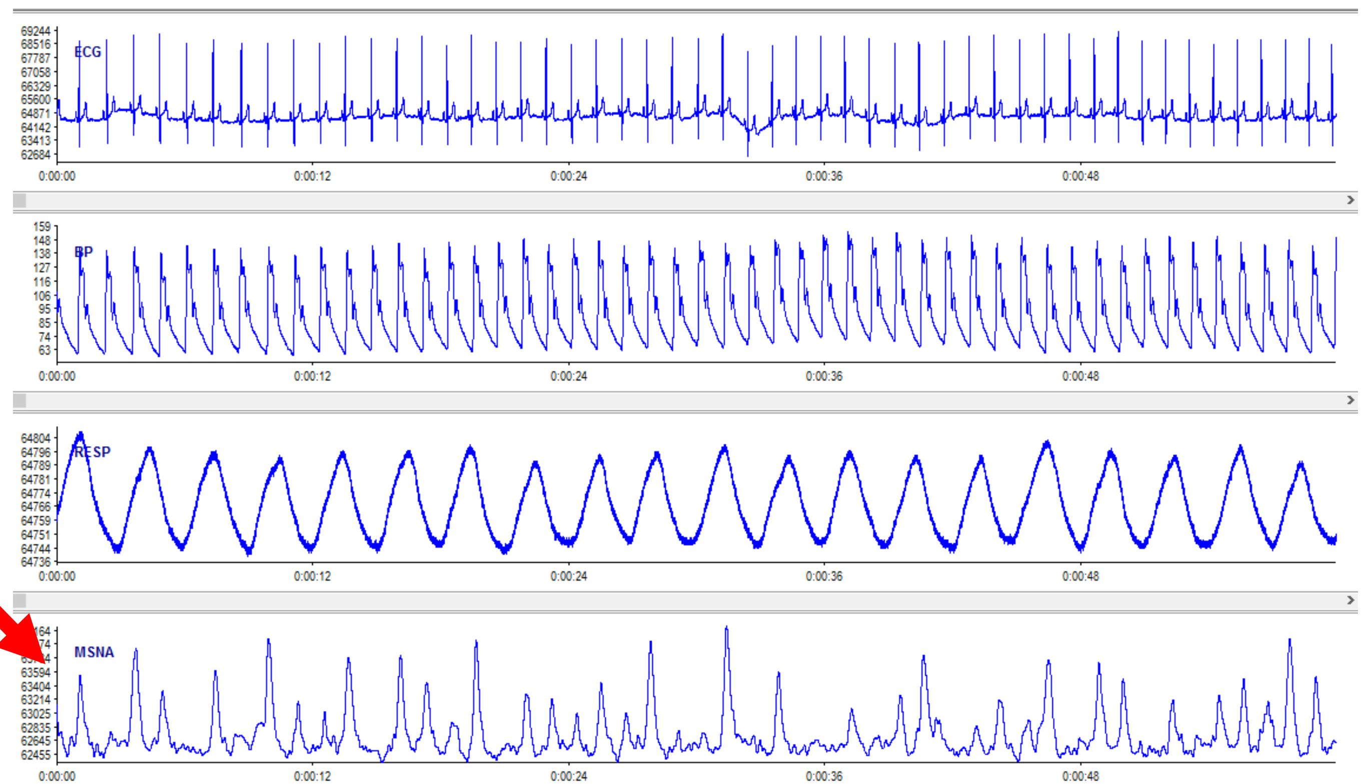
Ambiente em conforto térmico ~22°C

Posição supina - 10min	***Cuff release*** - 5min	*Recuperação – 15 minutos*

Atividade simpática muscular periférica (*MSNA*)
Pressão arterial batimento-a-batimento (Finomiter, fotoplestimografia infravermelha)
Volume sistólico, débito cardíaco e ECG (Physioflow, bioimpedância transtorárica)
Pressão parcial de dióxido de carbono – $PetCO_2$ e ventilação (Ultima, analisador de gases)
Velocidade do fluxo sanguíneo cerebral (Doppler transcraniano)

Atividade simpática muscular periférica (MSNA)





Dados do laboratório

Considerações finais

- A HRV possui aplicabilidade no diagnóstico e seguimento de intervenções na saúde e na doença
- Pode contribuir para descrever o comportamento de mecanismos de regulação e integração entre diversas variáveis cardiovasculares e outros sinais biológicos

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E-26/190.370/2012

CAPES

Biology does not follow na Aristotelian logic: fortunately, as it would be quite boring. Discoveries are more likely to result from sound observations than from a priori reasoning. The Hegelian dialetic process in which a contradiction between thesis and antithesis is resolved by synthesis at a higher level of knowledge, still appears as a valid metaphor of biological organization and of our attempt to understand it.

Alberto Malliani (*Principles of cardiovascular neural regulation in health and disease*)