

Frequency-domain heart  
rate variability and  
physiology

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# Fluctuation of HR and its characterization

- Heart rate responds dynamically to instantaneous physiological and pathological hemodynamic perturbation and produce periodic and irregular fluctuation.
- Methods to characterize the fluctuation.
  - Time-domain measure: SDNN, ASDNN, SADNN, pNN50, and rMSSD.
  - Frequency domain measure: TP, ULFP, VLFP, LFP and HFP; nLFP and nHFP
  - Nonlinear dynamical measure: chaos and fractal etc.

# Cycle and physiology

- Even at rest, HR fluctuates or oscillates cyclically.
- Fourier transformation of a HR sequence.
  - The amplitude at a frequency corresponds to the magnitude oscillation at the cycle of HR.
- High-frequency cyclic fluctuation: modulated by ventilation mediated entirely by changes in vagal outflow.
- Slower Cycles: due to baroreflexes or due to thermoregulation or renin-angiotensin system
- More slower fluctuations due to circadian changes: due to complex and poorly understood neurohormonal rhythms.

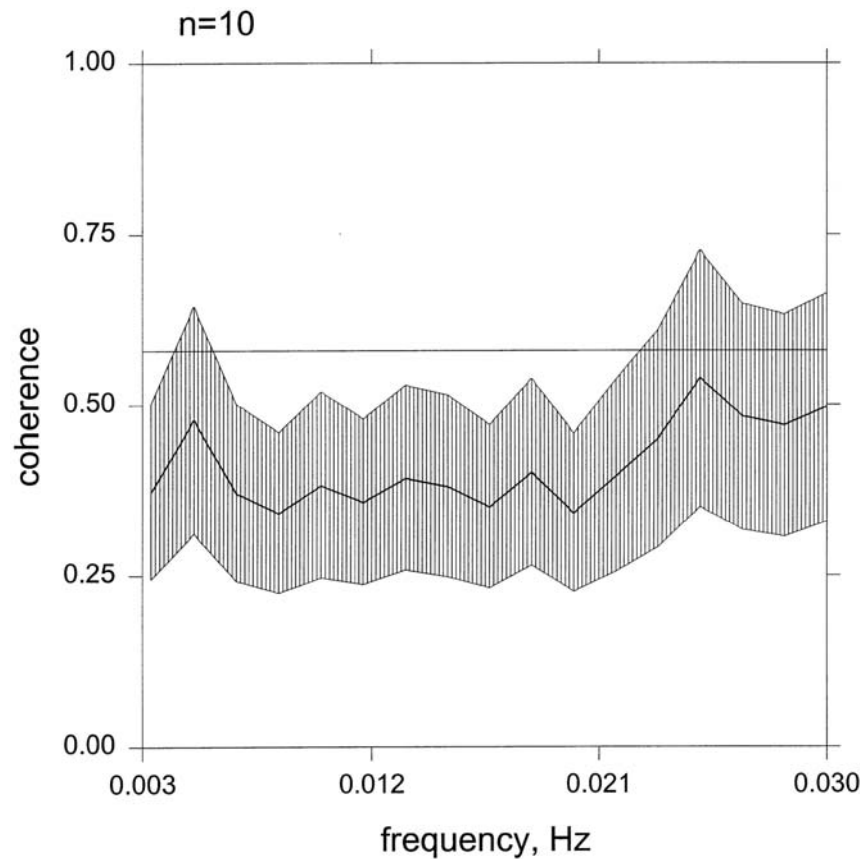
# Highly correlated frequency-domain and time domain measures

Time-domain	Frequency-domain
SDNN	TF
SDANN	ULF
ASDNN	VLF
PNN50, RMSSD	HF
Highly correlated Time domain measure	
SDNN	SDANN
RMSSD	PNN50

# Total power & Ultra-low frequency power

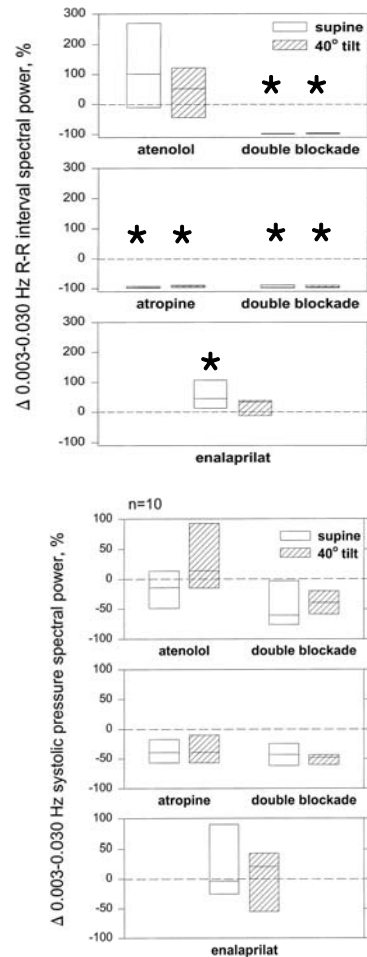
- Total power
  - 0~0.4Hz, CL > 2.5 seconds
  - Equivalent to the variance of a HR sequence, the square of SDNN.
- Ultra-low frequency power
  - < 0.003Hz CL> 5 minutes – 24 hours,
  - Strongly associated with SDANN.
  - Low ULFP in patients with chronic severe MR associated with RV and LV performance and a predictor for atrial fibrillation, mortality, and progression in valve surgery (Stein KM et al. *Circulation*. 88:127–35, 1993)

# Very low–frequency power



- 0.003–0.04Hz, CL>25s
- ASDNN
- About 12% of Total Power.
- No consistent linkage between SAP and RRI at this range.
- J. Andrew T et al. *Circulation*. 1998;98:547–555.

# Very low-frequency power



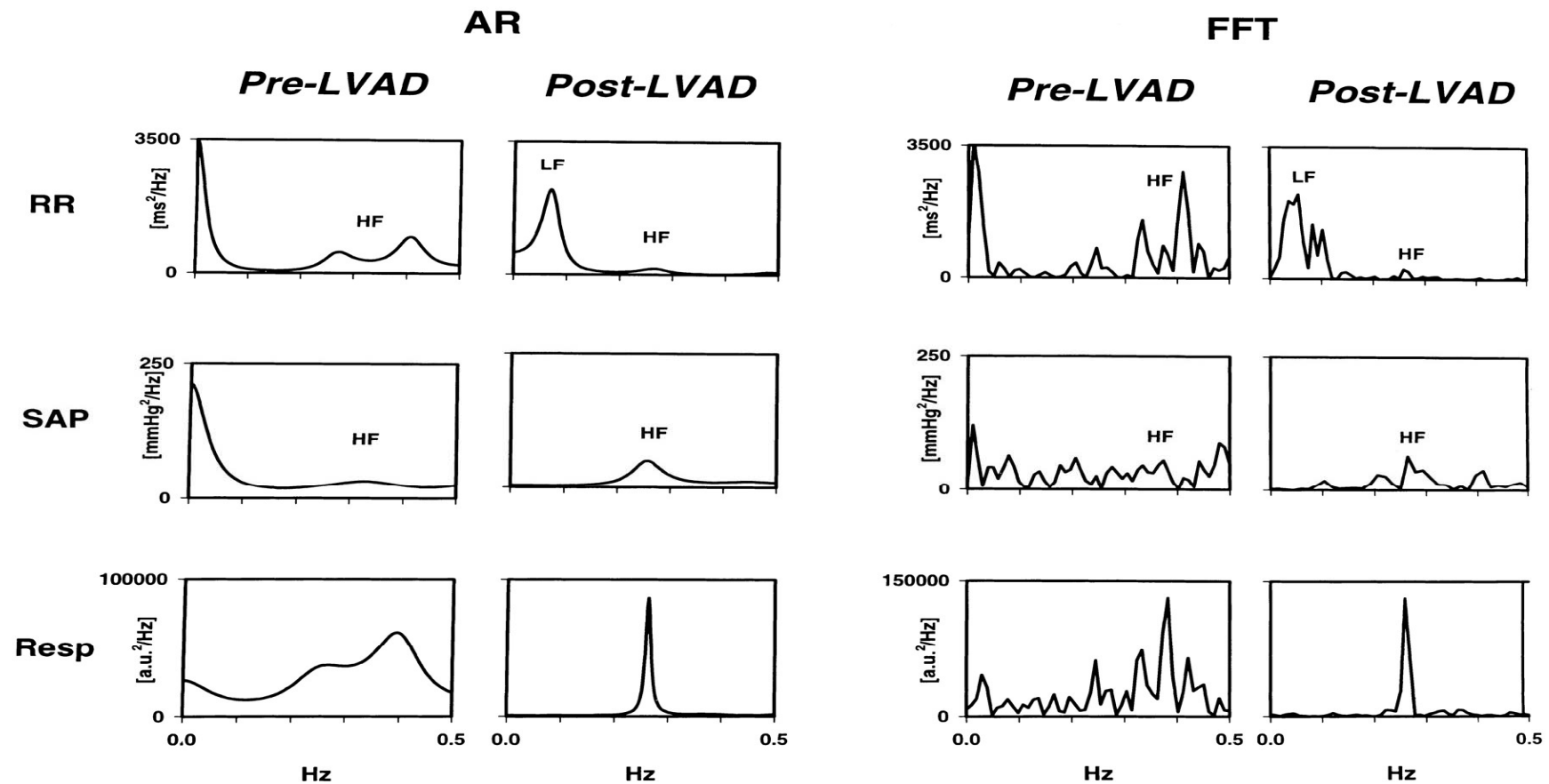
- In response to thermoregulation and vasomotor mechanism:
- Influenced by renin-angiotensin-aldosteron system:
  - Kidney can modulate the renin level in response to renal artery pressure change at the VLF range. ? Time lag from renin change to BP change: 15-30 minutes.
    - Tilting: Persistent deactivation of BR with consistently increase in renin level and no oscillation of renin level.
    - Above explanation is not inconsistent with the observation of in significant change in SAP VLF.
  - Renin: damping peripheral vasomotor tone fluctuation: ? No BP change
  - Block of angiotensin → ↑ vagal output
- Depends on parasympathetic outflow.
  - J. Andrew T et al. *Circulation*. 1998;98:547-555
- Prognostic significance of VLF in postinfacts patients (Bigger J Jr, et al. *Circulation*. 1992;85:164-171; Bigger J Jr et al. *Circulation*. 1993;88:927-934) is tied to reduction in efferent vagal-cardiac traffic.

# Low frequency power

- 0.04–0.15Hz, CL : 6 s–25 s)
- Coupled to 10 second wave in SAP and baroreflex function.
- A resonance phenomenon (at a frequency of 0.1 Hz) due to the slow sympathetic control loop of the baroreflex response to respiratory fluctuation of blood pressure (Akselrod S et al Am J Physiol. 249:H867–75. 1985)
- A central oscillator, the rate of which is entrained by the sluggish baroreflex mediated sympathetic response .
- Depends on vagal outflow.
- Total LF power or Normalized LF Power
- Additional information from specific distribution of spectral power in the LF band
  - Spectral power in Mid–frequency band
  - Central frequency derived from AR model
  - Median frequency from Fourier analysis
  - Dominant frequency at max coherence between RRI and SAP.
  - Prevalent low–frequency oscillation(PLF)
    - May be superior to the total LF power. (tendency to progressively shift to lower frequencies as severity of cardiovascular diseases increases)

# Central Origin of the Low-Frequency Oscillation in HRV

## Patient #1

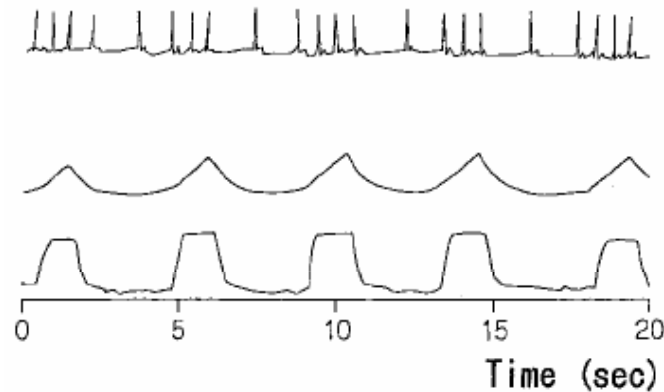


Spectral analysis of RR-interval (RR), systolic arterial pressure (SAP), and respiration (Resp) variabilities before and after implantation of LVAD. Ryan LC et al. *Circulation*. 1998;98:556-561

# High-frequency power

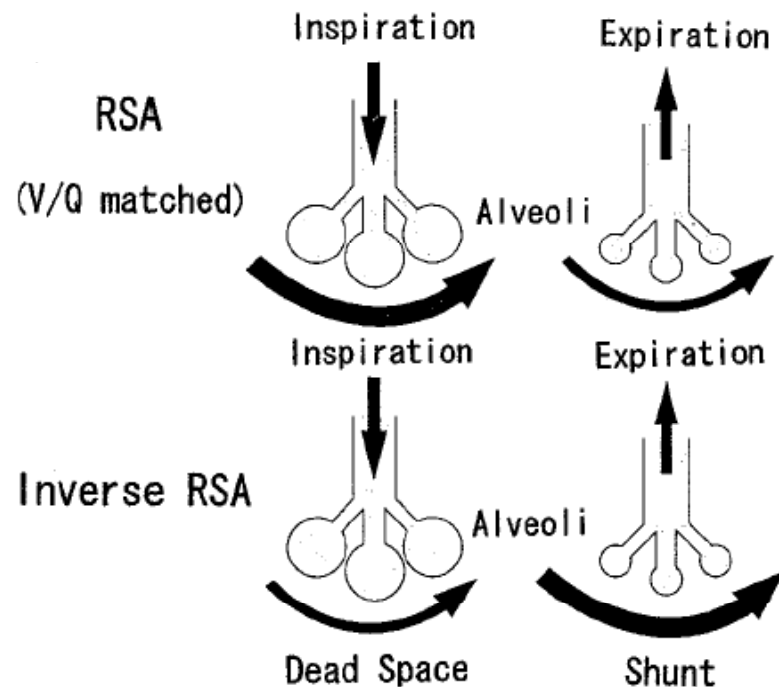
- 0.15–0.4 Hz (CL 2.5 s –6 s)
- Irregular respiration rate in healthy human (9–25 /minutes)
- Approximate measure of respiratory sinus arrhythmia (RSA). Fluctuation of HR synchronized with respiratory rhythm.
  - Amplitude of RSA: max RRI during late inspiration and early expiration phase– min RRI during early inspiration and late expiration phase.

# Teleology of RSA or HF



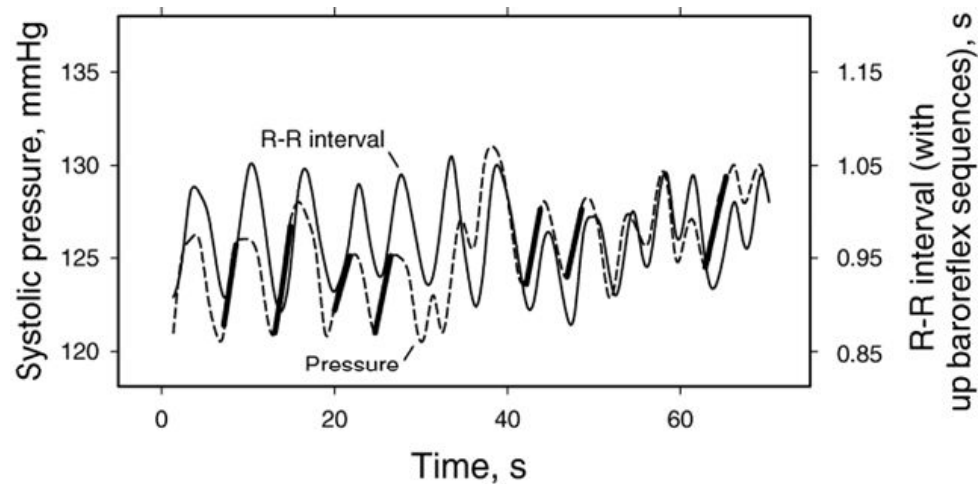
- Clustering of heartbeats during inspiration and a scattering during expiration.
- Improving efficacy of pulmonary gas exchange by synchronizing or entraining heartbeat with inspiration (synchronization of heartbeat within each respiratory cycle).

# Improving pulmonary gas exchange

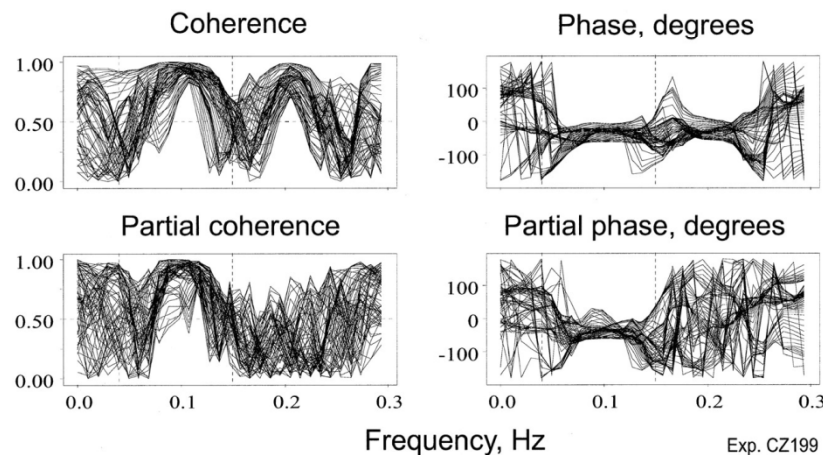


- Dead space/Tidal Volume; Shunt/Cardiac Output;  $O_2$  uptake
- RSA:  $\downarrow 10\%$ ,  $51\%$ ,  $\uparrow 4\%$
- Inverse RSA:  $\uparrow 14,64\%$ ,  $\downarrow 14\%$ 
  - Improving pulmonary  $O_2$  uptakes by V/Q matching within respiratory cycle
  - Suppress unnecessary heartbeats during expiration, and ineffective ventilation during ebb of perfusion
    - Yasuma F. et al. Chest 2004;125:683–690

# Origin of RSA

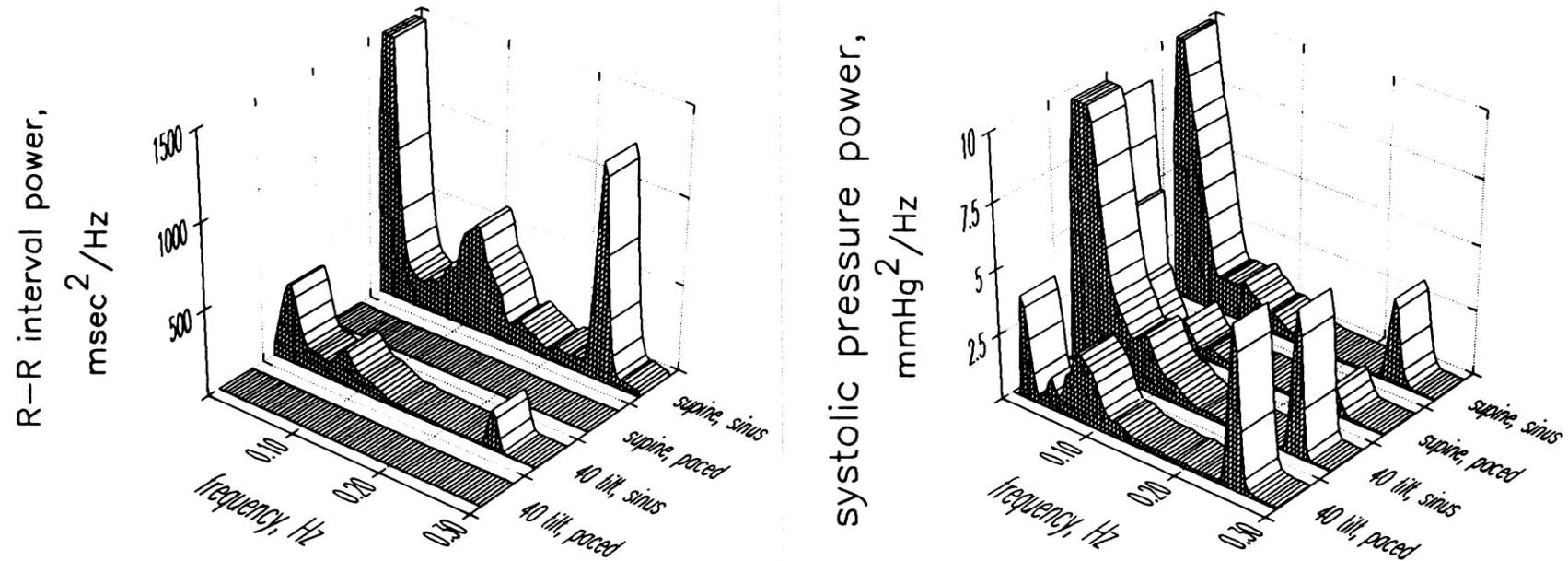


- Classic suggestion: Breathing triggers a cascade, such that intrathoracic pressure changes lead to changes of left ventricular stroke volume and SAP, and SAP changes provoke parallel RRI changes by means of BR physiology (Rothlisberger BW. *Clin Physiol* 2003 23,307–313)



- Parallel fluctuations of SAP and RRI at breathing frequencies are secondary to direct respiratory influences on both SAP and RRIs, (Badra LJ et al. (*Am J Physiol Heart Circ Physiol* 280: H2674–H2688, 2001,

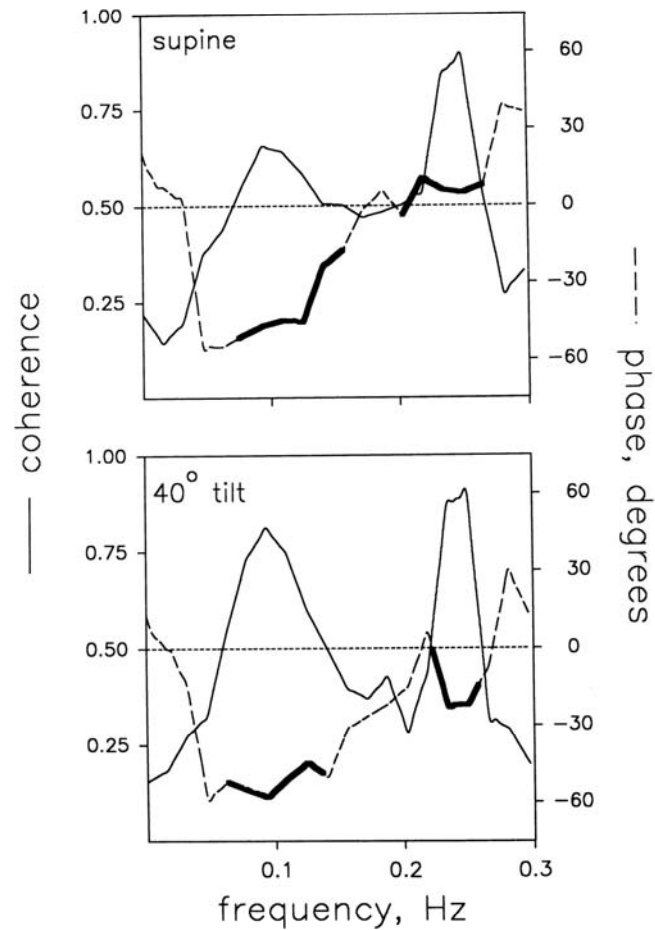
# Power spectral analysis during pacing



- After the elimination of RRI fluctuation:
  - Supine position: BP fluctuation – or  $\downarrow$ : no or negative contribution of HRV to BR mechanism
  - Tilting position: BP fluctuation  $\uparrow$  : positive contribution of HRV to BR mechanism.

Taylor A et al. *Circulation* 93:1527–1532, 1996

# Cross spectral analysis

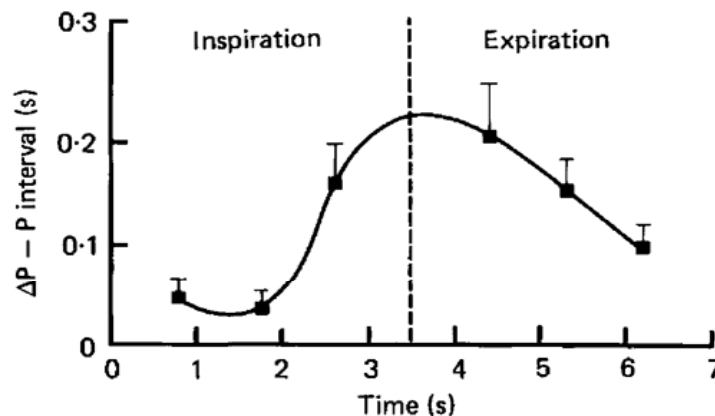
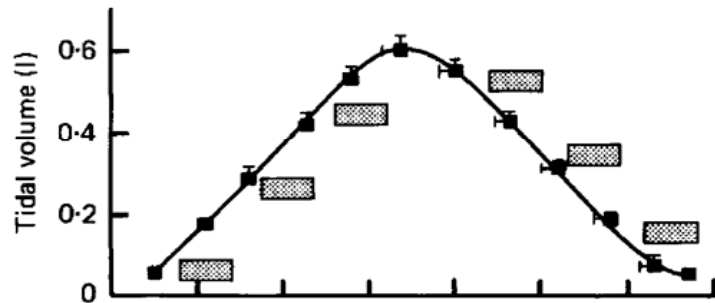


- Low frequency range
  - $\Delta$ RRI follows  $\Delta$ BP
- Respiratory frequency range
  - Supine position:  $\Delta$ RRI leads  $\Delta$ BP
  - Tilting position:  $\Delta$ RRI follows  $\Delta$ BP
- Taylor A et al. *Circulation* 93:1527–1532, 1996

# Respiratory activity directly influences autonomic nerve traffic by respiratory gating

- Respiratory activity phasically alters membrane potential of preganglionic vagal and sympathetic motoneuron and continuously modulates their responsiveness to stimuli input: respiratory gating.
  - RSA is a manifestation of respiratory gating on vagal nerve traffic and fluctuation of vagal nerve activity: not magnitude of vagal nerve activity but the magnitude of the vagal nerve rhythm.
    - Eckberg DL *J. Physiol.* 2003;548;339–352

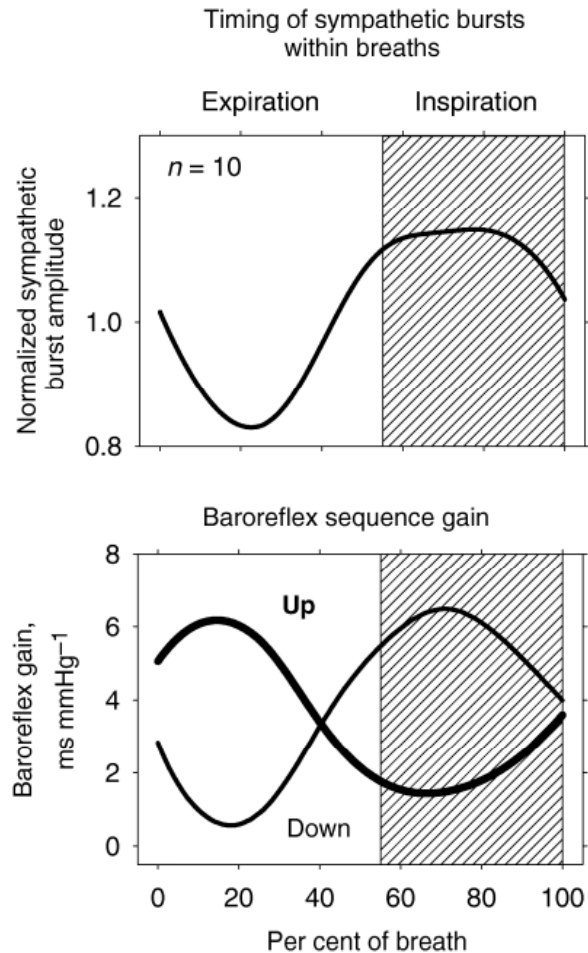
# Respiratory gating for vagal nerve traffic (RGVNT): time of respiratory gate opening



- Brief neck suction at six times during the normal breathing cycle was applied.
- Opens greatly during late inspiration and early expiration
- Close greatly during late expiration and early inspiration.

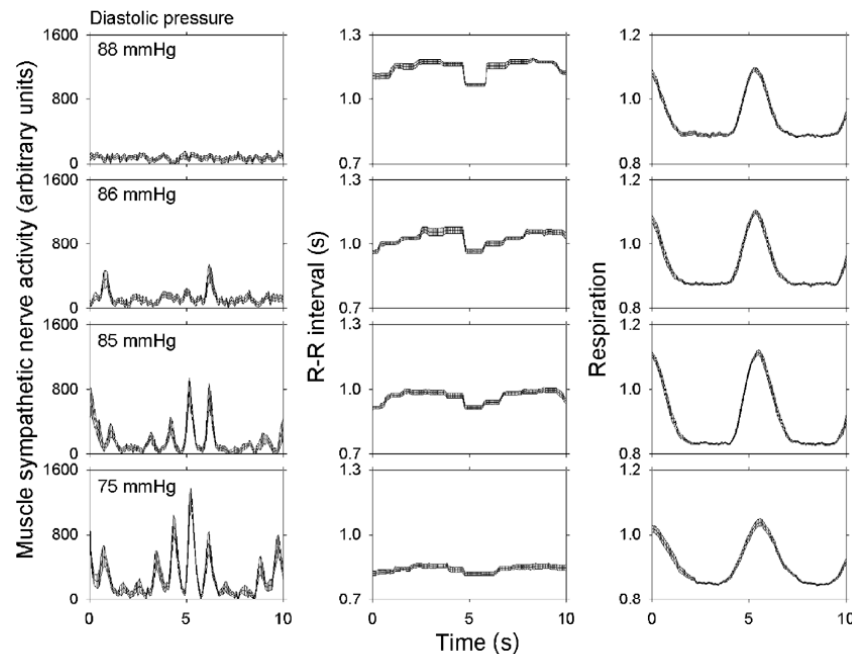
– Eckberg DL. *Circ Res* 1980;47: 208–216

# Respiratory gating for sympathetic nerve traffic (RGSNT)



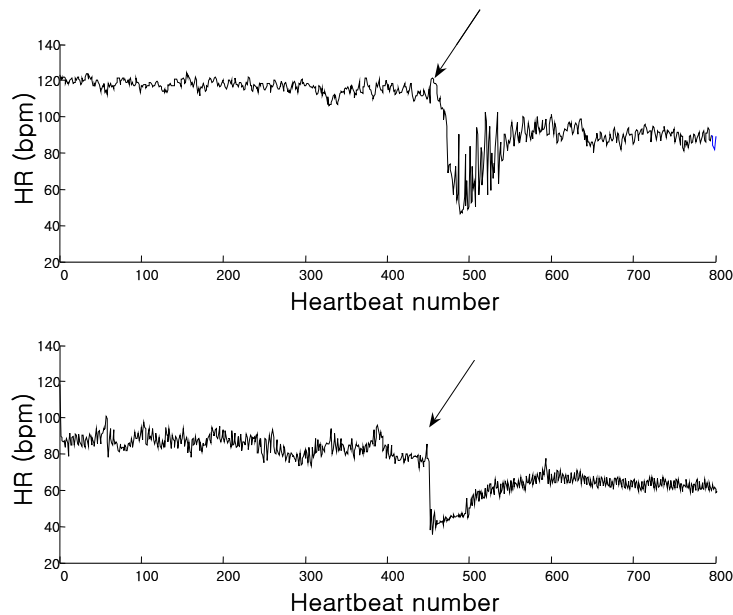
- Respiration gates not the quantity of sympathetic burst but the timing of sympathetic burst and upgoing and downgoing baroreflex sequences.
- Sympathetic burst occurs during inspiratory phase.
- Upgoing baroreflex sequences during expiration and downgoing baroreflex during inspiration.
  - Rothlisberger BW. *Clin Physiol* 2003 23,307–313

# Factors determining magnitude of respiratory gating (1)



- Level of stimulation of sympathetic and vagal nerve
- DBP  $\uparrow \rightarrow$ 
  - $\uparrow$  BR stimulation of vagal nerve  $\rightarrow \uparrow$  magnitude of RGVNT  $\rightarrow \uparrow$  RSA
  - $\downarrow$  BR stimulation of sympathetic nerve  $\rightarrow \downarrow$  magnitude of RGSNT  $\rightarrow \downarrow$  muscle sympathetic burst during inspiration
- Eckberg DL et al *Acta Physiol Scand* 1988;133: 221-231.
- At the usual intensity of autonomic input stimuli, the amplitude of respiratory rhythm of autonomic nerve traffic correlates well with the autonomic nerve activity.

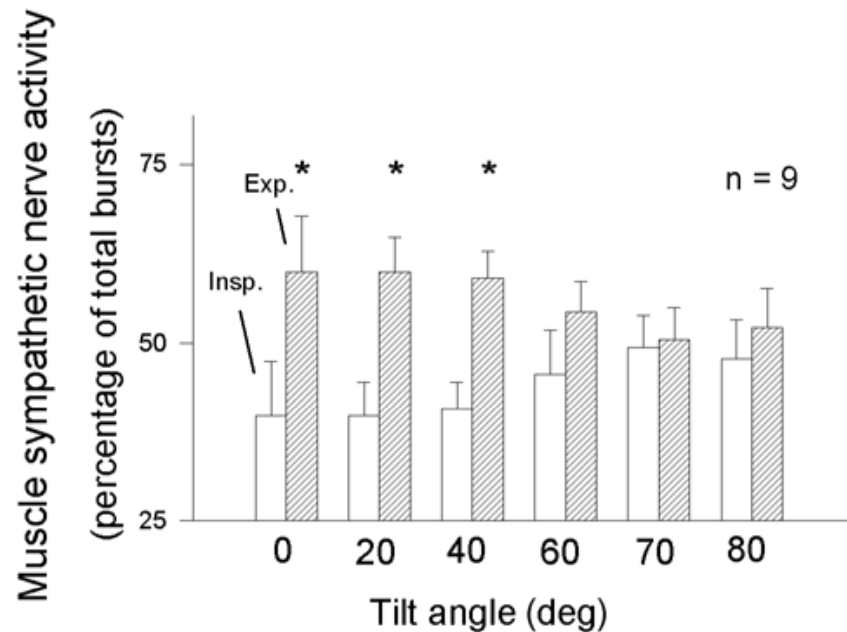
# Finitude in RGVNT



- The ability of RGVNT is finite.
- When vagus nerve is intensely stimulated by ice water application to face, it sometimes provokes equal vagal motoneuron response in expiration and inspiration; there is no RSA and no respiratory gating.

– Yum MK et al. *Cardiol Young* 1994; 4:358–365

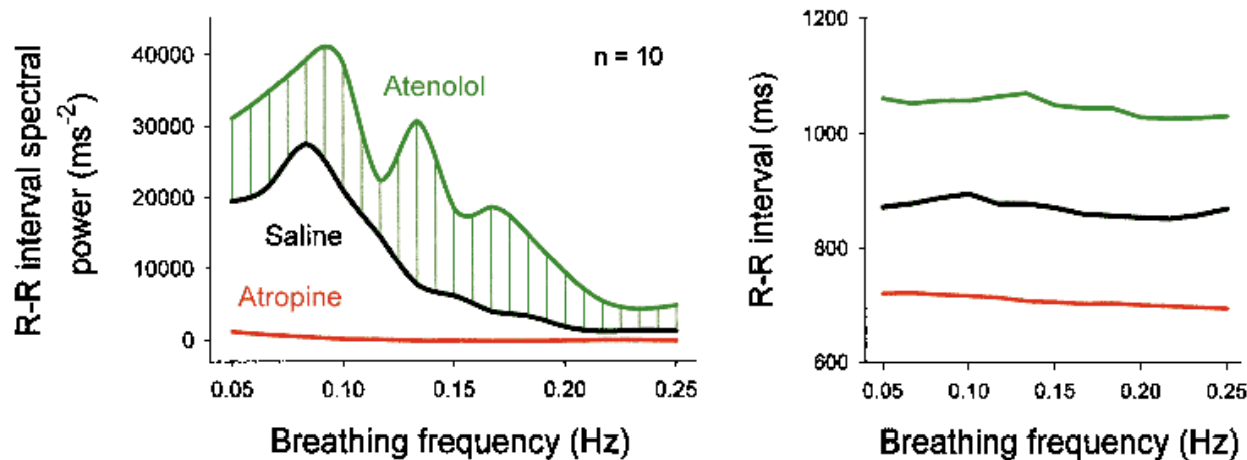
# Finitude in RGSNT



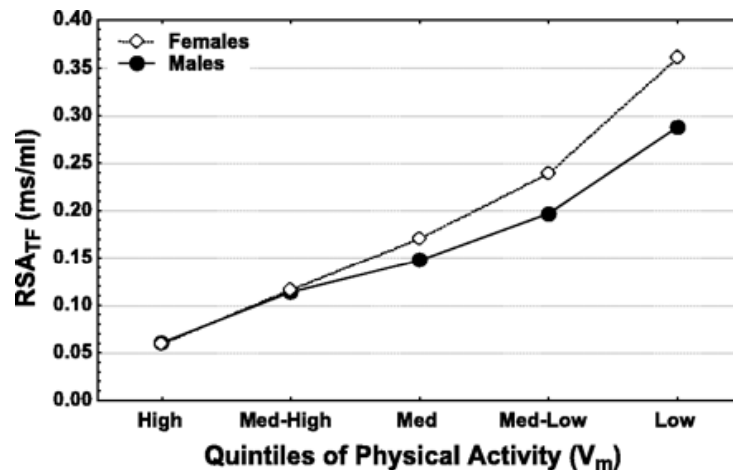
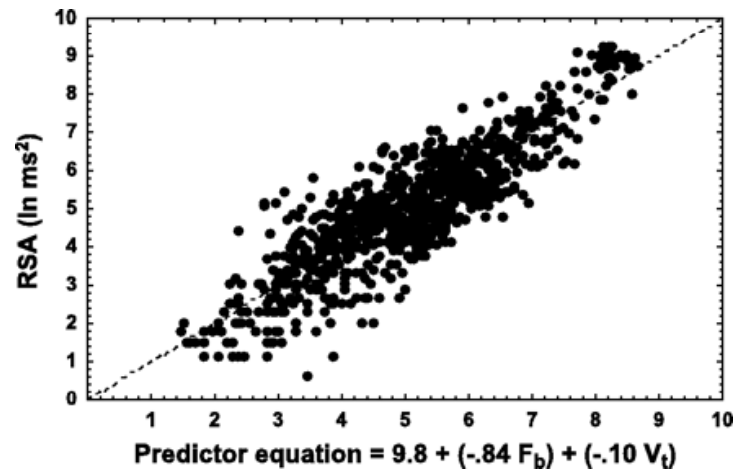
- The ability of RGSNT is also finite.
  - Intense BR stimulation provokes equal muscle sympathetic motoneuron responses in expiration and inspiration.
- Cooke WH et al. 1999; *J Physiol* 1999; 517:617–628.

# Factors determining magnitude of respiratory gating (2)

- RGVNT and RSA is determined importantly by breathing rate, this is not a simple linear function: RSA small at usual breathing frequencies 0.25 Hz, maximal at frequencies of about 0.1 Hz, and intermediate at very low breathing frequencies.
- Sympathetic stimulation reduces vagal inhibition at all breathing frequencies. However, sympathetic opposition to vagal effects is not uniform – inhibition is small at rapid breathing frequencies, and maximum levels at about 0.15 Hz
  - Taylor JA et al *Am J Physiol Heart Circ Physiol* 2001; 280, H2804–2814.



# Factors determining magnitude of RGVNT (3,4)



- RSA strongly depends on respiratory variables and physical activity.
- Concurrent assessment of respiration and physical activity
  - Grossman P. et al. *Am J Physiol Heart Circ Physiol* 2004; 287: H728–H734